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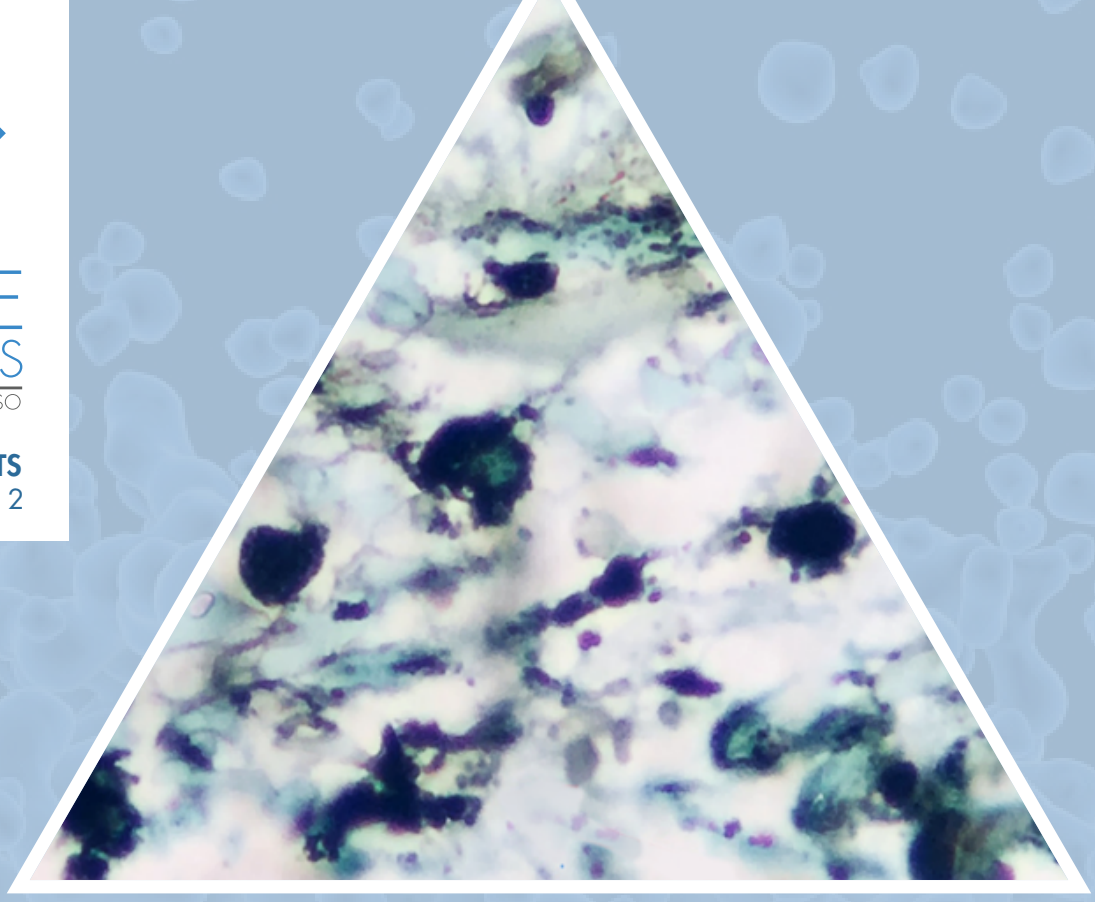
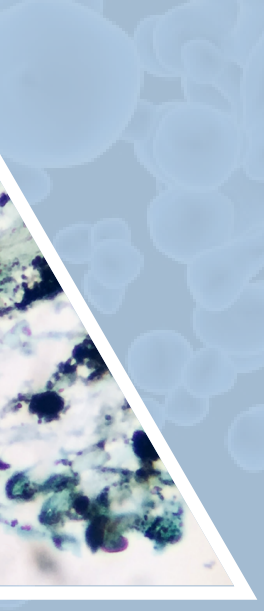
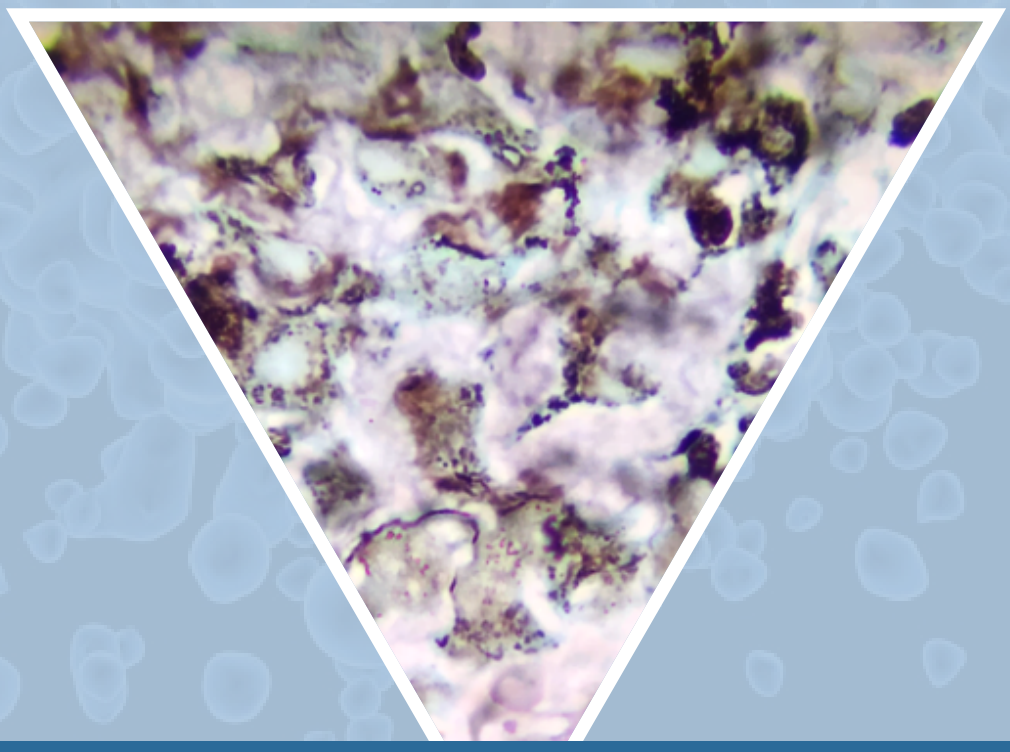
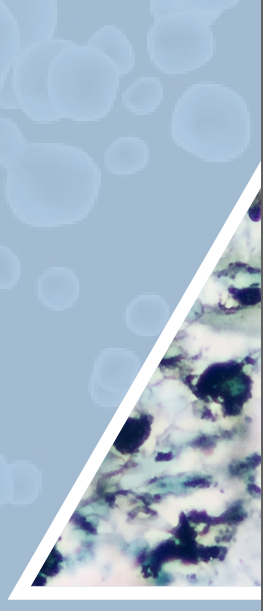


PERITONEAL HISTOPLASMOSIS

Case report







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HISTOPLASMOSIS: DIAGNOSTIC CHALLENGES

Editorial

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Histoplasmosis is an infection usually caused by a fungal pathogen that, in most cases, occurs in the respiratory tract, which explains the high frequency of clinical manifestations in the lungs. (1) This mycosis is endemic in the Americas (Mississippi and Ohio River Valley, USA; Central and South America; and the West Indies), while reports in areas of Asia, Africa, Australia, and Oceania are mainly associated with the pandemic of acquired immune deficiency syndrome (AIDS). In Europe, cases are on the rise because of the speculation of a global distribution of histoplasmosis, and emphasis has been on improving methods for its diagnosis. (2,3)

The etiological agent of histoplasmosis is the dimorphic fungus *Histoplasma capsulatum*, which is widely distributed in soils with high nitrogen content (contaminated with droppings from bats or birds) both in endemic areas and outside them. (2) From a taxonomic standpoint and based on molecular tests, Sepúlveda *et al.* (1) proposed a new classification of the species of *Histoplasma*. They were previously classified into three varieties: *H. capsulatum* var. *capsulatum*, pathogen for humans in America; *H. capsulatum* var. *duboisii*, pathogen for humans in Africa; and *H. capsulatum* var. *farciminosum*, pathogen for equines. Currently, the following classification is used: *H. capsulatum sensu stricto*, in Panama; *H. mississippiense sp.* nov. and *H. ohiense sp.* nov. in North America; and *H. suramericanum sp.* nov. in South America. The description of these species has clinical and epidemiological implications, as there are differences between them in terms of virulence and resistance to antifungal agents, as is the case of *H. mississippiense,* which is less virulent but has greater resistance to the most used antifungal antibiotics. (1)

Histoplasmosis mostly affects the lungs; however, the clinical presentation depends on two variables: the load of infectious particles in the inoculum and the immune status of the patient. It has been reported that in 5-10% of cases, the infection spreads systemically to other organs to be controlled by an immune system without alteration. Progressive disseminated disease occurs more often in patients with human immunodeficiency virus (HIV) infection and lower CD4 T-cell counts (<200 cells/mm^3), or in therapy with tumor necrosis factor inhibiting agents, in which mortality rates are high if diagnosis and treatment are not timely.

The symptoms of progressive histoplasmosis are nonspecific, so its differentiation with other infections, especially tuberculosis, is a challenge, even to determine the presence of coinfections that occur frequently in patients with HIV/AIDS. (1,2,4)

The laboratory tests available for the conventional diagnosis of this fungal infection have several limitations:

1) Collecting blood, respiratory tract or tissue samples for cultures is the golden standard, but sensitivity is variable based on the immunity of the patient, so the culture sometimes yields false-negative results. In addition, *Histoplasma* isolation may require up to six weeks for optimal growth.
2) Immunological tests can detect antigens or antibodies in serum and other biological fluids, but the detection of antibodies can give false-negative results due to its low sensitivity in immunosuppressed patients (particularly patients with AIDS, in whom the production of antibodies decreases); however, antigen detection in these individuals is more sensitive. Antigenic cross-reactivity with other fungi may also occur, causing

false-positive results in patients with other mycoses such as paracoccidioidomycosis, blastomycosis, aspergillosis, candidiasis and coccidioidomycosis. The detection of these antibodies is of great value to diagnose meningeal involvement in histoplasmosis. The detection of antigens in progressive disseminated histoplasmosis is more sensitive than the detection of antibodies, especially in urine. The detection of galactomannan antigen by enzyme immunoassay is the only commercially available methodology that has been validated and approved by the European Community for in vitro diagnosis. (5)

3) Histopathological analysis with different stains (Wright, Giemsa, Schiff periodic acid and methenamine silver) is a useful tool, but can have a sensitivity lower than 50%, depending on the experience of the observer since the *Histoplama* yeasts may be mistaken for *Candida spp., Penicillium marneffei, Pneumocystis jirovecii, Cryptococcus neoformans, Blastomyces dermatitidis* and *Leishmania spp.*, or for artifacts.
4) Molecular methods, in particular polymerase chain reaction (PCR), are a diagnostic alternative with suitable sensitivity and specificity to detect and identify *Histoplasma spp.* in biological and environmental samples in a rapid manner (6,7); however, their diagnostic use has not been approved by the Food and Drug Administration (FDA). (5,8)

All these limitations cause a delay in the diagnosis and subsequent mismanagement of patients. For this reason, a multiple approach to diagnosis is recommended, involving epidemiological and, especially, working knowledge of the patient, as well as laboratory, radiographic, histopathological, microbiological, serological and even molecular test results in complicated cases.

The initial treatment of choice for progressive disseminated histoplasmosis in immunocompromised individuals is lysosomal amphotericin B, while itraconazole is used in mild presentations of the disease and as reduction therapy. (4) Primary prophylaxis with itraconazole (200 mg/day) is recommended to reduce the risk of histoplasmosis in HIV-infected patients with CD4 cell counts <150 cells/mm^3 living in endemic areas. (9)

It is worth mentioning that since 1987 histoplasmosis has been considered an AIDS-defining infection because it is the first manifestation of the syndrome in 50-75% of HIV-infected patients; furthermore, disseminated infection may occur in 2-5% of them, particularly in patients living in endemic areas. (10) In Latin America, where there are areas of high endemicity (Colombia, Argentina, Mexico, Brazil, Venezuela, etc.), it has been estimated that about 1 600 000 people live with HIV, of which 24 000 develop disseminated histoplasmosis with a mortality rate of ≥40%. Although antiretroviral therapy has helped to reduce the incidence of histoplasmosis, it is a fact that in Latin America this infection continues to be a serious health problem, since there are still many people who do not have access to this therapy, which, together with the lack of tests that would allow a timely diagnosis, increases the risk of death. (11)

With all this in mind, it is evident that histoplasmosis is a disease of great medical interest due to its association with the population of individuals living with HIV/AIDS and its clinical similarity with tuberculosis. The public health problem posed by this fungal infection should be addressed comprehensively, considering that it is not a disease that is compulsorily reported

and its real incidence is unknown, reason why prevention and control programs have not been developed for the population most vulnerable to developing it. It is important that, in the presence of clinical suspicion, physicians have knowledge of the set of tests that can be used, as well as of their limitations, in order to confirm the diagnosis, provide the most appropriate therapeutic management for each patient, and influence the reduction of the mortality rate.

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PERITONEAL HISTOPLASMOSIS. CASE REPORT

Keywords: Histoplasmosis; Acquired Immunodeficiency Syndrome; Dialysis; Systemic Lupus Erythematosus.
Palabras clave: Histoplasmosis; Síndrome de inmunodeficiencia adquirida; Diálisis; Lupus eritematoso sistémico.

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RESUMEN

Introducción. La histoplasmosis es una infección micótica oportunista granulomatosa. La histoplasmosis peritoneal (HP) es una forma rara de histoplasmosis diseminada (HD).

Presentación del caso. Paciente masculino de 44 años con antecedentes de infección por VIH, lupus eritematoso sistémico con nefropatía lúpica y enfermedad renal crónica en diálisis peritoneal, quien presenta ascitis recurrente sin etiología en estudio seriado de líquido ascítico. Se realiza tomografía de abdomen contrastada que evidencia lesión peritoneal inespecífica, luego estudiada con laparoscopia y biopsia, documentándose infección por *Histoplasma capsulatum.* El sujeto recibe 15 días de tratamiento intrahospitalario con anfotericina B deoxicolato con buena evolución, sin recurrencia de ascitis, y continúa con manejo ambulatorio indefinido con itraconazol.

Discusión. El primer caso de HP se describe en 1970 y el primero en Colombia es el que aquí se presenta. La mayoría de los casos de este tipo de infección se han asociado a diálisis peritoneal, su diagnóstico se basa en el estudio de líquido ascítico y su tratamiento depende de los lineamientos de otras formas de HD.

Conclusiones. La HP es una entidad rara que requiere alta sospecha clínica, principalmente en pacientes con inmunocompromiso.

ABSTRACT

Introduction: Histoplasmosis is an opportunistic granulomatous fungal infection. Peritoneal histoplasmosis (PH) is a rare form of disseminated histoplasmosis (DH).

Case description: A 44-year-old male patient with history of HIV infection, systemic lupus erythematosus with lupus nephritis, and chronic kidney disease on peritoneal dialysis, presented with recurrent ascites without clear etiology in the serial study of ascitic fluid. Contrast computed tomography of the abdomen showed a nonspecific peritoneal nodule, for which laparoscopy and biopsy were performed, identifying Histoplasma capsulatum infection. The subject received 15 days of in-hospital treatment with amphotericin B deoxycholate with good evolution, no recurrence of ascites, and indefinite outpatient management with itraconazole.

Discussion: The first case of PH was described in 1970 but this is the first case reported in Colombia. Most cases of PH have been associated with peritoneal dialysis. Its diagnosis is based on the study of ascitic fluid and its treatment follows the guidelines of other forms DH.

Conclusions: PH is a rare entity that requires high clinical suspicion, especially in immunocompromised patients.

INTRODUCTION

Histoplasmosis is an opportunistic fungal granulomatous infection with higher prevalence in tropical regions, mainly in Central and South America. It is caused by inhalation of microconidia of *Histoplasma capsulatum* var. *capsulatum*, a dimorphic fungus that develops in soil and plant debris, especially in areas with high nitrogen content usually associated with caves and bird droppings. (1)

Histoplasmosis has a wide range of clinical presentations that depend on three factors mostly: fungal load, virulence and histoplasma strain, and host immune status. (2) In addition, it can vary from asymptomatic patients with a less severe state to severe infections in the context of hematogenous dissemination or through the reticuloendothelial system, more frequently involving organs such as liver, spleen, bone marrow and skin. (3)

In patients with human immunodeficiency virus (HIV) infection, the most frequent clinical presentation is the progressive disseminated form, which usually has an acute or subacute course. (4)

Peritonitis associated with *H. capsulatum* is extremely rare, with few cases reported in the literature. Risk factors for developing fungal peritonitis include prior use of antibiotics, immunosuppression status, environmental exposure, intra-abdominal surgery, and extraperitoneal spread of fungal infection. (5) The following is a case report of a patient with HIV infection, systemic lupus erythematosus with lupus nephritis, and chronic kidney disease on hemodialysis diagnosed with peritoneal histoplasmosis (PH).

CASE PRESENTATION

Male patient of 44 years of age, from Río Viejo (Bolívar, Colombia) and resident in Bogotá D.C. for 3 years in a household classified as socioeconomic stratum 2 in the locality of Engativá; he was unemployed for the last year and previously worked as a heavy machinery operator. He had been diagnosed with HIV infection C3 category and AIDS (clinical stage 4), with a CD4 count of 416 cells/mm^3 and a viral load of 36,645 copies/mm^3, treated with anti-retrovirals including abacavir 600 mg/day, lamivudine 50 mg/day and dolutegravir 50 mg/day. He also had a history of systemic lupus erythematosus with lupus nephritis, and stage 5 chronic kidney disease previously treated with mycophenolate mofetil 500 mg/day and on renal replacement therapy with peritoneal dialysis.

The patient attended consultation due to a clinical picture of three months of evolution consisting of abdominal distention, early prandial satiety, nausea, anorexia and progressive dyspnea. The subject assisted to outpatient consultations on multiple occasions and was diagnosed with possible tense ascites, for which an evacuation and diagnostic paracentesis with conventional ascitic fluid studies was scheduled. No infectious etiology was documented in peritoneal liquid cultures (negative for common germs and fungi) or Ziehl-Neelsen staining (no acid-alcohol resistant germs observed); adenosine desaminase was reported as normal (data not available in clinical history) and there were no other relevant findings in basic studies of ascitic fluid.

On physical examination, the patient was in poor general condition, tachycardic, normotensive, afebrile and with cachexia; his weight was 48kg, and he presented with distended abdomen with shifting dullness, cardiopulmonary auscultation without alterations, positive ascitic wave and pain on palpation without signs of peritoneal irritation, and peritoneal dialysis catheter without local inflammatory signs. A computed tomography (CT) of the abdomen was performed, showing a single

nodular image of well-defined edges, with soft tissue density, of 12mm in diameter, located in the peritoneal plane of the right abdominal wall and associated with abundant ascites of free characteristics, splenomegaly and slight thickening of the parietal peritoneum (Figure 1 and 2).

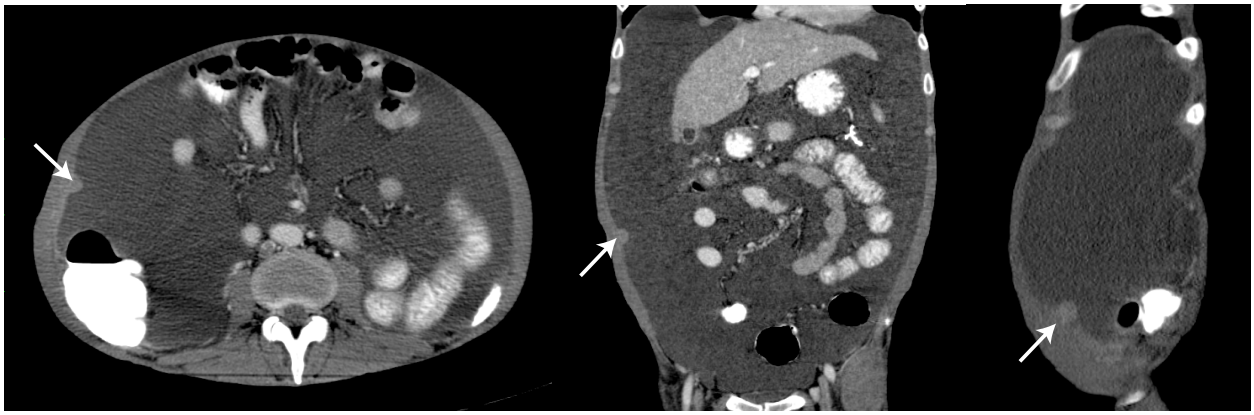

Figure 1. CT scan of the abdomen, axial, coronal and sagittal planes, showing nodular lesion (arrow) in the parietal peritoneum.
Source: Document obtained during the study.

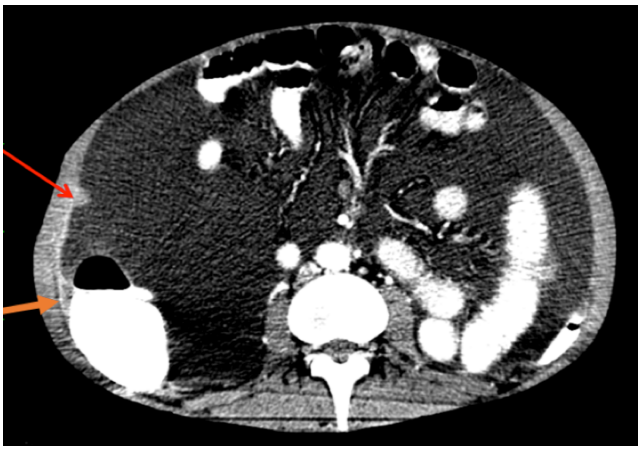

Figure 2. CT scan of the abdomen, axial plane, showing thickening (orange arrow) and nodular lesion (red arrow) in the parietal peritoneum.
Source: Document obtained during the study.

Subsequently, a diagnostic laparoscopy with biopsy of the peritoneal lesion was performed, revealing fibroconective stromal tissue with cells of reactive aspect; hemorrhagic and necrotic foci, and infiltrate of eosinophils, lymphocytes and, to a lesser extent, plasmocytes. No granulomas or tumor cells were obtained. Special stains were performed with findings in Grocott-Gomori's methenamine silver stain suggestive of histoplasma immersed in necrotic tissue (Figures 3 and 4).

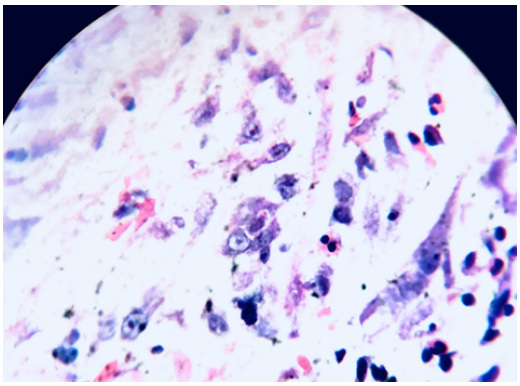

Figure 3. Hematoxyline-eosine staining of fibroconective stromal tissue with reactive cells, eosinophil infiltrates, and hemorrhagic and necrotic foci.
Source: Document obtained during the study.

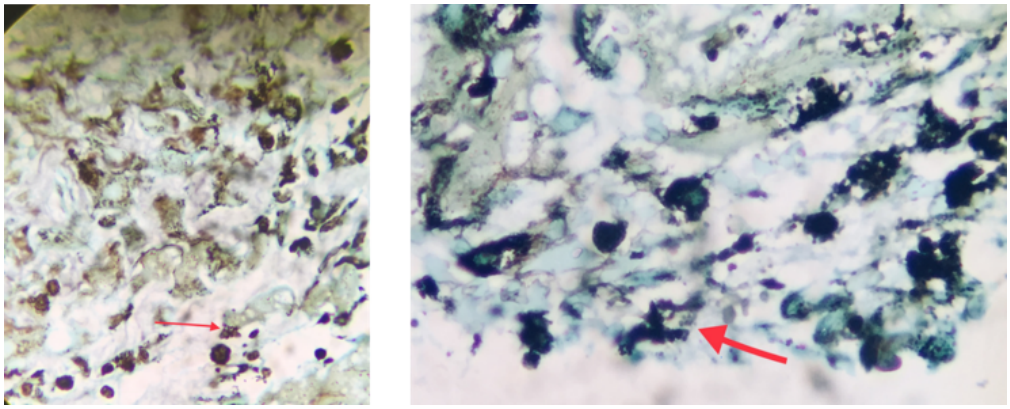

Figure 4. Grocott-Gomori's methenamine silver stain suggestive of histoplasma forms (red arrows) in a small necrotic tissue fragment.
Source: Document obtained during the study.

In addition, fungi were cultured in a peritoneal sample at 6 weeks, which confirmed the diagnosis of *H capsulatum* infection. Peritoneal dialysis catheter was removed, renal support was initiated with hemodialysis, as well as in-hospital treatment with amphotericin B deoxycholate 50 mg/day in continuous infusion for 15 days (indicated by the Infectious Disease Department for patients with chronic kidney disease on hemodialysis).

During the diagnostic approach, pulmonary involvement was ruled out by chest CT and negative blood cultures. During hospitalization follow-up, the nutrition service diagnosed him with severe protein-calorie malnutrition, thus conditioning an additional factor for immunocompromise that was managed with enteral nutritional support with satisfactory clinical response.

The treatment did not have any adverse effect and no adjustment of the dose scheduled for in-hospital management of amphotericin B deoxycholate was required. Once the amphotericin B scheme was completed with good tolerance, and considering his clinical improvement without

recurrence of ascitic syndrome and tolerance to enteral nutritional support weaning and the oral route, it was decided to continue outpatient management with itraconazole 200mg every 12 hours indefinitely, according to the concept of infectology. Control appointments were scheduled with nephrology, clinical nutrition, infectology and HIV program to continue with multidisciplinary outpatient management.

The patient was considered to have a good prognosis due to guided management of specific etiology, a multidisciplinary evaluation plan for physical rehabilitation and nutrition, and the management of comorbidities.

DISCUSSION

This report presents a case of peritoneal infection by histoplasmosis in a patient with HIV infection, systemic lupus erythematosus and severe protein-caloric malnutrition. This infection is found throughout the world, and since the twentieth century, it has been considered part of the definition of acquired immunodeficiency in HIV patients. (6,7) It is also characterized by respiratory symptomatology —either acute, subacute or chronic— when it involves only the lungs, and by systemic manifestations related to its disseminated form; the latter is more frequent in the elderly and in immunocompromised patients. (8)

In patients with AIDS, *H. capsulatum* is considered opportunistic, and is usually associated with low CD4 counts (<150 cell/mm^3), with higher incidence in patients coming from endemic areas for the disease and in patients with aspiration of a high inoculum of microconidias of the fungus. (9) Therefore, in the case described here, the risk factor was not the history of HIV infection, given that at the time of the PH diagnosis the patient had a CD4 count of 416 cell/mm^3. The risk factors for DH, in this case, involved immunosuppression determinants: systemic lupus erythematosus and its treatment, chronic kidney disease and severe protein-caloric malnutrition.

The disseminated form of histoplasmosis is characterized by the onset of respiratory symptoms, subsequently accompanied by hepatosplenomegaly, adenopathies, colonic masses, chorioretinitis, central nervous system lesions and skin lesions. (8) Peritoneal manifestation is part of the spectrum of disseminated histoplasmosis (DH) presentation, while peritoneal fungal infection in immunosuppressed patients is usually caused by *Candida spp*; infection by *H. capsulatum* is rare. (10) With regard to the DH diagnosis, skin lesion examinations are usually positive in 3-55% of the cases, while antibody and urinary antigen detection is positive in 70-90% and lung culture in 50-70%; sensitivity depends on the clinical form and immune status of the host. (11)

In diagnostic imaging, PH is characterized by diffuse nodular thickening of peritoneal surfaces that have soft tissue attenuation on CT and are enhanced by intravenous contrast administration. Other findings may include ascites, hepatic or splenic microabscesses of miliary distribution, peritoneal or hepatic granulomas, and diffuse striation of the omentum or mesenteric fat. (12,13)

Finding disseminated peritoneal lymphadenopathies or nodules is highly relevant as they suggest peritoneal involvement secondary to hematogenous dissemination. (13) Gastrointestinal involvement (thickening of the terminal or blind ileum) by histoplasmosis suggests dissemination by contiguity secondary to intestinal microperforations. PH is included in the spectrum of granulomatous peritonitis and, therefore, its imaging characteristics are indistinguishable from peritoneal tuberculosis infection. (12)

PH is a rare form of DH that has been seldom reported worldwide, with one case in South America and none in Colombia. The case described here takes on great importance as it is the first to be reported in the country and the second in South America, thus providing valuable information on this rare disease.

The first case of PH was described in 1970 by Reddy after conducting the necropsy of a woman with disseminated disease (14); the only case reported in South America was a woman of Lebanese origin without other related diseases that occurred in Venezuela in 1989. (15)

Most PH reports have been associated with peritoneal dialysis (5,14-17): the first was reported by Ma (16) in 1985 and the last by Ijaz & Choudhury (5) in 2010. The present case adds to this list of infections associated with peritoneal dialysis catheter, since the patient was under management with peritoneal dialysis for chronic kidney disease due to class V lupus nephritis at the time of diagnosis. Among the diagnostic methods used for PH, Lim *et al.* (17) cultivated *H. capsulatum* in the peritoneal dialysis fluid of a patient who presented signs and symptoms consistent with peritonitis. In 1993, Lopes *et al.* (18) and Lopes *et al.* (19), besides performing the culture of peritoneal dialysis fluid, observed fungal forms compatible with the disease on direct examination. The clinical approach presented here focuses on the invasive peritoneal study of a patient with recurrent ascites in the context of multifactorial immunosuppression, in whom conventional ascitic fluid studies failed to establish an etiology and whose abdominal diagnostic imaging showed focal lesion amenable to study.

In Colombia, histoplasmosis is frequent, especially in risk groups according to the national survey of 1992-2008, which found that 70.5% of patients with histoplasmosis had AIDS and 7% had other types of immunosuppression (20); both situations were found in the reported patient. It is important to note that PH should be treated as DH in the absence of a specific guideline for treatment (21), with a duration based on the clinical evolution and extrapolation of other types. The initial management with amphotericin B was administered in the hospital for 15 days, during which time the patient presented progressive clinical improvement; he was finally discharged with an indication of indefinite management with voriconazole and follow up by infectology to determine the suspension of the drug.

In patients with chronic kidney disease who are on renal replacement therapy, amphotericin B deoxycholate and voriconazole are used at the same doses as in patients without chronic kidney disease, without any further consideration being required. However, adverse effects to be considered in both types of patients should always be followed up.

CONCLUSIONS

PH is a rare entity that is part of the spectrum of clinical manifestations of DH and requires high clinical suspicion, especially in immunocompromised patients. Its diagnosis should be based on the study of ascitic fluid, being invasive peritoneal study an option in patients in whom microbiological isolation in peritoneal fluid is not achieved. Because of its low incidence, treatment should be based on what is described for other forms of DH. Likewise, the clinical evolution of any hospitalized patient must be interpreted in an appropriate way, since one or several diseases may share signs and symptoms, and the course of a disease may be different from one patient to another. In short, clinical suspicion allows for proper diagnosis and, in turn, determines a comprehensive and timely management.

There are clinical settings that make difficult reaching a conclusive diagnosis, requiring unusual tests or empirical treatments, depending on each context. The present case provides information on the diagnostic approach and in-depth evaluation required by immunocompromised patients, especially those with multiple comorbidities and psychosocial risk factors.

The strength of the current clinical case lies in the fact that it was possible to achieve the definitive diagnosis of a rare entity, which also had an unusual clinical and radiological presentation. Some of the limitations are the unavailability of complete data from the previous clinical history, which included serial peritoneal fluid studies and outpatient follow-ups, given that the patient did not attend the scheduled control appointments and there was no in-person or telephone contact after hospital discharge. Moreover, it was not possible to use other methods for immunological diagnosis, molecular diagnosis and detection of fungal antigens because they were not available at the facilities of the health service provider where the patient was treated.

CONFLICTS OF INTEREST

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FUNCTIONAL ASSESSMENT USING SHORT TESTS IN A PATIENT WITH POMPE DISEASE RECEIVING ENZYME REPLACEMENT THERAPY: CASE REPORT

Keywords: Glycogen Storage Disease Type II; Enzyme Replacement Therapy; Recovery of Function; Glycogen Storage Disease Type IIB; Minimal Clinically Important Difference; Muscle Disorders.
Palabras clave: Enfermedad del almacenamiento de glucógeno tipo II; Terapia de reemplazo enzimático; Recuperación de la función; Diferencia mínima clínicamente importante; Enfermedades musculares.

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RESUMEN

Introducción. La enfermedad de Pompe se caracteriza por una alteración de la enzima alfa glucosidasa ácida lisosomal que produce acumulación de glicógeno, principalmente en el músculo esquelético y cardiaco. Se presentan formas de inicio temprano y tardío, esta última de más difícil manejo dada la múltiple variedad de presentaciones. La terapia de reemplazo enzimático ha demostrado mejorar la función motora gruesa y pulmonar de los pacientes con esta patología.

Presentación del caso. Paciente femenino quien presentó cuadro crónico de cuadriparesia y a quien se le documentó enfermedad de Pompe, por lo que requirió terapia de reemplazo enzimático con mejoría franca de sintomatología, objetivizada con la realización de pruebas rápidas de evaluación funcional.

Discusión. La terapia de reemplazo enzimático en la enfermedad de Pompe modifica la historia natural de la enfermedad. Se realiza una breve revisión de la literatura acerca de las pruebas funcionales que pueden ser utilizadas dentro de la evaluación del paciente con este trastorno.

Conclusiones. La prueba de caminata de 10m, de equilibrio monopodal, de flexión cervical en supino, de levantarse-sentarse cinco veces y de la moneda resultan útiles para la evaluación clínica de los pacientes con enfermedad de Pompe en terapia de remplazo enzimático.

ABSTRACT

Introduction: Pompe disease is characterized by the deficiency of the acid alfa glucosidase enzyme, which leads to a glycogen accumulation mainly in cardiac and skeletal muscles. Its onset may be early or late; the late form is more difficult to handle given the variety of presentations. Enzyme replacement therapy has shown to improve gross motor function and lung function in patients.

Case description: Female patient who presented chronic quadriparesis. She was diagnosed with Pompe disease, which required enzyme replacement therapy that helped improve the symptoms, which was evident with the performance of rapid functional evaluation tests.

Discussion: Enzyme replacement therapy in Pompe disease modifies the natural history of the disease. A brief review of the literature about the functional tests that can be used to assess a patient with this disorder is presented.

Conclusion: The 10-meter walk test, one-leg stance test, cervical flexion in supine position, five times sit to stand test, and coin rotation task are useful for clinical evaluation in patients with Pompe disease receiving enzyme replacement therapy.

INTRODUCTION

Pompe disease is characterized by a deficiency of the acid alpha-glucosidase enzyme, which is responsible for glycogen accumulation in cardiac and skeletal muscles. Its presentation may be early or late, and its diagnosis requires a high index of clinical suspicion and confirmation by molecular tests. (1) Enzyme replacement therapy has proven to improve general motor and lung function, albeit unpredictably.

In adults, enzyme replacement therapy improves or stabilizes skeletal muscle strength, muscle function, respiratory function, and survival; however, the magnitude of response varies among individuals. In 2017, the European POmpe Consortium (EPOC) reached a consensus on when to start and stop enzyme replacement therapy in patients with Pompe disease. Based on the experience of several countries, it was recommended to start when the following conditions were met: 1) diagnosis confirmed through leukocyte enzyme activity or genetic test, 2) symptomatic patient during clinical assessment, and 3) monitoring carried out at least once a year to evaluate the response to treatment.

This effect is even greater when moderate to vigorous aerobic activities and muscle strengthening activities are accompanied by enzyme replacement therapy, showing significant increase in muscle strength and distance traveled in the 6-minute walk test, and a decrease in fatigue and pain. (2-4) This appears to be caused by mechanisms that are not associated with the reduction of glycogen content. (5) Furthermore, specific training of respiratory muscles (6) has shown improvement in the strength of the maximum inspiratory and expiratory pressure in muscles (MIP and MEP).

Short functioning assessment tests may be useful for follow-up in patients with Pompe disease, and the minimal detectable change (MDC) must be taken into account for their application. The following is a clinical case of a patient with late-onset Pompe disease who underwent enzyme replacement therapy with marked improvement in symptomatology, which was evident when performing functional evaluation tests.

CASE PRESENTATION

This is the case of a 34-year-old female mestizo patient, housewife, who consulted due to a clinical picture of proximal weakness experienced since adolescence, which progressively interfered and limited her activities of daily living. The symptoms included hypersomnia, dyspnea and snoring during sleep. On physical examination, she had normal muscle tone and sensitivity, proximal 3/5 and distal 4/5 quadriparesis, thoracic hyperkyphosis, lumbar hyperlordosis and global hyporeflexia, without evidence of tongue muscle involvement or skin lesions. Her family history included a sister with a diagnosis of Pompe disease.

The patient presented with a chronic and progressive pure motor stroke which, given the clinical characteristics of her symptoms (proximal weakness, apparently symmetrical), required ruling out a myopathy first, as some of them frequently involve the respiratory muscles, as is the case of Pompe disease.

Creatine phosphokinase (CPK) was requested as an extension study, yielding an elevated value (790 U/L). Electrodiagnosis of the four limbs was performed, showing fibrillation potentials, especially in the evaluated thoracic paraspinal and proximal muscles, early recruitment, and short duration motor unit potentials. The diagnosis of Pompe disease was confirmed by enzymatic study in leukocytes, finding a marked reduction in the enzymatic activity of alpha-glucosidase

(21%). The genetic study demonstrated an abnormal OAG sequence.

Enzyme replacement with alpha-glucosidase was initiated at a rate of 20 mg/kg every two weeks by continuous infusion. One month after the start of treatment, her sleep pattern improved and dyspnoea decreased, but functional performance showed no significant change. After five months of enzyme replacement, respiratory pattern and physical capacity improved (Table 1). There were no adverse drug reactions during the follow-up period.

Table 1. Changes in physical test.

Variable \ Date	Before treatment	One month after starting treatment	Five months after starting treatment	Difference pre- and post-TRE evaluation	MCID
10-min-walk	8.05 s	7.50 s	7.44 s	0.61 m/s	0.05-0.13 m/s
Coin rotation task - right hand	15 s	13 s	12.5 s	2.5 s	1.55 s
Coin rotation task - left hand	16 s	17 s	14.21s	1.79s	1.3 s
Right leg stance	20 s	26 s	50 s	30 s	4.77 s
Left leg stance	41 s	47 s	44.8 s	3.8s	4.77 s
Five times sit-to-stand	12.7 s	13 s	9.56 s	3,14 s	2.3 s
Cervical flexion in supine position	23 s	27 s	47.62 s	24.62 s	4.4-5.3 s

ERT: enzyme replacement therapy; MCID: minimal clinically important difference.

Source: Own elaboration.

Changes in short functional tests were observed from before the start of enzyme replacement therapy until 5 months after beginning the treatment.

DISCUSSION

Pompe disease, also known as glycogen storage disease type 2, is an autosomal recessive disorder considered as a rare inborn error of metabolism, with an estimated frequency of 1 per 40 000 live births. (1) It is characterized by an acid alpha-glucosidase deficiency that causes excessive accumulation of lysosomal glycogen and defects in autophagy, mainly in cardiac and skeletal muscles. Two clinical presentations have been described according to the age of onset: early onset (infantile with or without cardiomyopathy) and late onset (juvenile and adult), which poses greater diagnostic difficulty.

To date, the literature has not described which rapid clinical assessment tests are most appropriate for Pompe disease. The systematic review by Savegnago *et al.* (7) on functional assessment scales in children and adults with Pompe disease included 14 studies, and scales with grade of recommendation (Grade C) were found for the pediatric population (Alberta Infant Motor Scale and Pompe-Pedi). Regarding the adult population, only the Rotterdam Handicap Scale was described —with good reproducibility (ICC=0.94)—, as well as the GMFM (Gross Motor Function Measure) and the FIM (Functional Independence Measure); the last

two were used only in one case report. (7) The limitation of these tests lies in the fact that their application is time consuming and must be done by trained personnel.

Functional assessment tests have been widely used in patients with diseases in muscle fibers, so they can be a cost-effective tool to monitor the response to enzyme replacement therapy in patients with Pompe disease and detect changes over time.

In Colombia, several cases of Pompe disease in its juvenile (8) and adult (9) forms have been described; nevertheless, no information has been provided on the improvement of patient's functionality, at least not in an objective manner. In this case, even though the patient showed improvement in symptoms related to respiratory muscle weakness, during the "classical" physical examination no objective functional changes were reported that could be confirmed when the patient performed the functional assessment using simple tests such as the 10 meter walk, coin rotation task, five times sit to stand test, cervical flexion time in supine position and one leg stance (Table 1).

In order to interpret the results and the changes observed in the functional tests, it is important to consider the populations in which they have been validated. To objectively determine whether the change obtained between two consecutive assessments is outside the margin of error, the minimal clinically important difference (MCID) or the minimal detectable change (MDC) are useful if these outcome measures are known. (10,11)

For example, the 10 meter test calculates the walking speed in m/s in a short duration, which is useful for monitoring and evaluating the ability to perform safe and independent walking both in the community and at home in adult patients with neuromuscular diseases; it also evaluates the activity domain of the ICF (International Classification of Functionality). During this test, the patient is asked to walk a distance of 10 meters, leaving a space so that the subject can accelerate/decelerate —said space is not included when determining the distance—, and then three trials are averaged to find the speed. This test has excellent test-retest reproducibility (ICC=0.91), and MCID of 0.13 m/s and MDC of 0.05 m/s. (12)

The five times sit to stand test measures the strength of the lower limbs and balance when evaluating the IFC activity domain. Three trials are administered and then the average of the three trials or only the value obtained in the first trial is considered. The MDC in patients with vestibular pathology is 2.3s (13); in Parkinson's patients a score >16 is the cut-off point to differentiate subjects with a high risk of falling. (14) Times >12s in older adults were recently described as one of the strongest evidence for predicting risk of future falls. (15)

The coin rotation task was designed as a rapid assessment test to measure fine motor dexterity of the fingers. For this assessment, the patient must rotate a coin 20 times using the thumb, index and middle fingers, and the time it takes to develop the activity is measured; the MDC for all ages is 1.55 for the right hand and 1.3 for the left hand. (16)

Finally, the single leg stance test screens for balance control and thus the risk of falls. It measures the time that the patient is able to maintain balance using only one leg, without assistance, and with open or closed eyes. It has established normative values for healthy individuals by age group (17); the MDC for the test with closed eyes is 0.48 and with open eyes is 4.77. (18)

CONCLUSIONS

Pompe disease is characterized by glycogen accumulation in skeletal muscles, which leads to generalized weakness that progressively limits

the functionality of affected patients. Enzyme replacement therapy, along with physical activity interventions, has shown to improve weakness and thus the quality of life of the patients.

This is the case of a rare pathology — late-onset Pompe disease—, which describes the usefulness of functional tests as a quick and effective way of observing the response to treatment in an objective manner. Consequently, these tests are indispensable tools for physiatrists to monitor response to treatment. (19)

One of the limitations of this work is that comparisons were not made with other standardized tests to follow up neuromuscular pathologies, although there is broad literature regarding the usefulness of performing such comparisons. The interpretation of these tests must take into account the minimal clinically important difference. Therefore, the coin rotation task, cervical flexion time in supine position, one leg stance, five times sit-to-stand test, and the 10 meter walk test are proposed as tools to objectively measure the response to treatments during interventions.

CONFLICT OF INTEREST

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MULTIPLE ORGAN FAILURE CAUSED BY POISONOUS CONTACT WITH A *LONOMIA SP* CATERPILLAR. CASE REPORT

Keywords: Lonomia; Larva; Lepidoptera.
Palabras clave: Lonomia; Larva; Lepidópteros.

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RESUMEN

Introducción. El accidente lonómico se ha convertido en un evento de gran interés, ya que supone una problemática de salud pública enfocada en las comunidades rurales y un reto para el personal de salud dadas las múltiples complicaciones, el difícil diagnóstico y las variantes terapéuticas.

Presentación del caso. Paciente masculino de 41 años quien tuvo contacto con oruga del género *Lonomia sp.* y presentó síntomas de sangrado y posterior falla multiorgánica que se resolvió con el uso de suero antilonómico.

Discusión. Se presenta un cuadro clínico que progresó a falla multiorgánica y síndrome hemorrágico asociado a dificultades en su diagnóstico y que requirió intervención terapéutica en primer nivel de urgencia con posterior necesidad de tratamiento en un centro de mayor complejidad por deterioro y no disponibilidad de suero antilonómico.

Conclusiones. A partir de las estrategias de intervención médica intrahospitalaria, la administración del suero lonómico y el seguimiento del paciente a través del sistema, se pudo constatar la mejoría en el estado de salud y dar el alta médica. Es importante poner en tensión los conocimientos de los profesionales en salud que atienden estos casos en las zonas rurales y la disponibilidad del suero de tratamiento.

ABSTRACT

Introduction: Lonomic accidents have become of great interest as they represent a public health problem in rural communities. These accidents are challenging for health personnel given their multiple associated complications, difficult diagnosis and therapeutic variants.

Case presentation: This is the case of a 41-year-old male patient who had contact with a caterpillar of the genus *Lonomia* sp. He presented with symptoms of bleeding and subsequent multiple organ failure that resolved with the use of antilonomic serum.

Discussion: The patient presented with symptoms that progressed to multiple organ failure and associated hemorrhagic syndrome due to the difficulties for diagnosis. He required therapeutic intervention in a primary care institution with subsequent need for treatment in a more complex center considering the deterioration and non-availability of the antilonomic serum.

Conclusions: Based on in-hospital medical intervention strategies, the administration of the lonomic serum and the patient's follow-up through the system, it was possible to confirm the improvement of his health condition and discharge him. It is important to stress the knowledge of the health professionals who treat these cases in rural areas and the availability of the serum.

INTRODUCTION

Lonomic accident or lepidopterism- erucism is understood as the disease caused by direct contact with caterpillars of the family *Lonomia* sp. Currently, there are about 26 variants of this species distributed throughout the Americas, where different denominations have been used to describe these larvae: fire caterpillars, churruscus (Colombia) or muchiras (southern Colombia and Ecuador). (1)

Accidents and diseases caused by poisonous terrestrial animals, such as caterpillars, amphibians and myriapods, or aquatic animals, are rarely reported in Colombia, and there is little information on their diagnosis and management. Culturally speaking, it is known that most affected people belong to indigenous communities and are exposed due to their economic and social activities, sociocultural particularities, the scarce or lack of protection of the hands, feet and skin, and even by the use of *Phyllobates* sp. venom in hunting activities. (2)

The caterpillars of the *Saturniidae* species (Figure 1) are characterized by pointed and branched spicules, bristles or hairs that contain a complex mixture of enzymes and toxins. (3) These substances are released into the skin after contact, causing activation of the kinin–kallikrein system and fibrinogen-lytic enzymes that produce a wide arrange of signs and symptoms because of the alteration in the coagulation cascade involving factors VIII-XIII-X. (3,4) Authors have reported cases of caterpillar poisoning that start with multiple symptoms at the inoculation site and then progress to general symptoms. Initial symptoms include general malaise, headache and nausea, followed by hemorrhagic syndrome, which leads to multiple organ failure and even death. (5)

Figure 1. *Lonomia obliqua* larva.
Source: Taken from Manosso (6).

Blood dyscrasia is closely correlated to the symptoms and is the most serious complication; it is usually established within the first 48 hours after contact. Moreover, hemorrhagic lesions may vary from ecchymotic lesions to episodes of massive and intraparenchymal bleeding. (7)

The main treatment involves the use and administration of antilonomic serum, depending

on the classification and description of symptoms in the patient (Table 1). The process that counteracts the mechanisms of the pathological lesion and reduces the symptomatology is currently known. (7-9)

Table 1. Clinical classification of lonomic accident.

Classification	Description
Mild	Patient exposed to caterpillars who has only local but no hemorrhagic symptoms.
Moderate	Patient with local symptoms, hemorrhagic signs and symptoms, and involvement of mucous membranes and skin, without vasopressor support.
Severe	Patient with hemodynamic instability, hemorrhagic syndrome that involves multiple organs and multiple organ failure.

Source: Elaboration based on Arocha-Piñango (4).

CASE PRESENTATION

A 41-year-old male patient from the Curipao indigenous ethnic group, residing in the municipality of Tame, Arauca (Colombia), with a history of chronic gastritis without pharmacological treatment and no other relevant condition, was admitted at a secondary healthcare center on September 26, 2016, with an apparent snakebite injury diagnosed in a primary healthcare center. The man reported that around 10:00 a.m. the day before, he left his home to carry out agricultural work and had contact with an animal (unidentified at first) in the back side of the right hand (Figure 2). He also reported the insertion of approximately 20 bristles into the skin that caused him intense localized pain, similar to stinging pain, with an intensity of 8/10 on a pain scale, which were removed a few minutes later with a sharp object (knife). After that, he expressed feeling irradiation of pain towards the elbow, sensation of paresthesia, pruritus, edema, redness and heat on the lesion site. He said that he applied a topical fungal cream 20 minutes after contact, improving the symptoms, pain and redness; however, edema of the hand persisted (Figure 2).

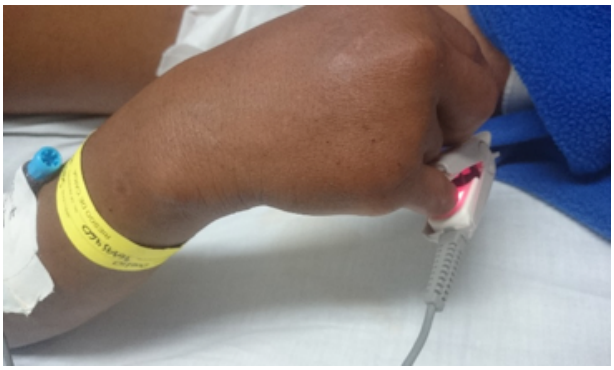

Figure 2. Primary site of contact with caterpillar *Lonomia* sp.
Source: Document obtained during the study.

The man manifested the onset of global headache and hematemesis —approximately 30 episodes during the day— and burning pain in the epigastric region without irradiation, and generalized arthralgia. The following day, he decided to seek medical help at the nearest center (primary healthcare center), where he reported persistence of symptoms and appearance of bleeding gums. The medical assessment resulted in a diagnostic impression of snakebite accident, and management with omeprazole and intravenous fluid therapy was initiated. Laboratory reports indicated 13 000 leukocytes, 86% neutrophilia, 14% lymphocytes, and prothrombin time and partial thromboplastin time >1 minute; no platelet count was available.

He was referred to a secondary healthcare center, where he was admitted for evaluation and management by an internist. The vital signs on admission were: heart rate: 87 /min, respiratory rate: 19/min, blood pressure: 146/83 mmhg, oxygen saturation: 98%, and fraction of inspired oxygen: 0.21. On initial physical examination,

slight skin paleness was observed, along with active bleeding in the gums, especially in the dental fracture of the right first molar (Figure 3); cardiopulmonary aspects without alterations; soft abdomen with pain in epigastrium region; and right upper limb with edema located in the dorsum, erythematous punctiform lesions, without redness or heat, and mild pain on palpation. No strength deficiencies were observed during the neurological examination and sensitivity was preserved.

Finally, two episodes of hematemesis occurred during hospitalization, for which hematology tests and blood chemistry were requested. Table 2 presents the results of the laboratory tests carried out on admission, revealing an increase in kidney function and alteration of liver function; deterioration of leukocyte and platelet function is also evident.

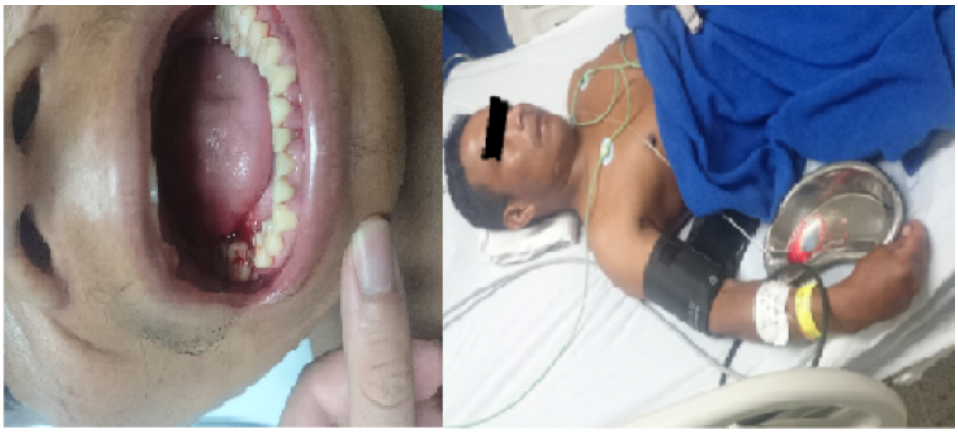

Figure 3. Bleeding of the gums.
Source: Document obtained during the study.

Table 2. Lab test reports obtained during clinical evolution.

Tests	25/09/16	26/09/16	27/09/16	27/09/16	28/09/16	29/09/16	30/09/16	01/10/16	02/10/16
Hematocrit for men: 42-54%		hematocrit: 40.5%	hematocrit: 24.8%	hematocrit: 18.6%	hematocrit: 20.1%		hematocrit: 16.9%	hemoglobin: 27.4%	
White blood cell count: 5 000-10 000/mm³	leukocytes: 13 000, neutrophils: 83%, lymphocytes: 8%	leukocytes: 9 400, neutrophils: 83%, lymphocytes: 8%	leukocytes: 18 200, neutrophils: 97%, lymphocytes: 2%	leukocytes: 11 192, neutrophils: 94%, lymphocytes: 2%	leukocytes: 11 160, neutrophils: 87% lymphocytes: 6%		leukocytes: 9 100, neutrophils: 76.1%, lymphocytes: 17.1%	leukocytes: 9 360 neutrophils: 71.3%, lymphocytes: 14.9%	
Manual platelet count: 150 000-450 000		platelets: 212 000 / mm³	platelets: 178 500 / mm³	platelets: 86 100/ mm³	platelets: 52 000/ mm³		platelets: 135 000 / mm³	platelets: 192 000 / mm³	

Continues.

Tests	25/09/16	26/09/16	27/09/16	27/09/16	28/09/16	29/09/16	30/09/16	01/10/16	02/10/16
Coagulation times PT: 12-15 seconds PTT: 25-35 seconds	PTT >1 minute, PT >1 minute	PTT >2 minutes, PT >2 minutes	PTT >2 minutes, PT >2 minutes	PTT: 106.1 seconds, PT: >2 seconds	PTT: 35.9 seconds, PT: 26.2 seconds	PTT: 23.6 seconds, PT: 17.9 seconds		PTT: 21.2 seconds, PT: 14.3 seconds	
Transaminases GOT: 10-40 u/L GPT: 7-40 u/L		GOT: 217 u/L, GPT: 42 u/L	GOT:217 u/L, GPT: 42 u/L				GOT: 30 u/L, GPT: 25 u/L		
Kidney function men Creatinine: 0.6 and 1.2 mg/dL BUN: 10 and 20 mg/dL		3.2 mg/dL		Creatinine: 3.27 mg/dL, BUN: 43 mg/dL	Creatinine: 2.65 mg/dL, BUN: 44.5 mg/dL	Creatinine: 2.48 mg/dL	Creatinine: 1.24 mg/dL, BUN: 27.7 mg/dL	Creatinine: 1.09 mg/dL, BUN: 17.6 mg/dL	Creatinine 1.03 mg/dL BUN: 15.2 mg/dL
Glucose: 60-110 mg/dL		95 mg/dL							
Electrolytes Potassium 3.5-4.5 mEq/L Sodium: 135-145 mEq/L		Potassium: 4.0 mEq/L, Sodium: 143 mEq/L				Potassium: 2.9 mEq/L	Potassium: 3.41 mEq/L, Sodium: 146.7 mEq/L	Potassium: 3.05 mEq/L, Sodium: 145 mEq/L	Potassium: 3,1 mEq/L, Sodium 139 mEq/L

PTT: thromboplastin time; PT: prothrombin time; GOT: glutamic-oxalacetic transaminase; GPT: glutamic-pyruvic transaminase; BUN: blood urea nitrogen.

Source: Own elaboration.

In order to assess and control hemodynamics, the patient was taken to intermediate care and received treatment with fluid therapy of 0.9% saline solution, 300mg hydrocortisone single dose, 6 vials of antiophidic serum IV, antibiotic management with third generation cephalosporins (ceftriaxone) 1g every 12 hours, 600mg lincosamides (clindamycin) every 6 hours, 1 vial of tranexamic acid every 8 hours, 1mg vitamin k every day, 40mg omeprazole every 12 hours, 20mg simple hyoscine and 10mg metoclopramide every 8 hours. Control lab tests were subsequently requested based on his clinical evolution and according to the need.

Medications were not applied intramuscularly due to the risk of hematomas as an adverse event. After initiating pharmacological administration and upon observation, it was concluded that there were no hemodynamic alterations, no need for vasopressor support,

no cardiac frequency alterations, oxygen saturation of 98%, and fraction of inspired oxygen of 0.21. Regarding the neurological condition, there were no focalizations or new episodes of hematemesis, no increase in hand edema, but there was persistence of pain in the epigastrium region and bleeding in the gums. Management with transfusion of five units of frozen plasma (Table 2) was initiated and a chest X-ray was performed to establish pulmonary involvement, which did not show relevant acute lesions.

Subsequently, a new physical examination was performed, leading to the impression of lonomic accident based on the recognition of the animal by the patient from graphic material, thus confirming suspicion of diagnosis of poisoning by *Lonomia* sp. Therefore, the Departmental Health Secretariat and the Bogotá Health Secretariat were immediately notified; they confirmed the availability of five vials of antilonomic serum in a tertiary referral hospital to where he was transferred for comprehensive management. He was admitted to this hospital with a diagnostic impression of septic shock versus hypovolemic, lonomic accident, upper digestive tract bleeding and normochromic microcytic anemia.

The patient was immediately assessed by the internal medicine service, which indicated the need for intravenous application of antilonomic serum and subsequent control tests for follow-up. During the application of the five vials of serum, no adverse events or reactions were observed; additionally, hemodynamic control did not present deterioration, neurological state was preserved and bleeding in the gums persisted.

With the passage of time, the bleeding in the gums resolved and control lab tests showed improvement and slight prolongation of coagulation times; there was also a decrease in neutrophilia without hemodynamic decompensation, but thrombocytopenia and a decrease in serum creatinine persisted. During hospitalization, a complete ultrasound of the abdomen was performed, showing liver with some degree of parenchymal destructuring of micro nodular aspect and findings compatible with diffuse liver parenchyma lesion, possible alcoholic hepatic cirrhosis, and bilateral pleural effusion. Modification of parenteral fluids was indicated considering possible signs of overload, as well as transfusion of two units of red blood cells.

During the night, a new transfusion of red blood cells was made. However, the patient showed no signs of hemodynamic instability and his neurological state was preserved. Correction of acute anemia, preserved kidney function, correction of hypokalemia, preserved coagulation times and corrected thrombocytopenia were observed; there was no evidence of bleeding in the gums. He was finally discharged to continue medical treatment and care on an outpatient basis.

DISCUSSION

Cases associated with poisonous contact with caterpillars that do not cause hemorrhagic syndrome have been described, therefore, not all poisoning mechanisms are the same and different enzymatic mechanisms may be involved. (10) Some species only cause acute kidney failure as the main complication, but this could also be caused by ischemia (Table 1). (11)

Despite the lack of case reports, this type of cases has been reported in Brazil, Venezuela, Argentina and French Guiana in Latin America. According to statistics, between 1989 and 2005, 354 cases were reported in Brazil, with a lethality that dropped from 20% in 1995 to 15% in 1998, being intracranial bleeding the cause of death in 50% of cases. (12)

In Colombia, the incidence of lonomic accidents and knowledge of this pathology is low,

making epidemiological notification difficult. According to the Colombian Toxicological Research, Management and Information Center, between 2006 and 2010, 68 cases of lepidopteran accidents occurred due to spontaneous and passive reporting, being the sixth cause of incidence of accidents by poisonous animals, with a relative frequency of 4% (Figure 4). (13) In 2000, the first cases of hemorrhagic syndrome secondary to Lonomia sp were reported; they occurred in the departments of Guainía, Valle del Cauca, Boyacá, Caldas, Antioquia, Cundinamarca and Meta, each case with especial characteristics concerning their evolution (Figure 5). (14)

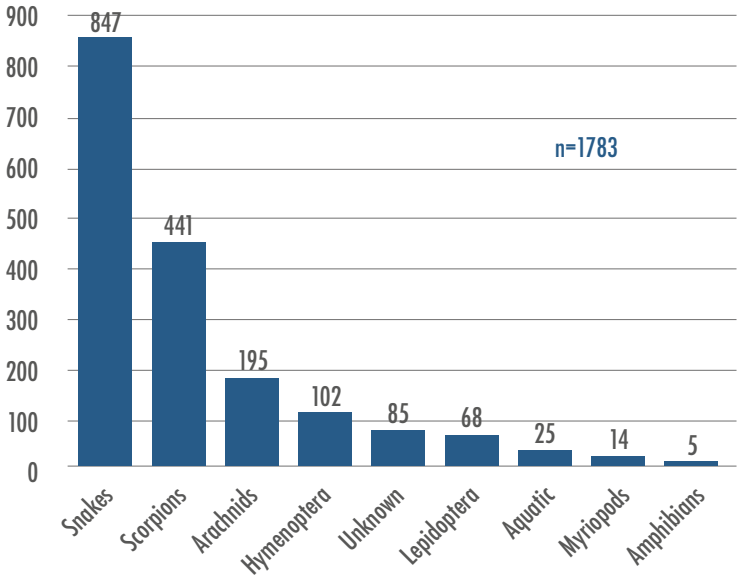

Figure 4. Frequency of accidents caused by poisonous animals in Colombia, 2006-2010.
Source: Elaboration based on Rodriguez-Vargas *et al.* (13).

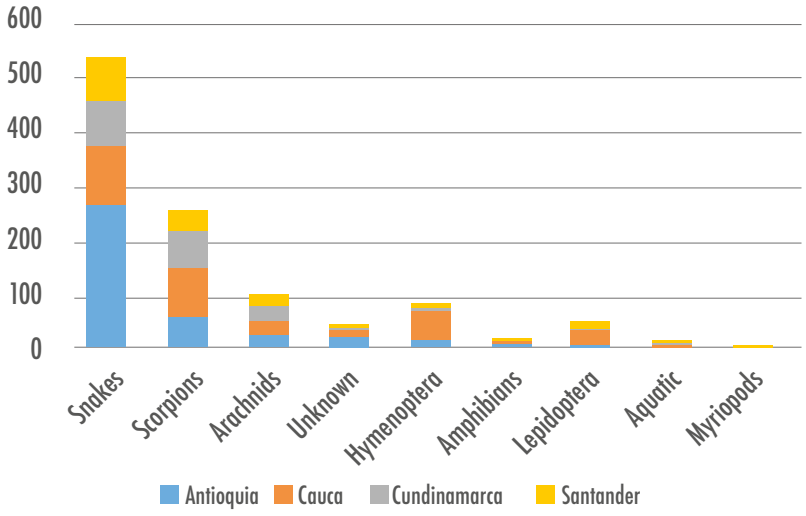

Figure 5. Frequency of accidental poisoning by department in Colombia. 2006-2010.
Source: Elaboration based on Rodríguez-Vargas *et al.* (13).

It should be noted that there is currently evidence of under-reporting, since it is impossible to notify a lonomic accident that was previously reported as ophidic, as in this case. In addition, this could be correlated with the lack of knowledge of health personnel to identify cases of lonomism. This last aspect was evident in the present case as it was initially treated as an ophidic accident and there were delays in the care process; consequently, the management of the patient was only adequate until he was referred to a high complexity health center.

In addition, it should be noted that the highly specialized professionals who attended the present case had basic notions and some degree of expertise in this accident and subsequent pathological manifestation. Basic knowledge for proper management is vital in correlations involving poor performance or intervention and the development of a pathology associated with injury to multiple vital organs, and even death.

CONCLUSIONS

The use of antilonomic serum therapy led to complete recovery 17 hours after initiating the treatment, without the presence of associated complications and coincides with the management described in other reports. (14) However, it is important to emphasize that management with intrahospital therapy allowed for a positive evolution of the patient and early diagnosis.

One of the disagreements between the system and health care lies in the lack of knowledge of the pathology and the lack of availability of fresh frozen plasma, devices for transfusion of red blood cells and antilonomic serum. For this reason, it was necessary to refer the patient to hospitals of all tiers of care, affecting his clinical picture and putting at risk his vital organs. It is important to mention that the latter two reasons are the most common causes of worsening. (14)

It is necessary to identify the medical centers and professionals that are in the areas where this species lives in order to provide training according to the socio-demographic context and to provide resources that allow them to have the necessary inputs to improve medical interventions and obtain better health outcomes.

CONFLICT OF INTEREST

None stated by the authors.

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COLONIC INTUSSUSCEPTION AS A RARE MANIFESTATION OF COLONIC LIPOMA: CASE REPORT

Keywords: Colon; Intussusception; Adiposis Dolorosa; Laparoscopy.
Palabras clave: Colon; Intususcepción; Lipomatosis; Laparoscopía.

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RESUMEN

Introducción. Los lipomas en el colon son lesiones con pocos riesgos de malignización que, según su tamaño y sintomatología, pueden requerir manejo endoscópico o quirúrgico. Sin embargo, es difícil establecer el diagnóstico de una lesión lipomatosa en el colon: los hallazgos clínicos o imagenológicos solo describen que la prevalencia de estas lesiones es baja y que es una patología común en el género femenino. Debido a que el abordaje laparoscópico causa menores traumas y por tanto la recuperación clínica es más rápida, en la actualidad suele elegirse esta opción.

Presentación de caso. Paciente femenino de 43 años, raza blanca, procedente de Bogotá D.C., ama de casa y sin antecedentes médicos. La sintomatología que presentó fue dolor abdominal de instauración aguda asociado a deposiciones melénicas, por lo que fue llevada a toma de imágenes diagnósticas donde se documentó intususcepción colocolónica originada en una lesión lipomatosa y localizada en el colon transverso. Se le practicó hemicolectomía derecha ampliada por vía laparoscópica.

Discusión. A partir de este caso se describe cómo la intususcepción colónica constituye una complicación preoperatoria que demanda la realización de un manejo quirúrgico desde el mismo diagnóstico dado el margen de los porcentajes de mortalidad.

Conclusión. El análisis del presente caso constituye parte de la evidencia científica indispensable para mejorar el abordaje diagnóstico y terapéutico de la intususcepción colónica que la literatura nacional e internacional no ha tratado suficientemente.

ABSTRACT

Introduction: Colonic lipomas are low-risk lesions that require endoscopic or surgical management depending on their size and symptoms. However, diagnosing a lipomatous lesion in the colon is a difficult task, as the clinical or imaging findings point to a low prevalence of these lesions and a higher frequency in the female sex. The laparoscopic approach is the current method of choice as it represents fewer traumas and, therefore, a faster clinical recovery.

Case presentation: 43-year-old female patient, Caucasian, from the city of Bogotá, housewife, without any medical history. She presented with acute abdominal pain associated with tarry stools. Diagnostic imaging tests were performed, finding colo-colonic intussusception, originated in a lipomatous lesion located in the transverse colon. This patient underwent an enlarged laparoscopic right hemicolectomy.

Discussion: This case describes how colonic intussusception constitutes a preoperative complication that requires surgical management since its diagnosis considering the associated mortality rates.

Conclusion: The analysis of this case is part of the scientific evidence indispensable to improve the diagnostic and therapeutic approach to colonic intussusception, as local and international literature have not addressed this condition sufficiently.

INTRODUCTION

Colonic lipomas are benign lesions that represent less than 4.4% of the tumors that affect this organ, being the location in transverse colon the least frequent. They can affect adults of any age, but they most often occur in people over age 50. (1)

These lesions are usually asymptomatic, and colo-colonic intussusception is one of the rarest complications, which appears in direct relation to the size of the lipoma. (2-4) Establishing a diagnosis based on the symptomatology or on imaging findings is difficult, so colonoscopy is the golden standard to confirm the presence of this type of tumor. (5,4)

Like other benign tumors, management depends not only on size, but also on symptoms. Most patients benefit from endoscopic resection, but surgery is required when that approach is not possible due to the morphological characteristics of the lipoma or because it is associated with complications such as bleeding, perforation or intestinal obstruction. (1-3,5)

Nevertheless, the literature (6) does not have sufficient reports about the best surgical approach to this pathology. In this regard, this article contributes to the literature with the description of a clinical case of proximal intussusception of the transverse colon, secondary to a lipomatous lesion located in the hepatic flexure of the colon, which required surgical management by laparoscopy, without early or late post-operative complications. It also presents a brief review of the literature detailing the clinical features and management options of this unusual pathology; this part shows the contribution of the case to the reviewed literature. Finally, it is concluded that colonic intussusception is a preoperative complication that requires determining surgical management since it is diagnosed, regardless of mortality rates.

CASE PRESENTATION

A 43-year-old female patient, Caucasian, from Bogotá D.C. (Colombia), housewife, from a low-income household was admitted after 2 days of colicky pain mainly in the mesogastrium, associated with nausea, hyporexia and hematochezia. Two weeks prior to her consultation, the woman reported a change in stool caliber and occasional abdominal pain with characteristics similar to those already described that resolved spontaneously with the use of conventional analgesics. She had no pathological, surgical or family history and, according to the physical examination, she had vital signs within normal values and mild pain on palpation in the mesogastrium with a sensation of a mass at this level.

Diagnosis and identification of preoperative complications

Extension studies were requested, including a contrast-enhanced computed tomography (CT) scan of the abdomen. It showed a submucosal lesion that affected the transverse colon with fat density, suggesting a lipoma that probably led to a proximal intussusception of the transverse colon (Figure 1).

Bearing in mind that the findings of the CT scan suggested a rare pathology and the fact that the patient's clinical picture pointed to a diagnosis of right colon cancer, a colonoscopy under sedation was considered necessary. Based on the study, a rounded subepithelial mass was observed in the proximal transverse colon in what seemed to be a hepatic flexure, with smooth edges and no findings compatible with infiltration. The mass occupied 50% of the circumference, obstructed 70% of the lumen, and tilted producing intussusception (Figure 2).

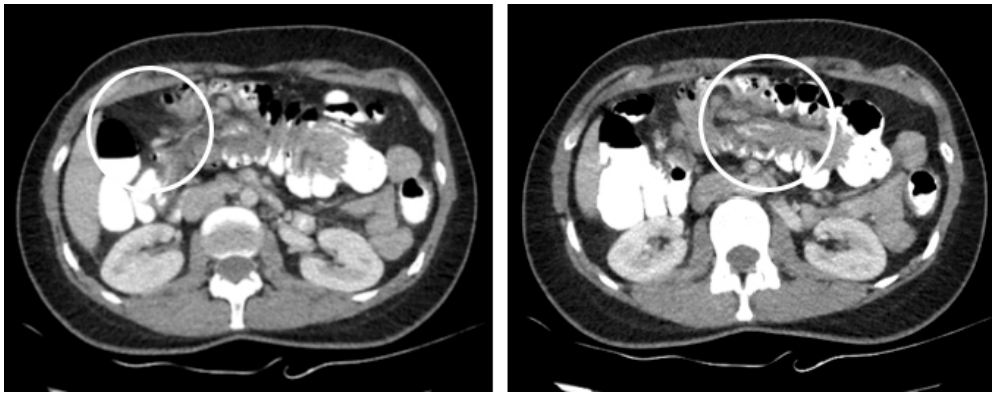

Figure 1. CT scan of the abdomen performed on admission showing colo-colonic intussusception.
Source: Document obtained during the study.

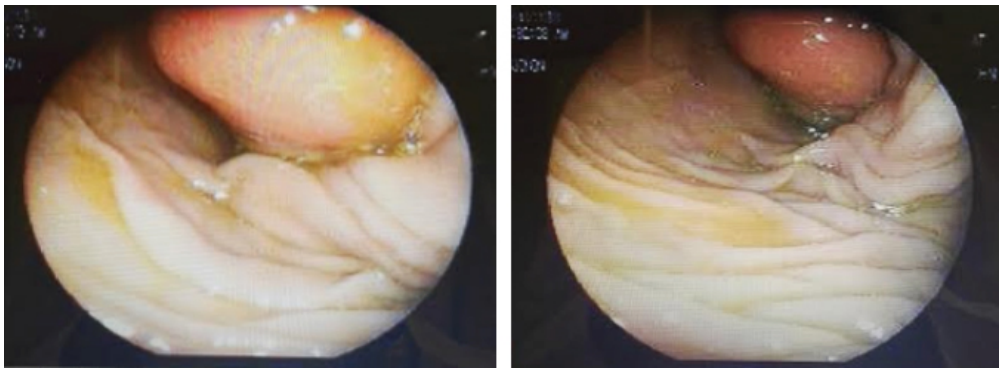

Figure 2. Preoperative colonoscopy showing submucosal lesion in the proximal transverse colon.
Source: Document obtained during the study.

Subsequently, because of the impossibility of endoscopic management due to the size of the lesion, the patient was taken to surgery, where a right hemicolectomy was performed by laparoscopy with side-to-side extracorporeal anastomosis with mechanical suture, without using drains. Mechanical bowel preparation was not considered necessary for this procedure; however, prior to surgery, prophylactic antibiotics (first-generation cephalosporin) were administered.

Intra-operative and post-operative findings

One of the intraoperative findings was a mobile pedunculated mass in the hepatic flexure of the colon, about 7x7cm, which protruded towards the lumen, without serosa involvement, causing colo-colonic intussusception (Figure 3).

In the post-operative period, the patient evolved without complications, so she was discharged on the third day with analgesic management and general recommendations.

The surgical pathology results concluded that the specimen was a submucosal lipoma with adjacent ulcerated mucosa and negative reactive changes for dysplasia and malignancy. Post-operative follow-up was carried out on the seventh day and the third week, and an adequate clinical evolution was observed, without complications related to the surgery. Consequently, coloproctology discharged the patient with nutritional recommendations and colonoscopic screening at age 50.

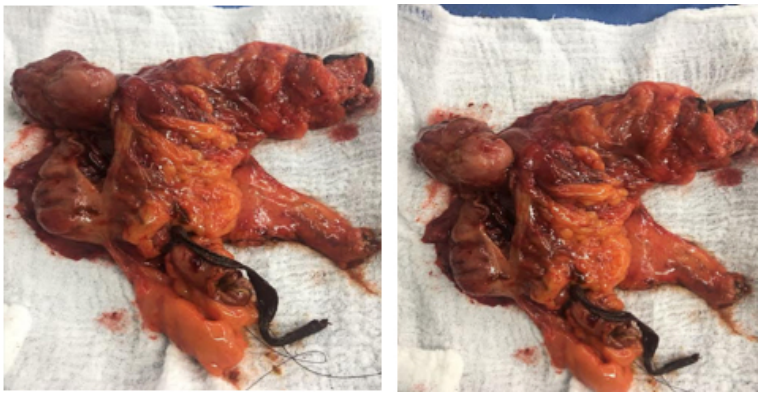

Figure 3. Lipomatous lesion observed in the surgical specimen obtained from enlarged right hemicolectomy.
Source: Document obtained during the study.

DISCUSSION

The case makes a significant contribution to the literature. The epidemiological, histological and clinical characterization of lipomas is presented below, including a description of colo-colonic intussusception with precise information on its incidence, clinical findings and types of intussusception. Additionally, details on what the literature has reported regarding the diagnostic approach to this type of lesions in the colon are provided, and the therapeutic approach is analyzed according to the literature.

Epidemiological, histological and clinical characterization

Lipomas of the gastrointestinal tract were first described by Bauer in 1757; later, a few other cases were reported in the literature, including the publications of Stetten (1909) and Hall (1985), who explained that these lesions could clinically resemble pathologies such as angiodysplasia and colon cancer. (7,8)

Classic lipomas are histologically formed by mature adipose cells without pleomorphism, localized more frequently in the limbs and the trunk. (9) In the digestive tract, despite being somewhat rare with an overall incidence of 1.8% (1.3), mature adipose cells without pleomorphism are found in the colon for the most part, with an incidence of 0.03-4.4%, and located 65% of the time on the right side, often in the cecum. (2,6) Most of these lesions originate in the submucosal layer, but up to 10% may arise from the submucosal layer and extend to the muscle layer. (6,3)

The systematic review by Crocetti *et al.* (1), published in 2014, describes a female predilection in 55% of cases. Furthermore, the pathology is observed in an age range between 32 and 82 years (61±9), and only 15% of the total evaluated lipomas were located in the transverse colon, as in the clinical case reported in this article.

Most lipomas are asymptomatic; however, as the size of the lesion increases, the chances of developing symptoms are as high as 25%. One of the most unusual pictures that patients with lipomatous lesions >4cm may present is colo-colonic intussusception, of which only 32 cases have been reported in the literature. (1,3,6)

Colo-colonic intussusception

Intussusception in adults originates 50-75% of the time in the small intestine, being usually secondary to a Meckel diverticulum or adhesions.

Less than 20% of intussusception cases originate in the colon, with adenocarcinoma of the colon being the most common cause at this level. (10)

In adults, this condition is generally secondary to an alteration in the normal peristaltic activity of the bowel wall, resulting from a pathological lesion that serves as the starting point for invagination from one bowel segment to another. (11)

Intussusception is much more common in children, but may occur in up to 10% of adults. Studies describe a classic triad for diagnosis consisting of abdominal pain, palpable mass and hematochezia (12,13); however, publications such as Paškauskas *et al.* (3) report that the most frequent symptoms, prior to emergency department consultation, are abdominal pain (100% of cases), followed by episodes of diarrhea and hematochezia (22-32% of cases). This pathology is usually limited to a single segment of the colon, and the least frequent is retrograde intussusception. (3)

There are four main types of intussusception which are entero-enteric, ileocolic, ileocecal and colo-colic; the latter is the most common type in adults, which is consistent with the case report described here. (11)

Diagnosis and findings of lipomatous lesions

The main diagnostic tools for lipomatous lesions are: 1) radiological studies, such as ultrasonography, which has many limitations inherent to the method and because it is an operator-dependent test (11); 2) computed tomography and abdominal nuclear magnetic resonance, which can determine fat density on many occasions by revealing infiltration of the colon wall, but can establish a less certain diagnosis as a malignant pathology (2); and 3) colonoscopy, which is the confirmatory method for this type of neoplasms due to their morphological characteristics. (5,4)

The endoscopic findings of a lipoma include smooth, spherical, slightly yellowish and usually broad-based polyps of variable size (0.5-5cm). In addition, they show some characteristic endoscopic signs that are observed during manipulation with biopsy forceps, namely, tent sign (elevation of the mucosa over the lipoma), cushion sign (indentation of the lesion), and naked fat sign (extrusion of fat after biopsy). (4)

Even so, some publications, such as Ghanem *et al.* (8), report that biopsies taken during colonoscopies are not obtained adequately because ulcerated and necrotic tissues, distinctive of atypical lipomas, can cover adipose tissue. In such cases, the recommendation is to perform a biopsy by echoendoscopy in order to have a better diagnostic yield. (8)

Therapeutic approach and association with the described case

The therapeutic options for colonic lipomas depend on the size of the mass: endoscopic resection is the first option for lesions <2cm, while surgical management is considered for larger symptomatic lesions or when they lead to complications such as intussusception. (1,2,3,6) Non-radical segmental colectomy via laparoscopy is generally the best therapeutic choice because there is less surgical trauma and a rapid post-operative recovery. (1,3,8,14)

The case described here presented intussusception secondary to a pediculated lipomatous lesion of the hepatic flexure of the colon of about 7x7cm. This is a rare pathology with marked influence on both diagnosis and treatment selection. According to the reports, it can be said that determining the exact etiology of colon lesions based on clinical findings alone is difficult. Although the first differential diagnosis is colon cancer in the majority of cases, it is necessary

to consider neoplasms of benign origin, despite their low incidence.

In this case, taking biopsy samples during the colonoscopy was not necessary because the size of the lesion and the symptomatology required priority surgery: laparoscopic right colectomy. Therefore, based on this report, it could be said that colonic intussusception is a preoperative complication for which surgery is the most recommendable option since it is diagnosed.

CONCLUSIONS

Colon lipomas are lesions that represent less than 4.4% of tumors affecting this organ and 1.8% of all tumors of the digestive tract. However, scientific discussion on this issue should not be disregarded only because of its low or high incidence, nor should it be forgotten that this pathology generally affects adults of any age, more often the population over 50 years of age. (1) With this in mind, knowing about cases that allow suggesting the best therapeutic approach is essential for medical practice.

The importance of this case also lies in the fact that colonic lipomas, as they are lesions considered incidental findings, can be clinically mistaken for other pathologies, mostly of malignant origin. Since both the size and macroscopic characteristics of these lesions can be determined from endoscopic imaging, colonoscopy is a diagnostic tool that avoids confusion with malignant pathologies and allows a better therapeutic approach.

In the case described here, the surgical approach was laparoscopic right colectomy, which is currently the most effective approach, the one that causes the least surgical trauma and the one that has the fastest post-operative recovery. The proper characterization and diagnostic approach of patients, as described above, avoids taking biopsies during colonoscopies and performing other procedures that are not always necessary.

CONFLICT OF INTEREST

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IMAGENOLOGICAL FINDINGS OF EXTERNAL SNAPPING HIP SYNDROME. CASE REPORT

Keywords: Hip Injuries; Femur; Ultrasonography; Diagnostic Imaging; Snapping Hip.
Palabras clave: Lesiones de la cadera; Fémur; Ultrasonido; Imágenes diagnósticas; Cadera en resorte.

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RESUMEN

Introducción. El síndrome de cadera en resorte externa es una entidad en la cual hay una sensación de dolor acompañada de un sonido palpable durante el movimiento de la cadera. Esta es una condición ampliamente conocida por los ortopedistas, pero aún es necesario que los hallazgos imagenológicos sean reconocidos por todos los radiólogos con el fin de brindar mayor información que permita un adecuado manejo multidisciplinario. La Z-plastia de la banda iliotibial es la técnica de tratamiento más reconocida y con mejores resultados.

Presentación del caso. Paciente femenino con síndrome de cadera en resorte externo bilateral sintomático en el lado derecho, quien fue manejada de forma conservadora sin adecuada respuesta y requirió manejo quirúrgico por vía artroscópica. Las técnicas utilizadas en la paciente no fueron exitosas y se presentó recurrencia de los síntomas.

Discusión. El diagnóstico del síndrome de cadera en resorte es principalmente clínico. Sin embargo, el aporte de las imágenes diagnósticas es importante para caracterizar las estructuras involucradas en este proceso nosológico, para realizar el planeamiento terapéutico y para hacer el seguimiento.

Conclusión. Conocer los hallazgos imagenológicos en ultrasonido y resonancia magnética del síndrome en cadera en resorte externa permite a los radiólogos identificarlo y hacer aportes al manejo de esta patología en forma oportuna.

ABSTRACT

Introduction: External snapping hip syndrome is characterized by a painful sensation accompanied by an audible snapping noise in the hip when moving. Even though orthopedists are widely aware of this condition, imaging findings still need to be recognized by all radiologists in order to provide more information that allows for the best multidisciplinary treatment. Z-plasty of the iliotibial band is the most used treatment with the best results.

Case presentation: Female patient with bilateral external hip snapping syndrome on the right side, who was treated initially in a conservative manner without adequate response; hence, she required surgical management with arthroscopy. All treatment options used for this patient were not successful, and symptoms recurred.

Discussion: The diagnosis of snapping hip syndrome is mainly clinical. However, the contribution of diagnostic imaging is important to characterize the structures involved in this nosological process, in order to develop the therapeutic planning and do the follow-up.

Conclusion: Knowledge on ultrasound and magnetic resonance findings related to this pathology allows radiologists to identify this syndrome and contribute to a timely treatment.

INTRODUCTION

The iliotibial band (ITB) is a flat morphological structure that is made up of connective tissue and is part of the tensor fasciae latae muscle. It extends the fibers of the anterior tensor fasciae latae, and involves the gluteal aponeurosis and the posterior fibers of the gluteus maximus muscle (1) (Figure 1). It originates at the iliac crest, runs parallel to the diaphysis of the femur, inserts at the Gerdy's tubercle —which is located in the anterior and lateral corner of the proximal tibia— and joins the lateral femoral condyle and the tibia. Its functions are to extend, abduct, and laterally rotate the hip, and it is also involved in maintaining posture and lateral knee stabilization.

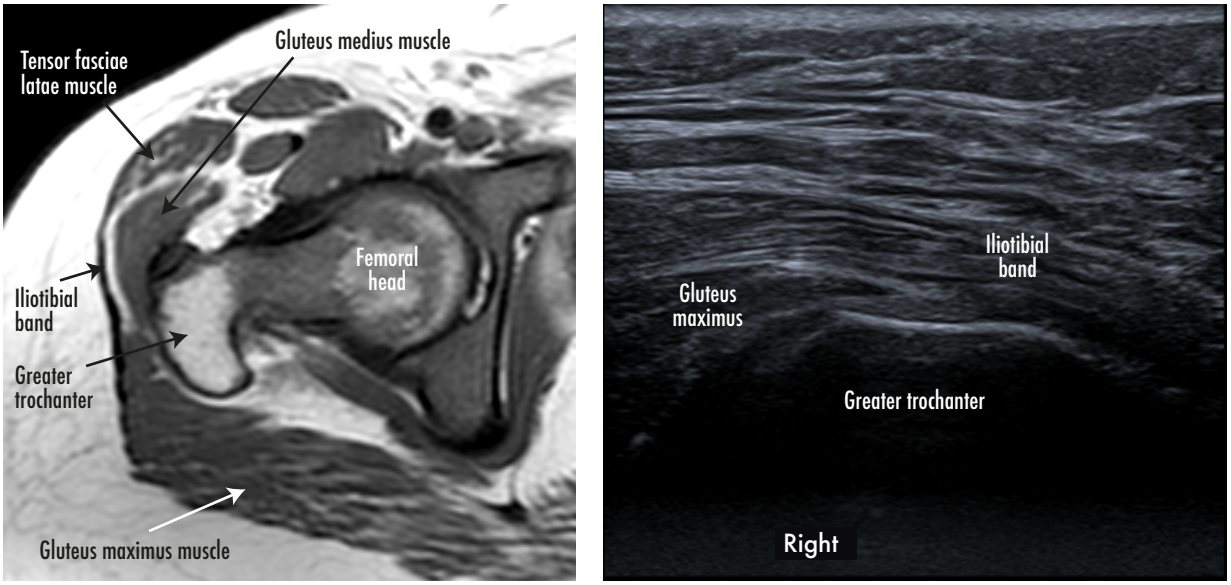


Figure 1. Magnetic resonance and ultrasound (cross-sectional plane) of the right hip of an asymptomatic patient, where the relationship between the iliotibial band, the tendon of the gluteus maximus and the greater trochanter is evident.
Source: Document obtained during the study.

Snapping hip syndrome is a complex condition in which there is an audible noise in the hip when moving (flexion or extension), usually accompanied by pain. (2) This condition was first described by Nunziata & Blumenfeld (3) in 1951; however, in 1995, Allen introduced the term "coxa saltans" to differentiate the causes. (2) At present, three types are described: internal, external (included by some authors in extra-articular) (1,2,4) and intra-articular. The first is caused by the IBT sliding over the femoral head or acetabular ridge, the second by the IBT sliding over the greater trochanter (2), and the third by different causes, mainly degenerative, such as labrum tears, damage to the liagementum teres or loose bodies in the hip. (1,2,4).

The external subtype is the most common type of "coxa saltans" and refers to the snapping sensation caused by a sudden motion of the IBT, whose posterior portion and, to a lesser extent, the distal and anterior portion of the gluteus maximus thicken during hip movements, most frequently during flexion, external rotation and abduction. (1,2,4) During hip extension, the IBT slides over the greater trochanter and returns

to the anterior portion during flexion. (2) Pain may or may not be observed during movement, and if it occurs, it coincides with the noise.

External snapping hip syndrome is associated with repetitive physical activities or overuse of anatomical structures related to IBT movements. Some intrinsic risk factors have been identified, such as decreased cervico-diaphyseal angle (coxa vara), the narrowing of the bi-iliac distance, increased distance between major trochanteres, prominence of the major trochanter, and fibrosis of the iliotibial band secondary to multiple intramuscular injections. (5-7)

The incidence and prevalence of this syndrome in the general population is not clear (2), although it is usually found in athletes and dancers, with a reported frequency of up to 62% in young women (8), and also in an asymptomatic manner in between 5% to 10% of the population. (9) Affected people visit their doctor because they have difficulty performing common activities such as running, climbing stairs, lifting heavy objects, and even, in some cases, walking. The physical examination is characterized by the reproduction of the noise or palpation of the dislocation during triggering maneuvers: hip flexion and extension.

CASE PRESENTATION

A 29-year-old female patient from Bogotá D.C., with a master's degree in education, white, who works as a psychologist, attended consultation due to symptoms with a year of evolution that began with a sensation of "snap" or prominence in the right greater trochanter, associated with pain, which occurred during walking and when flexing the hip to sit.

Medical history included ligamentous laxity (under study to confirm Ehlers-Danlos syndrome), flexible flatfoot treated with insoles with internal wedge in the hindfoot, length asymmetry in the lower limbs, severe lumbar hyperlordosis, scoliosis from infancy in management with orthosis and Raynaud's phenomenon under study with final diagnosis of vasculitis.

The physical examination showed height of 1.52m, weight of 45k and hypotonic posture caused by lumbar hyperlordosis and thoracic hyperkifosis. The evaluation in standing position revealed tendency to genu valgum with flat foot that compensates with the retraction of the tensor fasciae latae muscle; asymmetry of 4mm in the comparative length of the lower limbs, being greater on the right side; myofascial snapping of the gluteus medius with external extension and flexion hip rotation, without severe hamstring or tensor fasciae latae retraction due to its superimposed hyperlaxity; and significant weakness of the buttocks, predominantly on the right side. Hip impingement and pain were observed when internally rotating the hip bilaterally in a flexed position, especially on the right side, with localized pain in the greater trochanter.

The patient underwent multiple analgesic (until being prescribed with hydrocodone + acetaminophen, which she takes irregularly) and anti-inflammatory treatments, and received multiple physiotherapy sessions without improvement; in fact, her symptoms increased progressively. After assessment by Orthopedics, she was diagnosed with bilateral snapping hip syndrome, with retraction of the tensor fasciae latae. An ultrasound of the hip was performed on both sides, finding thickening of the right tensor fasciae latae (4mm), alteration of the fibrillary pattern and tendon protrusion over the greater trochanter during dynamic assessment, accompanied by an audible and palpable "snap" (Figure 2) (Video 1). Magnetic resonance imaging (MRI) of the hip showed bilateral edema of the ITB and slight thickening of the ITB on the right side (2.3mm) (Figure 3).

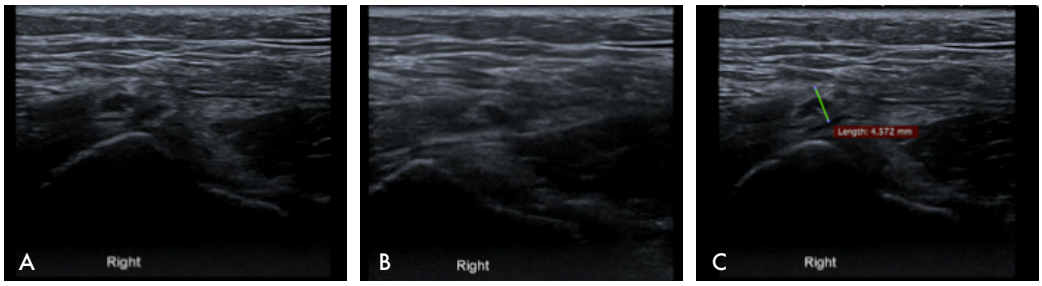
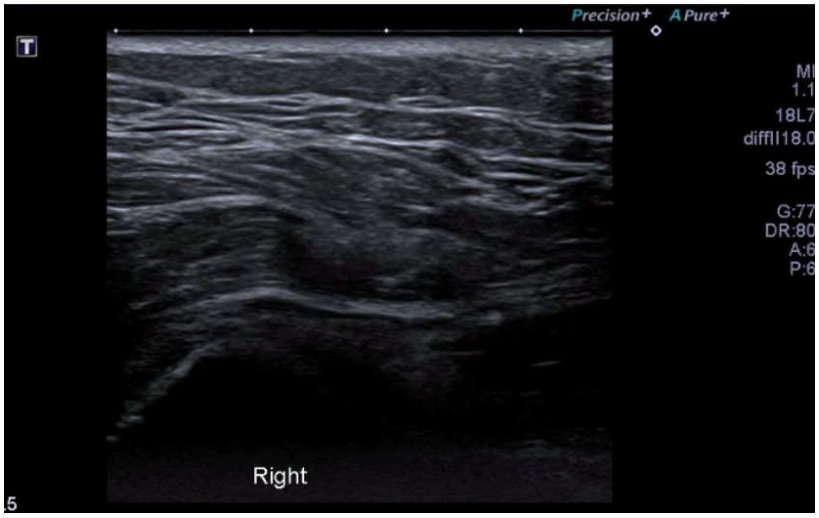


Figure 2. Dynamic ultrasound of the iliotibial band over the greater trochanter. A) neutral position of the right hip; B) hip internal rotation; C) thickening of the iliotibial band measured in the transverse plane associated with heterogeneous echogenicity of the tendon.
Source: Document obtained during the study.



Video 1. Dynamic ultrasound of the iliotibial band over the greater trochanter before the patient underwent the surgical procedure.
Source: Document obtained during the study.
Note: Dear reader in order to watch the video you need to download the PDF file and open it with Acrobat Reader (having previously installed the Adobe Flash Player add-on) and click on the video once.

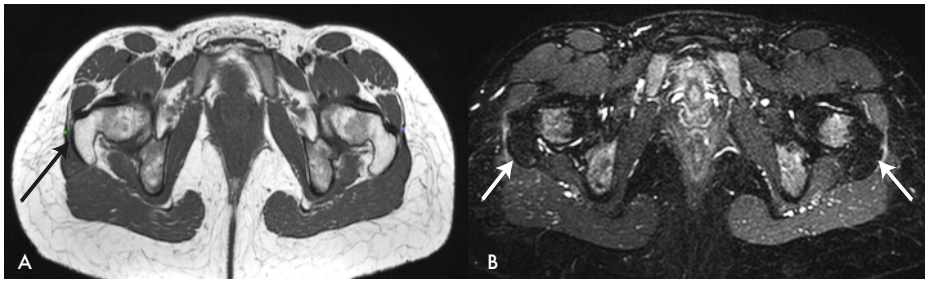


Figure 3. Magnetic resonance imaging. A) Enhanced axial T1-image showing slight thickening and undulation of the right iliotibial band (black arrow); B) axial plane with Short tau inversion recovery sequences, where an increase in signal intensity of the iliotibial band is identified on both sides (white arrows).
Source: Document obtained during the study.

Two years after the onset of the symptoms, the patient required an arthroscopy, so a T-shaped incision of the ITB was made in the right hip using radiofrequency. During a second surgery, an X-shaped incision was made in the fasciae latae muscle on the left side, also by radiofrequency, with subsequent formation of a rhombus and fixation. The patient presented recurrence of predominant symptoms in the right hip. A control ultrasound was performed again, showing greater tendon thickening and peritendinous fluid, probably of post-surgical origin (Figure 4) (Video 2).

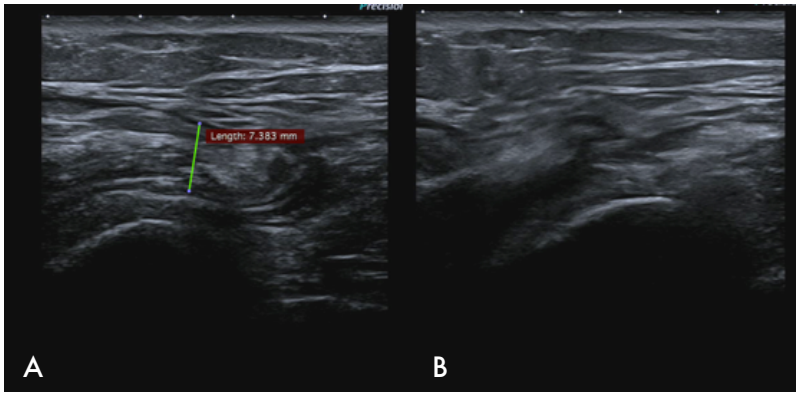
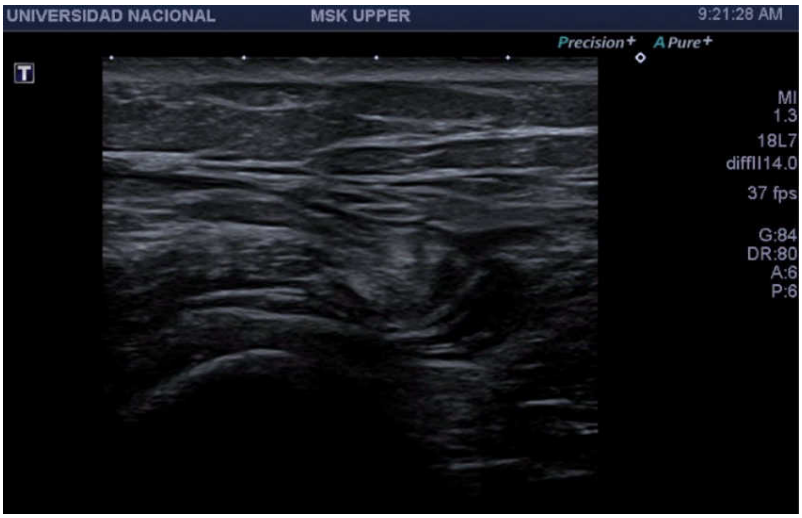


Figure 4. Ultrasound of the patient taken during post-surgical control 1 month after iliotibial band release. Persistence of symptoms. A) Increase in the thickness of the right iliotibial band (7.5 mm) with respect to the initial ultrasound. B) Dislocation of the iliotibial band during hip external rotation.

Source: Document obtained during the study.



Video 2. Ultrasound of the patient taken during post-surgical control 1 month after iliotibial band release.

Source: Document obtained during the study.

Note: Dear reader in order to watch the video you need to download the PDF file and open it with Acrobat Reader (having previously installed the Adobe Flash Player add-on) and click on the video once.

One year after the first surgery, the woman underwent a new surgical procedure on the right hip, consisting of ITB opening, partial synovectomy and tenotomy of the hip at two levels, and proximal and distal release. Severe tendon fibrosis secondary to previous surgical procedures was reported as an additional finding. At the time of completion of this case report, the patient had shown partial improvement of the symptoms and had not undergone any new imaging controls.

DISCUSSION

The main structure involved in external snapping hip syndrome is ITB; however, to a lesser extent, there may also be involvement of the tendon of the gluteus maximus. (10) Although the diagnosis is mainly clinical, diagnostic images allow ruling out other causes of hip pain such as bone or soft tissue alterations, bursa, labrum tear, among others. The most widely used and useful modality is dynamic ultrasound. Simple x-rays are usually normal, but allow ruling out intra-articular causes of this syndrome. There is still no consensus to determine diagnostic parameters. (2,11)

Dynamic ultrasound shows thickening of the iliotibial band and heterogeneous echogenicity of the fibers, as well as secondary findings such as distension of the greater trochanteric bursa. This dynamic evaluation is useful since it verifies movement of the ITB or the tendon of the gluteus maximus on the greater trochanter, and allows perceiving the dislocation or listening to the "snap", thus leading to the definitive diagnosis of this syndrome. (2,4)

The appropriate tool to perform the dynamic ultrasound evaluation is a high frequency linear transducer (12 MHz or higher), with the patient in supine or standing position. Based on the radiologist's preference, the transducer is placed transversely to the greater trochanter, and the exploration is performed with active and passive flexion and external rotation maneuvers of the hip. The abrupt displacement of the ITB or the gluteus maximus muscle is related to the painful "snap" perceived by the patient. (4,7)

According to the literature, the MRI findings include thickening of the iliotibial band (>2mm) and of the anterior edge of the tendon of the gluteus maximus (>2mm), with undulation of the contours of both structures (7); the signal is hypointense in T1 and hyperintense in T2. Inflammatory changes of the greater trochanter bursa, visualized as a hyperintense T2 collection, and peritendinous enhancement following administration of intravenous contrast medium can also be seen; however, these findings are nonspecific and should always be analyzed bearing in mind the patient's clinical features. (1) Retrospectively, ipsilateral gluteus maximus atrophy has been identified as an additional finding of this syndrome. It is important to enlarge the field of vision in order to fully visualize the region of interest: this includes the entire pelvis and its soft tissues.

Computerized tomography permit a better evaluation of bone structures, while the multiplanar reconstructions that can be carried out allow better characterizing the findings that predispose to the snapping hip syndrome, and ruling out intra-articular causes. This study should not be the first choice as the resolution of the soft tissues is not good. (8)

Taking into account the findings of the present case, a dynamic ultrasound was the diagnostic modality that best allowed evaluating the patient and corroborating what was identified during the physical examination. Besides identifying the key finding, which was the subluxation of the ITB over the greater trochanter accompanied by pain, changes in the soft tissues (in the second ultrasound) were found that could explain the persistence of symptoms.

Treatment in these patients includes rest, physical means (local heat), stretching exercises, release of loads during daily activities, and analgesics and non-steroidal anti-inflammatory drugs. Conducting anesthetic or corticosteroid infiltration of the trochanteric bursa or iliotibial band has been proposed if there is no response. (8)

When there is no response to conservative treatment, surgery should be done in order to eliminate tendon protrusion. Possible surgical procedures include resection of the major trochanteric bursa, trochanter osteotomy and, in refractory cases, arthroscopic release of the ITB or lengthening of the ITB by Z-plasty. (1,2)

The failure of surgery in the reported case is still cause for study. Specialists believe that the recurrence of symptoms may be associated to a marked fibrotic process following the two surgical procedures; however, that baseline hyperlaxity may be associated with recurrence of symptoms is considered a possibility.

CONCLUSIONS

This case report describes the ultrasound and MRI imaging findings of external snapping hip syndrome, which allow radiologists to recognize and contribute to the management of this pathology in a timely manner.

Dynamic ultrasound is the most useful technique for the diagnosis of snapping hip syndrome, as it allows confirming the main finding, which is the protrusion of the ITB or the tendon of the gluteus maximus over the greater trochanter. Other techniques, such as x-ray and MRI, provide secondary information on possible differential diagnoses of painful hip or help rule out the intra-articular variant of this syndrome.

CONFLICT OF INTEREST

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FALSE-POSITIVE FOURTH-GENERATION HIV TEST ASSOCIATED WITH AUTOIMMUNE HEMOLYTIC ANEMIA. CASE REPORT

Keywords: Enzyme-Linked Immunosorbent Assay; HIV; Anemia; Hemolytic.
Palabras clave: Ensayo de inmunoadsorción enzimática; Serodiagnóstico del sida; Anemia hemolítica.

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RESUMEN

Introducción. La prueba de tamizaje para virus de la inmunodeficiencia humana (VIH) con ELISA de cuarta generación tiene gran sensibilidad y una especificidad >99% para detectar tanto antígenos como anticuerpos. Se estima que solo el 0.5% son falsos positivos.

Presentación del caso. Paciente femenino de 61 años con cuadro clínico consistente en malestar general, fiebre no cuantificada, astenia y adinamia. En los paraclínicos se evidenció anemia, por lo que se realizó prueba de Coombs, la cual resultó positiva junto con otros hallazgos de anemia hemolítica autoinmune mixta. Se realizaron dos pruebas de tamizaje para VIH con técnica ELISA de cuarta generación que fueron positivas. Dadas las recomendaciones nacionales sobre el diagnóstico de la infección por VIH, se realizó una carga viral que resultó ser negativa, por lo que se consideró el resultado como un falso positivo.

Discusión. Factores clínicos y biológicos se relacionan con resultados falsos positivos. Existen descripciones sobre fenómenos de autoinmunidad, como el lupus eritematoso sistémico o la anemia hemolítica autoinmune, con pocos casos en adultos mayores.

Conclusiones. Las pruebas rápidas han cambiado el diagnóstico de la infección por VIH en el mundo; sin embargo, como toda prueba diagnóstica, tienen falsos positivos con diagnósticos diferenciales, incluidos la anemia hemolítica autoinmune.

ABSTRACT

Introduction: The fourth-generation ELISA human immunodeficiency virus (HIV) screening test has a high sensitivity and specificity >99% to detect both antigens and antibodies. Estimates are that only 0.5% yield false positive results.

Case description: 61-year-old female patient with a clinical picture consisting of malaise, unquantified fever, asthenia and adynamia. Laboratory tests revealed anemia, so a Coombs test was performed, obtaining a positive result along with other findings of mixed autoimmune hemolytic anemia. Two fourth-generation ELISA HIV screening tests were performed obtaining positive results. Given the national recommendations on the diagnosis of HIV infection, a viral load was performed, which turned out to be negative, so the result was considered a false positive.

Discussion: Clinical and biological factors are related to false positive results. There are descriptions about autoimmunity phenomena, such as systemic lupus erythematosus or autoimmune hemolytic anemia, with few cases in older adults.

Conclusions: Rapid tests have changed the diagnosis of HIV infection worldwide; however, like any other diagnostic test, they may yield false positive results with differential diagnoses, including autoimmune hemolytic anemia.

INTRODUCTION

The number of people living with human immunodeficiency virus (HIV) worldwide rose to 36.9 million in 2017, with 1.8 million new cases that same year. Latin America ranks fifth in prevalence, with a heterogeneous distribution among the countries of the region; Colombia is one of the countries with the highest incidence rates with 150 000 cases. (1)

Autoimmune hemolytic anemia has an annual incidence of 1 case per 80 000 inhabitants in America and Europe, and is defined as the production of erythrocyte autoantibodies that cause a decrease in the lifespan of erythrocytes due to increased hemolysis. This condition is classified depending on the temperature at which the immunoglobulins sensitize the red blood cell; the most frequent form is warm autoantibody, which reacts at temperatures >37°C, mostly mediated by IgG, while cold autoantibodies do it at temperatures <32°C by IgM. (2,3)

The fourth-generation ELISA test detects HIV-1 and HIV-2 specific antibodies in blood using the HIV-1 p24 antigen. (4) Although this test has a very high sensitivity and specificity, estimates are that there may be a 0.5% chance of obtaining a false positive result, especially in pregnant patients with hyper IgM syndrome and hematologic diseases. (4-6)

The purpose of this case report is to present an older patient who was diagnosed with autoimmune hemolytic anemia, but whose HIV testing yielded a false positive result. It should be noted that this is a rare situation considering the high specificity and sensitivity of the ELISA test.

CASE PRESENTATION

Female patient, 61 years old, from Bucaramanga, housewife and white, who was treated in a tertiary care hospital from Bucaramanga, Colombia, in March 2017 due to a clinical picture of approximately 3 months of evolution. It was characterized by general malaise, unquantified fever, asthenia, adynamia and, for several weeks, edema of the lower limbs. The woman did not report hair loss, skin lesions, photo sensitivity, or mucosal lesions.

She had a history of diabetes mellitus type 2 without pharmacological treatment, primary pulmonary hypertension and chronic kidney disease. She had also been hospitalized several times for anemia, requiring transfusion support since November of the previous year. The physical examination performed on admission showed generalized mucocutaneous pallor and grade 3 edema in the lower limbs; her vital signs were: blood pressure: 220/110 mmHg, heart rate: 110/min, respiratory rate: 18/min, temperature: 38.3°C and oxygen saturation on air: 95%. Different tests were done, including serial hemograms that showed severe anemia since her admission in March 2017 until May of the same year (Table 1).

Table 1. List of hemograms.

Variable / Date	Hgb	HCT	MCV	MCH	RDW	Leucocytes	Platelets
4/03/17	5.5	15.4	89	33	18	9 800	425 000
20/04/17	7.7	23	87	33	16	19 700	400 000
22/04/17	3.8	10	86	97	18	13 000	307 000
23/04/17	3.7	9.5	86	97	18	13 200	327 000

Continues.

Variable / Date	Hgb	HCT	MCV	MCH	RDW	Leucocytes	Platelets
23/04/17	6.3	12	86	97	18	18 600	331 000
25/04/17	8.2	23	83	35	16	28 300	390 000
27/04/17	7.6	19	88	36	18	11.7	298 000
28/04/17	6.1	19	88	36	18	6 700	267 000
2/05/17	6.2	18	88	36	18	7 400	267 000
3/05/17	7.7	19	88	36	18	9 200	397 000
18/05/17	7.9	20	95	36	18	5 000	333 000

Hgb: hemoglobin; HCT: hematocrit; VCM: mean corpuscular volume; MCH: mean corpuscular hemoglobin; RDW: red blood cell distribution width.

Source: Own elaboration.

Due to the presence of anemia, different complementary tests were done, including the Coombs test, which was positive for IgG3+ / C3d 4+ on several occasions. Considering the diagnosis of anemia with possible autoimmune origin, studies were expanded to rule out the etiology with complement C4 levels at 8 mg/dL and C3 at 77 mg/dL, which were below the reference value. In addition, antinuclear antibodies tests were made, yielding a moderately positive value of 34.37 international units (U). An anti-double stranded DNA test was also done, obtaining negative results (66.02 U/mL; reference value: 60-200).

The other studies were a partial urine test that revealed significant proteinuria of 500 mg/dL, for which a test for protein in urine was performed 24 hours later, revealing nephrotic-range proteinuria of 13101.24gr. A routine fourth-generation HIV ELISA was performed, with a positive result of 0.34 (normal value: <0.25). Due to this result, the recommendations of the national guidelines for the diagnosis of HIV infection (7) were followed and a second test was performed, which was also positive with a value of 0.29. Considering these results and following again the recommendations of the national guidelines (7), a viral load test was performed, obtaining negative results (number of copies <5 000).

DISCUSSION

This is the case of an older patient with autoimmune hemolytic anemia, with suspected systemic lupus erythematosus (SLE) by nephrotic syndrome and weakly positive antinuclear antibodies. However, despite the presence of these signs, symptoms and findings, lupus was ruled out through a lab test because the patient only met 3 of the 17 criteria established by the Systemic Lupus International Collaborating Clinics for classification of the disease (6), and did not have clinical symptoms such as hair loss, skin manifestations or photosensitivity.

The presence of nephritis was not demonstrated since kidney biopsy could not be performed due to the unavailability of that service in the institution where the patient was treated. After two positive fourth-generation ELISA tests, in accordance with the national guidelines, a negative viral load test (7) was carried out, ruling out the disease and considering the tests as false positives.

A similar case occurred in Japan in 2011, where a patient with autoimmune hemolytic

anemia and angioimmunoblastic T-cell lymphoma had a false positive result for HIV in an enzyme immunoassay test. (5)

According to the literature, there is a correlation between multiple autoimmune and non-autoimmune diseases with false positive results in ELISA tests due to the production of immunoglobulins that generate cross-reactions with antibodies against the HIV virus. (8-11)

According to Barthel & Wallace (11), the first reports of false positive results were described in the 1980s with studies by Perentice *et al.* in 1985 and Calabrese *et al.* in 1986, in which 41 SLE patients had HIV-positive ELISA test results. The researchers considered that this was caused by antibodies against altered H9 nuclear antigens. (11)

In fact, these two processes can be immunologically exclusive in cases of HIV infection and SLE. (10) On the one hand, SLE may prevent HIV infection as a result of polyclonal antibodies and stimulation and, on the other hand, it may not develop in a low CD4 environment, as in the cell depletion process seen in HIV.

Descriptions for autoimmune hemolytic anemia with pathophysiological explanations are scarce in the reported cases (5); in this scenario, the high production of CXCL13 and IL-21 may be associated with the function of T follicular helper cells (TFH) for immunopathogenesis in SLE. (5) These cells were identified as the origin of autoimmune hemolytic anemia and their cytokines CXCL13 and IL-21 play a key role in the activation and expansion of plasmacytic B cells, differentiation and hypergammaglobulinemia. (5) Immune aberrations may produce the same autoimmune response observed in hemolytic anemia in SLE patients.

All the mechanisms described above are ways of trying to explain why these tests may yield false positive results, especially with autoimmune diseases, since no single way of producing these cross-reactions between antibodies has been established. In 2003, Muta & Yamano (12) considered that the reactivity mechanism with HIV P24 antigen was an antigenic mimesis among autoimmune epitopes, such as small ribonucleoproteins (also known as Sm) or retroviral antigens. Other researchers have considered that autoimmune hemolytic anemia has numerous subtypes of polyclonal gamma globulins that coincidentally react with HIV P24 antigen. (11,12)

A study conducted in sub-Saharan Africa found that there is a correlation between the presence of schistosomiasis and false-positive results in the same test, especially in infection by *Schistosoma mansoni* and *Schistosoma haematobium*. (13) This is the consequence of a cross-relationship between HIV-1 peptides and antibodies against these HIV-1 *Schistosoma* species. (14)

SLE is one of the autoimmune diseases related to false positive results for HIV, of which there are several cases reported so far. (11-15) One such case occurred in China in 2015, where a SLE patient tested positive for HIV by ELISA, result that was later considered to be a false positive by Western blot. (11-15) Other cases have reported patients with HIV infection who later develop SLE that has been difficult to diagnose due to overlapping symptoms and positive antibodies. (10)

All this evidences the cross-reaction leading to such results, and confirms the need to perform a different post-ELISA test to confirm or rule out the disease, in accordance with the international and national recommendations of the clinical practice guidelines. (7)

Considering the above and based on a bibliographic review, this may be the first case in Colombia to report cross reaction of antibodies associated with autoimmune hemolytic anemia and false positive results for HIV, which allows

stressing the importance of making a proper diagnosis by implementing appropriate tests. It should also be borne in mind that despite their high sensitivity and specificity, any diagnostic test can yield false positive results.

There is evidence in the literature of a higher frequency of false positive ELISA test results in young Hispanic women and pregnant women (13-16), which contrasts with the case presented here as the patient was an older adult. However, autoimmune conditions, kidney failure, cystic fibrosis, multiple pregnancies, blood transfusions, liver disorders, lymphomas, intravenous drug abuse, hemodialysis, and recent vaccines for hepatitis B, rabies, or influenza have also been described in young women with false-positive HIV tests. (13-16)

CONCLUSIONS

Although this is a single case, this report shows that autoimmune diseases, including SLE and conditions that lead to generalized immune stimulation with increased production of anti-HLA-DR or other antibodies —such as those produced in autoimmune hemolytic anemia— may cross-react with HIV antigens from the ELISA assay.

It is not yet known how a test as sensitive as the fourth-generation ELISA can generate false positive results, especially in relation to autoimmune conditions; however, this case allows providing the literature with a rare case to further investigate the physiopathology of autoimmune diseases and to be cautious when performing antibody-based diagnostic tests with the implications that a positive result must have, especially when dealing with HIV infection.

ETHICAL CONSIDERATIONS

The study was conducted with the patient's verbal and written informed consent to use her medical history and photographs that did not reveal her identity. The provisions of Resolution 8430 of 1993 of the Ministry of Health of Colombia (17) and the Declaration of Helsinki (18), which determine the guidelines for research on human beings, were taken into account.

CONFLICT OF INTEREST

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RETINAL VASCULITIS ASSOCIATED WITH EPSTEIN-BARR VIRUS INFECTION IN A YOUNG IMMUNOCOMPETENT PATIENT. FIRST COLOMBIAN CASE REPORT

Keywords: Epstein-Barr Virus Infections; Retinal Vasculitis; Acyclovir.
Palabras clave: Infecciones por virus de Epstein-Barr; Vasculitis retiniana; Aciclovir; Retinitis.

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RESUMEN

Introducción. La infección por virus de Epstein-Barr (VEB) suele ser asintomática y persiste durante toda la vida. La afectación ocular es infrecuente, y aunque existen informes de casos, ninguno de ellos proviene de Colombia o Latinoamérica.

Presentación del caso. Paciente masculino inmunocompetente con vasculitis retiniana unilateral generalizada, con vasos sin sangre temporales e inferonasales en la periferia, hemorragias intrarretinianas, vitritis intensa y desprendimiento de retina. La presencia de VEB se definió con una técnica de reacción en cadena de la polimerasa en humor vítreo. El paciente recuperó la agudeza visual con el tratamiento oral antiviral convencional.

Discusión. La afectación ocular asociada con el VEB se describe en pacientes inmunocomprometidos, en especial con infección por virus de inmunodeficiencia humana donde puede haber afectación retiniana. En este caso particular se discute la presencia de esta patología en pacientes inmunocompetentes.

Conclusiones. La vasculitis retiniana es una entidad rara con mayor asociación a la inmunodepresión. No existe un algoritmo de diagnóstico de esta enfermedad y la afectación ocular puede ser variable; tampoco existen líneas estándar de tratamiento. La evidencia reportada en el presente caso podría justificar estudios en pacientes seleccionados que muestran un compromiso de la agudeza visual sin una etiología establecida.

ABSTRACT

Introduction: Epstein - Barr virus (EBV) infection is usually asymptomatic and persists throughout life. Eye involvement is rare, and even though there are some case reports, none of them comes from Colombia or Latin America.

Case presentation: Immunocompetent young man with generalized unilateral retinal vasculitis, temporal and inferonasal bloodless vessels in the periphery, intraretinal hemorrhages, intense vitritis and retinal detachment. Epstein-Barr virus presence was determined using a polymerase chain reaction technique in vitreous humor. The patient recovered visual acuity with conventional antiviral oral treatment.

Discussion: Eye involvement associated with Epstein-Barr virus is observed in immunocompromised patients, especially with HIV infection, where retinal involvement may occur. This case reports the presence of this pathology in an immunocompetent patient.

Conclusions: Retinal vasculitis is a rare entity, frequently associated with immunocompromise. There is no diagnostic algorithm for this disease and eye involvement may be variable; there are no standard lines of treatment either. The evidence reported here explains the need for studies in selected patients showing visual acuity involvement without an established etiology.

INTRODUCTION

Epstein-Barr virus (EBV) was described in 1964 in cell cultures from Burkitt lymphoma samples; however, infectious mononucleosis is the clinical syndrome most frequently associated with this infection. (1,2)

EBV, or human herpesvirus type 4, belongs to the *Herpesviridae* family, *Gammaherpesviridae* subfamily, and is the prototype for the *Lymphocryptovirus* genus. It has a double-stranded 172kb DNA encapsulated in a 100nm icosahedral capsid that protects genetic information, and surrounds itself with a complex proteolipid envelope. To date, only 2 types of this virus have been identified: EBV-1 and EBV-2. (1,2)

Its role as an infectious agent in eye pathologies is still little known, since 95% of the healthy population has positive antibody titers; it is only observed in immunocompromised patients with rare severe ophthalmological involvement. Occasionally, conjunctivitis or uveitis may occur, although some other herpesviruses, such as herpes simplex and varicella-zoster virus, may cause retinal involvement with necrosis. (3-5)

EBV has been ascribed several ophthalmological pathologies, including multifocal choroiditis and, in the presence of systemic infections, all segments of the eye are involved. Ocular manifestations related to EBV infection may range from oculoglandular syndrome to conjunctivitis, dry eye syndrome, keratitis, uveitis, choroiditis, retinitis, ophthalmoplegia, or papillitis; specifically, conjunctivitis, dacryoadenitis, epiescleritis, keratitis, and iritis are observed in the anterior segment. Reported neurological complications include papilledema and optic neuritis. (5,6)

Retinal involvement is rare in cases of EBV associated with infectious mononucleosis; however, a variety of presentations, including retinochoroiditis, have been associated with systemic disease. Definitive evidence of EBV with acute retinal necrosis or vasculitis is scarce and has few cases reported in the literature. (3-6) Retinitis is a cause of impaired visual acuity, which should lead to differential diagnosis given its impact on patients with human immunodeficiency virus (HIV) infection. (3-6)

Based on the above, the objective of this report is to present a case of retinitis by EBV in an immunocompetent young adult patient, highlighting, on the one hand, that this presentation is rare in this population group and, on the other, the success of treatment with Aciclovir despite the little evidence available in the literature.

CASE PRESENTATION

An 18-year-old male, high school student from Bogotá D.C., Colombia, white, of a middle-income household, was treated at a quaternary care hospital in December 2017 for symptoms characterized by loss of visual acuity and myodesopsia in the right eye, which appeared suddenly three months earlier. Since the onset of symptoms until the time of consultation, the man was empirically managed with Acyclovir at a dose of 400mg every 12 hours with partial improvement of symptoms; the dose was adjusted to 400mg every 4 hours by indication of the Infectious Diseases Service in December 2017.

In the initial ophthalmology evaluation, the external eye examination was normal in both eyes; biomicroscopy showed clear cornea, well-formed anterior chamber, round central pupil and normal iris in both eyes. Ocular pressure was 12 in both eyes, and the lens was transparent in both eyes. Retina and vitreous body examination showed retinal detachment with abundant subretinal hemorrhage in the lower region and mild vitreous hemorrhage with macular involvement in the right eye. The initial

visual acuity of the right eye was 20/400, and 20/20 in the left.

One month after the onset of symptoms, during the second ophthalmology evaluation, the visual acuity of the right eye was 20/200 and of the left eye, 20/30, with biomicroscopy of the right eye that showed grade 2 vitreous hemorrhages and subhyaloid hemorrhage with temporary exsanguinated vessels in the inferior nasal quadrant in the periphery, pale colored macula with exsanguinated vessel in the inferior temporal arch, and difficult detail of the papilla. The subhyaloid hemorrhage also presented with temporary intraretinal hemorrhages, so a possible infectious etiology was considered; management was initiated with Aciclovir at the doses described above.

In October 2017, an ocular ultrasound showed severe low and medium reflectivity vitreous opacities with denser membrane formation in the lower quadrants, posterior vitreous detachment with inferior traction and severe subhyaloid opacities; the head of the optic nerve had normal appearance, so a picture compatible with severe vitritis, mixed opacities suggestive of bleeding areas, and inferior traction of the retina was considered.

Because of the reported changes, the patient was taken to subsequent vitrectomy with endolaser plus air for diagnostic purposes in order to take samples for PCR (polymerase chain reaction), cytomegalovirus (CMV), herpesvirus and EBV processing, by means of the LightMix technique using primers for EBV and specific probes. 10 copies of the amplified gene were obtained, being positive from cycle 31.4, which led to consider the sample as positive for EBV. No intravitreal treatment was provided. The remaining results are shown in Table 1.

In November 2017, different tests were carried out to rule out immunodeficiency disorders or other concomitant conditions that explained the symptomatology, but they were negative (Table 2).

Table 1. Vitreous humor tests using the PCR technique.

Test	Patient outcome	Reference value
Real-time PCR for herpesvirus	Not detected	<10 copies
Real-time PCR for EBV	Positive from cycle 31.4	<10 copies
Real-time PCR for *Toxoplasma gondii*	Not detected	<10 toxoplasmas
Real-time PCR for CMV	Not detected	<10 copies

PCR: polymerase chain reaction; EBV: Epstein-Barr virus; CMV: cytomegalovirus.

Source: Own elaboration.

Table 2. Blood tests.

Test	Patient outcome	Reference value
IgG CMV	>500 U/mL	>1
IgM CMV	Negative 0.04	>0.9
IgG Herpes	Positive 39.9	>11
IgM Herpes	Negative 0.74	<9
Elisa HIV	Negative 0.18	<0.9
CD4 lymphocyte count	611 cell /mm^3	
Serology syphilis screening		
Chemiluminescence method	0.09 non-reactive	<0.9

CMV: cytomegalovirus; HIV: human immunodeficiency virus.

Source: Own elaboration.

Also in November 2017, fluorescein angiography of both eyes was performed (Figure 1), which showed mild media opacity in the right eye, poorly defined optic disc, fibrovascular proliferation in the optic disc area and the lower area, adequate filling and transit of the dye

through retinal vessels since the beginning, with hyperfluorescence observed in the optic disc that increased as the angiographic transit progressed. Given the findings, a treated viral vasculitis was considered with secondary viral neovascularization and persistence of proliferative activity with suspicion of diffuse macular edema, the latter according to the reading of the retina specialist.

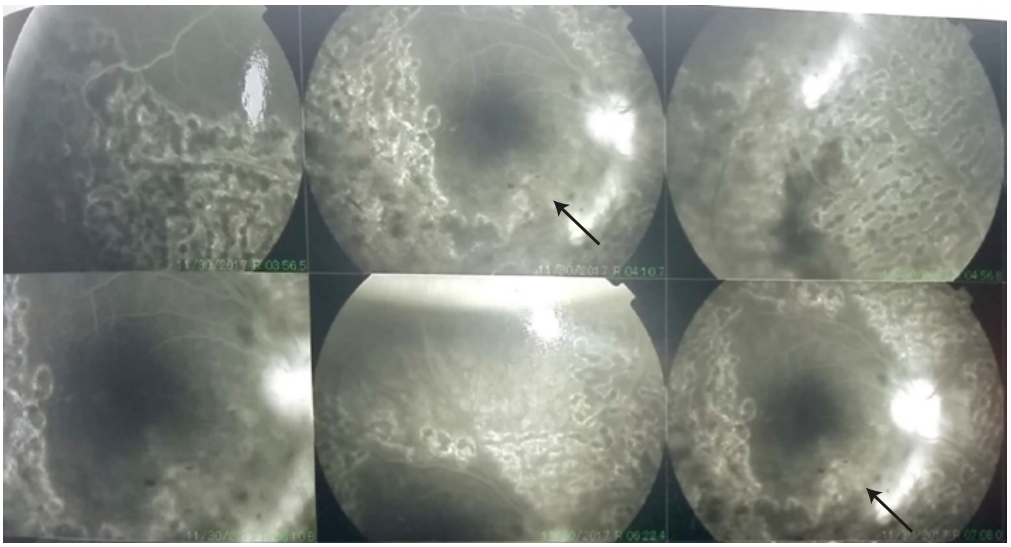

Figure 1. Findings of fluorescein angiography in the right eye.
→ Fibrovascular proliferation in the area of the optical disc and in the lower area.
Source: Document obtained during the study.

Finally, the patient was followed by the Infectious Diseases Service on a monthly basis from December 2017 to February 2018. The evolution was satisfactory, so management with Aciclovir was suspended after almost 6 months of treatment. The young man presented complete resolution of right eye symptoms with evolution of visual acuity to 20/40 with respect to initial values of 20/400. This case was considered as retinal vasculitis by EBV with adequate therapeutic response to Acyclovir despite having few literature data on doses and duration of management. This could be the first case reported in Colombia so far.

DISCUSSION

This paper reports a case of unilateral retinal vasculitis due to EBV in an immunocompetent young adult, who was successfully treated with Acyclovir for 6 months with complete resolution of symptoms and almost complete improvement of visual acuity. In spite of having insufficient initial doses of the drug, almost complete resolution of the symptoms was achieved after the adjustment.

The cases previously described in the literature on EBV retinitis only describe inflammation of the posterior pole, which contrasts with the reported case of generalized vasculitis of the eye with retinal detachment. This symptomatology is not an ocular manifestation of this virus as frequent as the involvement of the anterior chamber. (5-8) It is important to point out that this is a young patient without HIV infection, condition that is closely related to severe ocular involvement.

The pathogenic capacity of EBV is well known, and it can also cause intraocular inflammation and acute retinal necrosis (9); however, given its ubiquity, it has also been associated with multiple ocular pathologies ranging from mild conditions to severe impairment of visual acuity with retinal detachment, as in the case presented here. All this has been described in both immunocompetent and immunocompromised patients, especially HIV-infected patients where EBV and CMV are responsible for severe necrotizing retinitis. (10,11)

The diagnosis of intraocular infection by EBV and other herpesviruses is based on molecular tests that, in this case, were performed in vitreous humor with real-time polymerase chain reaction (RT-PCR). Although genotype detection is not available, this was the only positive test and was, therefore, considered a confirmed case of EBV retinal vasculitis. (3,12)

Appropriate management of an unknown condition, as is the case of eye involvement by EBV, is unclear because there are no clinical trials of this type of case. Virus identification leads to the use of antivirals, especially in patients with high viral load, study that was not performed in the reported patient. (13)

Andersson *et al.* (14) found a significant decrease in the spontaneous growth of EBV-infected B lymphocytes in vivo after Acyclovir therapy, but given the poor number of cases analyzed, the use of this medication is considered debatable. The review by Rafailidis *et al.* (13) suggests that antiviral agents could be considered for severe manifestations of EBV infections, including meningitis, meningoencephalitis, cerebritis, peripheral nerve palsy, myocarditis, hepatitis, and hematopoietic or kidney disease in immunocompetent patients, as well as an adjunct to steroid treatment. Nevertheless, there is no description of management with antivirals for eye involvement, only one case described by Keorochana (12) in which the use of antivirals showed a similar result to that obtained in the present case. It remains to be established whether joint use with steroids decreases the progression of the pathology and whether it is determinant in visual loss in these cases.

It is not possible to define if management with oral Acyclovir is the best therapeutic option, given that this is a single case and there is no extensive documentation of case series or clinical trials with other antivirals or intravitreal medication, which was not done in this case and leaves open the possibility of using such a strategy in the management of this pathology.

Eye involvement by EBV may include all segments of the eyeball. Cases reported so far include conjunctivitis, dacryoadenitis, episcleritis, keratitis, iritis, and optic nerve neuritis. In addition, Keorochana (12) reported their most recent case of involvement by retinal vasculitis, suggesting eye involvement with decreased visual acuity.

EBV should be considered within differential diagnoses, even in immunocompetent patients, leading to the implementation of vitreous humor sampling since, as in this case, as this was the only way to obtain the diagnosis.

CONCLUSIONS

PCR allowed the diagnostic confirmation of retinal vasculitis by EBV, which demonstrates the importance of vitrectomy, even with therapeutic intent. The patient had an adequate response to Acyclovir despite the disagreements regarding its use and the different doses received. This is the first case of this type reported in Colombia so far.

In spite of the fact that this is a single case, there were limitations such as access to the clinical history of the patient and vitrectomy —which was performed for taking samples only—,

and the fact that treatment with Acyclovir was sometimes empirical. The present report shows the importance of reporting similar cases in order to determine specific treatments and procedures to be carried out when eye involvement with a suspicion of infectious origin is found.

ETHICAL CONSIDERATIONS

The study was conducted after obtaining the patient's signed informed consent to participate in the study and to use his medical history and photographs, which did not compromise his identity.

CONFLICT OF INTEREST

None stated by the authors.

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ACQUIRED ACRODERMATITIS ENTEROPATHICA AFTER ABDOMINAL SURGERY: CASE REPORT

Keywords: Acrodermatitis; Zinc; Malnutrition.
Palabras clave: Acrodermatitis; Zinc; Desnutrición.

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RESUMEN

Introducción. El tratamiento de la acrodermatitis enteropática adquirida es la suplementación de zinc, sin embargo la dosis óptima y la duración de esta aún son objeto de estudio.

Presentación del caso. Paciente femenino con antecedente de bypass gástrico, resección intestinal y 2 meses de erupción cutánea que ameritó biopsia lesional con hallazgos histológicos compatibles con una dermatitis carencial. La mujer recibió suplemento de zinc elemental por 11 días, con lo que se logró mejoría de lesiones cutáneas. Posteriormente, presentó 2 reingresos por reactivación de la enfermedad con necesidad de reiniciar suplementación y, hasta el momento de la presente investigación, había permanecido 3 años con zinc elemental oral con dosis de hasta 240 mg/día.

Discusión. En pacientes con malabsorción intestinal la dosis de zinc de rutina de 8-11 mg/día puede ser insuficiente y los puede colocar en riesgo de acrodermatitis enteropática adquirida. En reportes de caso similares la dosis de suplementación va desde 2 mg/kg/día de zinc elemental venoso hasta 300 mg/día oral, en tanto la duración de la suplementación no ha sido establecida.

Conclusiones. La suplementación oral por 3 años con hasta 240 mg/día ha sido adecuada para el control de la enfermedad; el seguimiento a través de la medición de los niveles de zinc en sangre y la exploración física de la piel ha sido clave en el ajuste de la dosis a suplementar.

ABSTRACT

Introduction: The treatment of acquired acrodermatitis enteropathica involves zinc supplementation; however, further research is required to establsih the optimal dose and duration of the supplementation.

Case presentation: Female patient with a history of gastric bypass, intestinal resection, and 2 months of skin rash that required biopsy with histological findings compatible with dermatitis associated to nutritional deficiency. She received elemental zinc supplementation for 11 days, achieving improvement in skin lesions. She was later readmitted twice due to reactivation of the disease with the need to restart zinc supplementation. At the time of this study, she had been receiving oral elemental zinc treatment for 3 years, at doses of up to 240 mg/day.

Discussion: In patients with gastric bypass and intestinal malabsorption, the usual zinc dose of 8-11 mg/day may be insufficient and put patients at risk for acquired acrodermatitis enteropathica. In similar case reports, the supplementation dose ranges from 2 mg/kg/day of venous elemental zinc to 300 mg/day orally, while the duration of supplementation has not been established.

Conclusions: Oral supplementation for 3 years with a maximum dose of 240 mg/day has been adequate for controlling the disease. Monitoring blood zinc levels and physical examination of the skin have been key factors for adjusting the dose to be supplied.

INTRODUCTION

Acrodermatitis enteropathica (AE) is caused by zinc deficiency and may be inherited or acquired. The acquired form may occur due to inadequate intestinal absorption of this trace element in conditions such as alcoholism, anorexia nervosa, cystic fibrosis, celiac disease, bariatric surgery, inflammatory bowel disease and any form of chronic diarrhea. (1)

Rash is usually one of the first clinical manifestations of this disease: perioral and acral lesions in the form of vesicles, blisters, pustules, honey-colored crusts and well-defined scaly plaques that later take on a psoriasiform pattern. (1-3) To date, there is no specific and sensitive biochemical indicator for the diagnosis of acquired AE (4); the diagnosis is suspected due to clinical manifestations that are sometimes accompanied by low plasma zinc levels, and is confirmed when there is improvement of the symptoms after initiating supplementation. (1,5)

The treatment of acquired AE is zinc supplementation, but there is still some doubt about the dose and duration of the supplement needed. Some indicate that a dose of 15-30 mg/day is sufficient for adults (1,6), while others report the need to supplement about 3 mg/kg/day of elemental zinc. (1,7-10)

The following is a case of acquired AE in an adult patient with a history of bariatric surgery and intestinal resection. The nutritional management for this patient is described below.

CASE PRESENTATION

A female patient, 46 years old, mestizo, from Medellín (Colombia), with a technical degree and unemployed for about a year, entered the emergency department due to a trauma to the chin secondary to a fall from her own height. The woman had a history of gastric bypass 10 years ago and intestinal gangrene a year and a half ago, which required intestinal resection and correction of gastric bypass surgery; during the procedure, one and a half meters of residual small intestine was left between the proximal intestinal anastomosis and the bowel. Considering her surgical history, she received 300mg of ferrous sulfate, 600mg of elemental calcium, 1 tablet of folic acid (she did not remember the amount of mg), 2000 IU of vitamin D3 plus 80mg of magnesium, and 20mg of omeprazole daily.

The patient had also a history of hypothyroidism that was being treated with levothyroxine 75 µg/day, trigeminal neuralgia surgery being managed with pregabalin 75 mg/day, bipolar II disorder, and alcohol and opioids dependence in treatment with quetiapine XR 300 mg/day, bupropion 150mg (interdia), escitalopram 20 mg/day and lamotrigine 50 mg/day. Also, 2 weeks earlier, she started valproic acid 750 mg/day due to a paroxysmal attack which was interpreted as a convulsion.

On physical examination, the patient was conscious, alert and oriented. She presented bilateral grade 3 edema in arms and legs, eroded and erythematous plates of different sizes in the lateral region of both thighs, and more livedoid lesions with dorsal involvement in the posterior region and the soles of both feet. These findings were also evident but more moderate in the buttocks (Figure 1). In addition, she presented with erythema with scaling in the vagina and labia majora and fissures in the tongue and labial commissures. During the examination, she stated that she had been presenting with the skin rash for 2 months, which began in back of her feet and later compromised thighs, oral mucosa and vagina. She also referred a burning sensation and pruritus, and liquid depositions of several months of evolution.

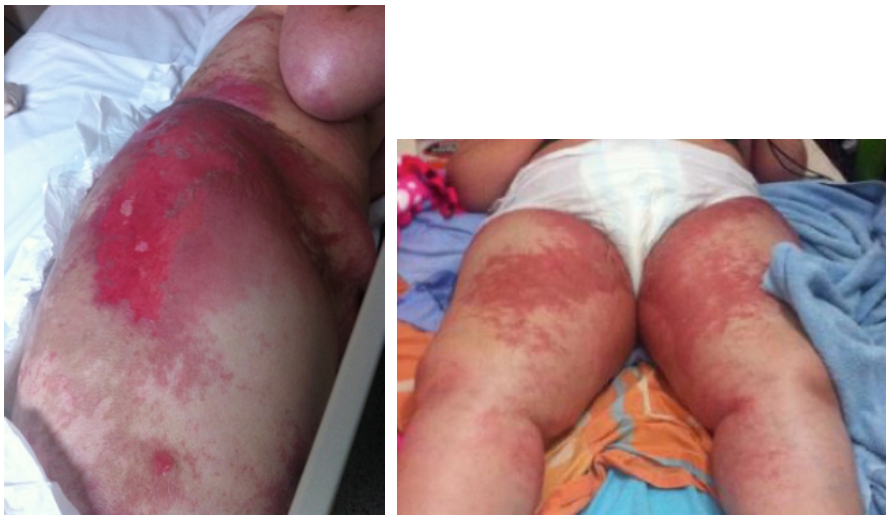


Figure 1. Skin lesions.
Source: Documents obtained during the study.

Clinically, toxicodermia versus zinc deficiency with acrodermatitis was suspected, so skin biopsy with pathology was scheduled for differential diagnosis. Treatment of skin lesions with emollient and epidermal barrier repairer was initiated.

While awaiting the pathology report, the patient was admitted to the intensive care unit (ICU) 5 days after her admission due to a septic shock with no clear focus and status epilepticus. Enteral nutrition was initiated by gastric tube due to the need for tracheal intubation and neurological alteration. Moreover, the patient received supplementation with vitamin C: 500 mg/every 12 hours, vitamin E: 200 IU/day, and multivitamin associated with minerals: 1 tablet/day, which included zinc 22.5mg. At that point, there were no signs of improvement in the skin lesions.

During her stay at the ICU, pathology reports were obtained (10 days after hospital admission and 5 days after ICU admission) indicating skin with hyper and confluent parakeratosis, absence of granular layer, irregular epidermal hyperplasia in some areas with psoriasiform pattern and some superficial keratinocytes of clear cytoplasm, and spongiosis. The dermis had dilated capillaries and superficial perivascular lymphocytic inflammatory infiltrate, findings that correlated with a clinical picture compatible with zinc deficiency, even though, from a histological viewpoint, the symptoms could not be differentiated from other diagnoses involving deficiency dermatitis, such as pellagra or necrolytic migratory erythema.

The treating medical team opted for a diagnosis of acquired acrodermatitis enteropathica and began treatment with enteral administration of elemental zinc 200 mg/day (3.3 mg/kg, dry weight: 60kg) for 6 days, with subsequent change to 100 mg/day intravenously for 5 days to avoid possible fluctuations in enteral absorption. Zinc supplementation improved the clinical picture with less erythematous and xerotic skin, in residual pigmentation phase, and residual desquamation. Upon completion of intravenous zinc treatment, a maintenance dose of 22.5mg of oral zinc was continued.

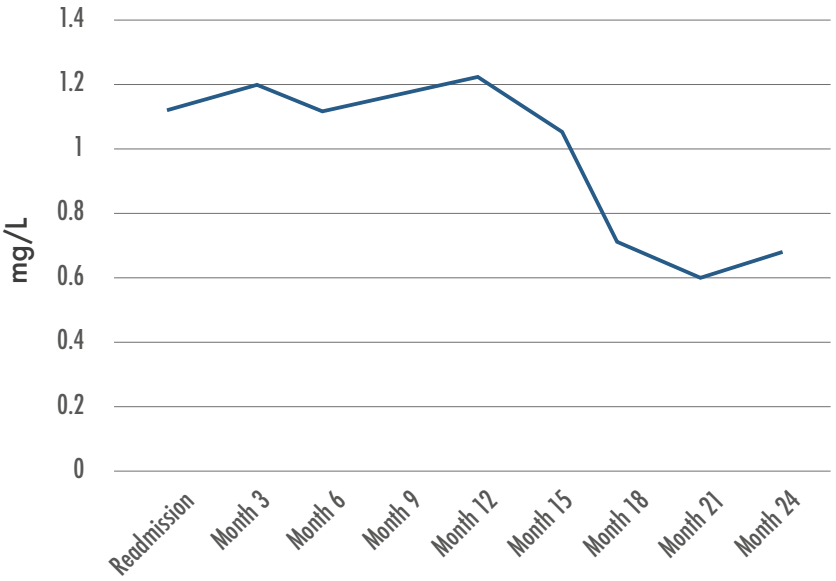
During her stay at the hospital, the patient said she felt sad about her health condition, with a feeling of loss of autonomy and independence, and tired due to her state and long period of

hospitalization, for which she received support from the psychology service. The woman remained in the ICU for 31 days with prolonged mechanical ventilation, and was discharged after 50 days with healthy skin and indications to continue with all supplements on an outpatient basis, including 22.5mg of zinc per day.

The patient was readmitted twice (on the 20th day and on the 7th month after discharge) due to reactivation of skin lesions clinically compatible with acrodermatitis enteropathica. In the first readmission, she had serum zinc levels of 0.29 mg/L (normal value: 0.66-1.020 mg/L), so she was prescribed 78mg (1.3 mg/kg, dry weight: 60kg) of elemental zinc per day and was indicated to continue with this same dose on an outpatient basis. The woman was hospitalized for 12 days.

During the second readmission, the patient received total parenteral nutrition (TPN) for severe lesions that affected the oral cavity and prevented her from eating; she was also diagnosed with intestinal failure by malabsorption associated with residual small bowel. A new skin biopsy was performed, showing, once again, histological findings compatible with deficiency dermatitis. Zinc values of 1.12 mg/L were obtained and the elemental zinc supplement dose was increased to 180 mg/day (2.7 mg/kg, weight: 67kg). The patient was discharged on day 17 with indication to continue supplementation at home.

At the time of writing this paper, outpatient follow-up had been performed and the patient had been on zinc supplementation for 3 years; the dose was adjusted according to blood zinc levels and the recurrence of skin lesions (Figure 2). The last dose she received was 240mg of elemental zinc/day (2.8 mg/kg/day, weight: 84.4kg), achieving normal levels and healthy skin. No intolerance or complications associated with zinc supplementation had been observed.



Since readmission until month 21, she received 180mg/day of oral elemental zinc. By month 24, she was receiving 240 mg/day of oral elemental zinc.

Figure 2. Plasma zinc levels during outpatient follow-up.
Source: Own elaboration.

DISCUSSION

Acquired AE should be suspected in adult patients with intestinal malabsorption who present dermatological symptoms. Intestinal malabsorption seems to be the main cause of zinc deficiency in this case report; a history of intestinal resection leading to chronic diarrhea with malabsorption may explain the deficiency of this trace element, which is absorbed and excreted mainly in the intestinal tract. (1)

In case of clinical suspicion, it is important to analyze skin lesions and measure blood zinc levels. In the described case report, a diagnosis of acquired AE was suspected due to the clinical manifestations and histological characteristics of the biopsy, and it was confirmed based on the improvement of the symptoms after initiating the supplementation. Zinc levels in plasma were not initially measured in this case, however, in future cases, this could be an important aspect to consider because it can contribute to the differential diagnosis, since the clinical manifestations and histological characteristics of acquired AE are indistinguishable from other nutrient deficiency diagnoses such as pellagra. (1,11,12)

Plasma zinc represents less than 0.2% of body reserves, thus limiting its usefulness as a method to diagnose acrodermatitis. (4,10) Zinc deficiency with normal plasma levels (13,14) have also been reported, such as the one observed in the patient's second hospital readmission when her skin lesions reactivated even though she had normal zinc levels. Measuring only the levels of this element in plasma in search of a deficiency may have limitations, but a proper correlation between clinical manifestations, histopathological findings from skin biopsy and plasma zinc levels is essential to identify the deficiency and initiate supplementation.

In the present case, supplementation was initiated with 3 mg/kg of oral elemental zinc with subsequent adjustments to the dose according to the evolution of the lesions and the values of this mineral in plasma, first monthly and then quarterly. The patient received up to 240mg of oral elemental zinc on an outpatient basis without adverse events.

In case reports of patients with a history of abdominal surgery, supplementation doses ranged from 2 mg/kg/day of venous elemental zinc to as much as 300 mg/day orally. (7-9,15,16) The recommended duration of the supplementation is not clear, since the available case reports do not specify the time of the intervention, although they show improvements of the lesions with only days or weeks of treatment. (7-9,15,16)

Oral zinc intake of 8-11 mg/day or parenteral zinc of 2.5-5 mg/day is considered sufficient to meet the mineral requirements in adults; in patients with intestinal malabsorption, the requirement could increase to 12-17mg of parenteral administration per liter of fluid lost. (5,17-19) In the treatment of acquired AE, the doses of supplementation used exceed previous recommendations, so it is important to follow up on the occurrence of adverse effects related to excess zinc, such as gastric irritation, abdominal pain, nausea and vomiting. (10) Copper should also be supplemented and its plasma levels monitored because excess zinc interferes with its absorption; thus, it is generally recommended to supplement 1mg of copper for every 8-5mg of zinc. (20)

The strength of this case report is the long-term outpatient follow-up received by the patient under a structured bowel rehabilitation program. The assessments were made during joint consultations that involved the bowel rehabilitation physician and the nutrition professional. This resulted in adequate control of acquired AE and

intestinal malabsorption. Limitations included not having measured plasma zinc levels from the beginning, which could have been an important aspect for differential diagnosis, and that copper levels were not included in the monthly or quarterly follow-up lab tests, although the appearance of possible adverse events due to excess zinc was monitored.

CONCLUSIONS

Health professionals should suspect acquired AE in patients with inadequate nutrient intake or intestinal malabsorption, who also have a confluence of relevant dermatological findings. For the differential diagnosis of acquired AE and for the early initiation of zinc supplementation, it is important to correlate clinical manifestations, histological findings of skin biopsy, and plasma zinc levels. In this patient with intestinal malabsorption, oral supplementation for 3 years at up to 240 mg/day was adequate for controlling the disease; follow-up through blood zinc levels and physical examination of the skin were also essential to adjust the supplemented dose.

CONFLICT OF INTEREST

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https://doi.org/10.15446/cr.v5n2.78952

SPONTANEOUS VULVAR HEMATOMA AS A RARE MANIFESTATION OF CONGENITAL HYPOFIBRINOGENEMIA. CASE REPORT

Keywords: Afibrinogenemia; Fibrinogen; Hematoma; Vulva.
Palabras clave: Afibrinogenemia; Fibrinógeno; Hematoma; Vulva.

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RESUMEN

Introducción. Los trastornos congénitos del fibrinógeno son una rara condición donde se presentan alteraciones cuantitativas y cualitativas del factor I, siendo asintomáticos la gran mayoría de pacientes.

Presentación del caso. Paciente femenino de 19 años con antecedente de hipofibrinogenemia congénita, quien cursa con hematoma espontáneo en vulva y presenta hipotensión, taquicardia, estupor y hematoma de 20cm en labio mayor derecho. Al ingreso, la joven registra hemoglobina 6.6 g/dL, fibrinógeno 74 mg/dL y prolongación de tiempos de coagulación. Se transfunden glóbulos rojos y crioprecipitados; luego se hace drenaje quirúrgico y reposición de fibrinógeno ajustando dosis acorde a fibrinógeno plasmático. La paciente presenta mejoría progresiva sin recurrencia hemorrágica y niveles de fibrinógeno en metas hasta egreso hospitalario.

Discusión. La afibrinogenemia y la hipofibrinogenemia hacen parte de los trastornos cuantitativos del factor I, con ausencia total para la primera y niveles <150 mg/dL para la segunda. El hematoma espontáneo de vulva como manifestación hemorrágica severa no es una presentación habitual en pacientes sintomáticos; su tratamiento se basa en la reposición de fibrinógeno de forma individualizada y manejo quirúrgico cuando sea requerido.

Conclusión. La hipofibrinogenemia es una enfermedad rara, donde el reemplazo de fibrinógeno es uno de los pilares de tratamiento.

ABSTRACT

Introduction: Congenital fibrinogen disorders are rare conditions in which there are quantitative and qualitative alterations of factor I; the vast majority of patients are asymptomatic.

Case presentation: A 19-year-old female patient with a history of congenital hypofibrinogenemia presented with spontaneous vulvar hematoma along with hypotension, tachycardia, stupor and hematoma of 20cm in the right labium majus. On admission, the young woman had hemoglobin 6.6 g/dL, fibrinogen 74 mg/dL and prolonged clotting times. She received red blood cells transfusion and cryoprecipitates, followed by surgical drainage and intravenous fibrinogen replacement, adjusting the dose according to fibrinogen levels in plasma. The patient presented progressive improvement without hemorrhagic recurrence and fibrinogen levels within the target values until hospital discharge.

Discussion: Afibrinogenemia and hypofibrinogenemia are part of the quantitative factor I disorders; in the first case, there is total absence of circulating fibrinogen, and in the second case the levels are below 150 mg/dL. Spontaneous vulvar hematoma as a severe hemorrhagic manifestation is not frequent in symptomatic patients; its treatment is based on fibrinogen replacement in an individualized manner and surgical management when required.

Conclusion: Hypofibrinogenemia is a rare disease, and fibrinogen replacement is one of the mainstays of treatment.

INTRODUCTION

Hypofibrinogenemia is a congenital disorder consisting of low levels of fibrinogen, a key glycoprotein for the hemostasis system and inflammatory response. (1,2) This abnormality occurs as a result of a heterozygous mutation in one of the three genes encoding for the fibrinogen protein chains and autosomal recessive inheritance. There is no exact data on its incidence, since most patients are asymptomatic or do not have clinically significant bleeding. When severe hemorrhagic manifestations, such as gastrointestinal bleeding with unknown etiology, are observed, the corresponding studies should be carried out to look for the cause. (1,3-6)

The severe form of hypofibrinogenemia is similar to afibrinogenemia (1), and also manifests itself mainly in the neonatal period, in 85% of cases through umbilical cord bleeding. Its presentation in older individuals is rare, and its hemorrhagic manifestations may be gastrointestinal, genitourinary, cutaneous, by spontaneous splenic rupture and central nervous system; the latter is the main cause of death in these patients. (2,3,5)

To diagnose hypofibrinogenemia, immunoreactive fibrinogen levels are evaluated, obtaining results that show very low values that should be associated with prolonged clotting times. (1,2,7) Treatment in symptomatic individuals consists mainly of fibrinogen replacement therapy and strict daily follow-up of fibrinogen levels in plasma in order to ensure adequate hemostasis. (2,6) This is the report of an unusual hemorrhagic presentation (spontaneous vulvar hematoma) in an adult patient with a history of congenital hypofibrinogenemia.

CASE PRESENTATION

19-year-old female patient, from Bogotá (Colombia), housewife and of a low-income socioeconomic status household, with history of congenital hypofibrinogenemia diagnosed during the neonatal period in a hemorrhagic context (without information on a specific event), compatible genetic study confirmed in anamnesis (not available in clinical history), without hemorrhagic manifestations subsequent to diagnosis nor pharmacological treatment. The young woman consulted the emergency department due to clinical symptoms of six hours of evolution and spontaneous appearance of expansive genital hematoma at the level of the right labium majus with hemorrhage associated with dissection of superficial tissues and altered state of consciousness. The physical examination showed hemodynamic instability and signs of low expenditure, presence of hematoma of approximately 20cm in diameter at the level of the right labium majus and active hemorrhage in its medial and inferior portion (Figure 1).

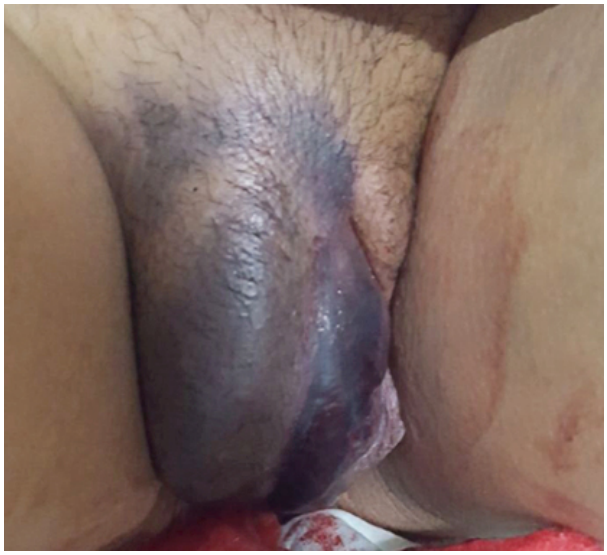

Figure 1. Vulvar hematoma at the level of the right labium majus with active inferomedial hemorrhage.
Source: Document obtained during the study.

A hypovolemic shock secondary to major hemorrhage was considered, for which Ringer's lactate infusion 3 000mL for 2 hours was prescribed, as well as intravenous tranexamic acid 1g and

compression at bleeding site. Laboratory tests on admission showed complete blood count with hemoglobin of 6.6 g/dL and no other alterations. Due to her history of hypofibrinogenemia, fibrinogen activity test was requested, which reported 74 mg/dL associated with prolonged clotting times (Table 1); based on the results, the patient received a transfusion of six units of cryoprecipitates and two units of packaged red blood cells.

The patient was assessed by the gynecology service, which considered the benefit of immediate surgical management. The hematoma was drained with intra-surgical size estimated at 17x7cm without complications. The hematology service assessed her again, confirming menstrual cycles without alterations and absence of family history of coagulopathies, bleeding or complications during invasive procedures (no surgical history) and episodes of involuntary pregnancy loss. In the immediate post-operative period, fibrinogen supplementation was initiated with doses adjusted according to weight; the dose were subsequently adjusted based on the fibrinogen values in plasma obtained every 8 hours, with an average daily dose of approximately 1.5 to 2 grams, administered for 8 days (Figure 2).

Table 1. Laboratory tests on admission.

Test	Value
Leukocytes	6 000 cell/uL
Neutrophils	5 260 cell/uL
Lymphocytes	570 cell/uL
Hemoglobin	6.6 g/dL
Hematocrit	21.3%
Mean corpuscular volume	82 fL
Mean corpuscular hemoglobin	25.5 pg
Platelets	159 000 cell
Partial thromboplastin time/day control	180/29 sec
Prothrombin time/day control	120/11.1 sec
Fibrinogen	74 mg/dL

Source: Own elaboration.

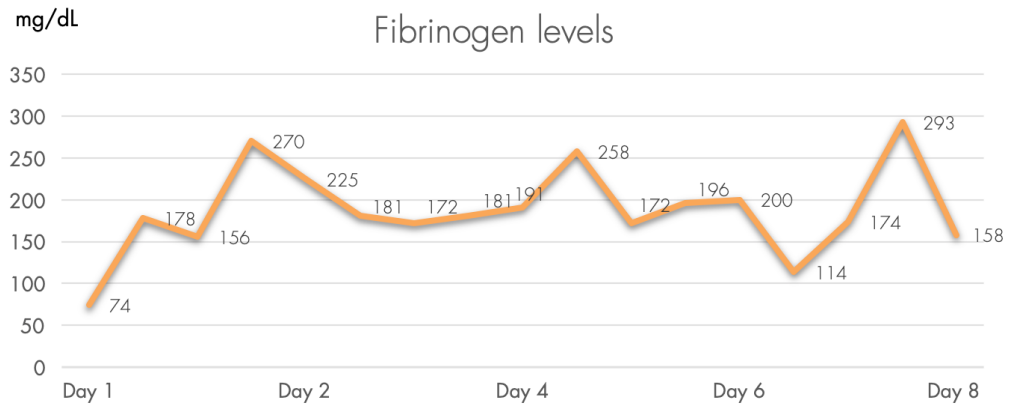

Figure 2. Fibrinogen values in plasma.

Source: Own elaboration.

The patient did not have any side effects to the administration of fibrinogen, and the treatment by intravenous administration was adequately tolerated without changes between doses until discharge from hospital.

DISCUSSION

Fibrinogen is a glycoprotein essential for hemostasis, and it is the soluble precursor of fibrin, which is required for clot formation; it also plays a key role on platelet aggregation and fibrinolysis. It is synthesized in the liver and circulates in plasma at concentrations of 2-4 g/L. (8-10)

Hypofibrinogenemia is a rare hematologic disorder that has no established incidence due to the absence of symptoms in most affected patients; it has a recessive inheritance pattern as does afibrinogenemia. In patients with hemorrhages of unknown etiology, studies should look for coagulation disorders. (1,2) The hereditary abnormalities of fibrinogen are divided into two: type 1 or quantitative, and type 2 or qualitative. (11)

The most frequent clinical manifestations of hypofibrinogenemia are umbilical cord hemorrhage, intracranial hemorrhage and mucosal hemorrhage; other less frequent manifestations are skeletal muscle hemorrhage, joint bleeds, paradoxical arterial and venous thrombotic events (9), ruptured spleen (3,12) and hepatic hematoma. (13) There are no reported cases describing spontaneous vulvar hematoma as a clinical manifestation.

For the case described here, the clinical history of the patient allowed guiding the diagnostic and treatment approach. However, it is important to highlight that an individual without a history of coagulopathy who presents unusual thrombotic or hemorrhagic events —which in some cases compromise life— must be a candidate for studies that include the evaluation of fibrinogen. Moreover, vulvar hematoma is a rare clinical finding in medicine, occurring mainly in obstetrics with an incidence of 1 to 2 per 1 000 births (14), and even more rare in non-obstetric population with an incidence of 3.7%. (15) Although in both cases it is usually associated with perineal trauma, vulvovaginal hematomas can rarely be triggered by spontaneous injury to a blood vessel or result from a hematological disorder. (16) In this case, a hematological disorder caused an expansive vulvar hematoma in a patient with a history of congenital fibrinogen disorder.

First-line treatment for a vulvovaginal hematoma is usually conservative, especially when the hematoma has a small to moderate size; however, if the hematoma has expansive behavior (16,17) or is >12cm, it is usually associated with decreased hematocrit, hemodynamic disorders, and transfusion requirement, suggesting the need for surgical management. Still, there is no clear scientific evidence to support this approach and the optimal timing for surgical management remains controversial.

On the other hand, it has been suggested that if the size of the hematoma is sufficient to trigger urological or neurological symptoms (16) or if its behavior is clearly expansive, surgical management should be urgent. (16,17) This was the approach determined for the patient described, achieving early hemostasis and stabilization, and avoiding complications derived from the procedure. Hemostasis can be achieved by ligation of the bleeding vessels, but another hematoma may occur as a complication, and in this context, embolization of the compromised blood vessels should be chosen as the second line of treatment. (17)

In the present case, transfusion of red blood cells concomitant to surgical management was necessary given the significant decrease in hemoglobin levels associated with hemodynamic instability.

The treatment of severe hemorrhages secondary to hypofibrinogenemia and afibrinogenemia is based on fibrinogen replacement, either with fresh frozen plasma, cryoprecipitate or concentrated fibrinogen, the latter being the treatment of choice due to its greater clinical safety. (8) Regarding fibrinogen concentrates replacement therapy as the mainstay of treatment for afibrinogenemia, it is recommended to individualize the clinical hemorrhagic context and the fibrinogen levels in plasma, aiming at a level not less than 75 mg/dL. (2,6,7) For the case described here, a dynamic dose of fibrinogen was indicated according to weight and with adjustment according to the plasmatic levels of fibrinogen evaluated every 8 hours during the entire hospital stay. This, along with surgical management and transfusion, allowed achieving a rapid and adequate clinical evolution, with discharge after 8 days of hospitalization without hemorrhagic recurrence, hemodynamic and hematological stability, and normal fibrinogen levels.

Given the impossibility of conducting large-scale studies on the treatment of fibrinogen disorders and their hemorrhagic manifestations, the best level of evidence available should be used for an early and appropriate approach; case reports are the main scientific contribution, and that is precisely the relevance of the information provided in this article.

The strengths of the current case report include the diagnostic and therapeutic approach of an unusual hemorrhagic presentation of hypofibrinogenemia that compromises life, highlighting the need, in this type of cases, for surgical management, transfusion and dynamic replacement of fibrinogen to prevent complications and seek the rapid improvement of the symptomatology. This is the first case of hypofibrinogenemia reported in Colombia, and the first in the world describing vulvar hematoma as a severe spontaneous hemorrhagic manifestation that compromises life.

The limitations of the study are the unavailability of the clinical history of the neonatal hemorrhagic event —which was useful to suspect the diagnosis— and the genetic studies carried out to confirm the diagnosis. Nevertheless, the lack of these data from the clinical history does not diminish the importance of what has been reported here, as this is the background anamnesis of the current clinical history described, with clarity and certainty, by the patient and her family, as is commonly observed during the evaluations made every day in the medical assistance field.

CONCLUSIONS

Afibrinogenemia is a rare disease that usually manifests itself with hemorrhagic events. Local control of such events includes supportive therapy, and fibrinogen replacement is the mainstay of therapy. It is important to suspect coagulation disorders in patients with bleeding at unusual sites, severe spontaneous bleeding, and unexpected thrombotic, obstetric, or adverse surgical events.

Having an adequate record of patients' clinical histories and their background information is essential to achieve a better diagnostic and therapeutic approach; in turn, this brings greater strength to the research and generates new knowledge, as all reported data could be relevant, this being one of the main lessons of the case report described here.

CONFLICT OF INTEREST

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