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Case Report

Disseminated histoplasmosis in pediatrics

Histoplasmosis diseminada en pediatría

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Abstract

A case of disseminated histoplasmosis is presented in a 2-year-6-month-old patient, immunocompromised due to her severely malnourished state. Histoplasmosis is a fungal infection of worldwide distribution, reported on all continents except Antarctica; it is endemic in the region of the Americas. It is produced by Histoplasma capsulatum, a dysmorphic fungus that grows in soils with a high content of bird and bat faces. Histoplasmosis offers a wide spectrum of clinical manifestations, it should be suspected in patients from endemic areas with risk factors for the development of the disease; in Ecuador its actual incidence is unknown. In immunocompetent infants it is usually a self-limited process, while in immunocompromised patients it is often life-threatening if not diagnosed and treated in time.

Keywords: Histoplasmosis, Child nutrition disorders, Diseases of the immune System.

Resumen

Se presenta un caso de histoplasmosis diseminada en una paciente de 2 años 6 meses, inmunocomprometida a causa de su estado de desnutrición severa. La histoplasmosis es una infección micótica de distribución mundial, reportada en todos los continentes, excepto en la Antártida; resulta endémica en la región de las Américas. Es producida por el Histoplasma capsulatum, un hongo dismórfico que crece en suelos con alto contenido de heces de aves y murciélagos. La histoplasmosis ofrece un amplio espectro de manifestaciones clínicas, debe ser sospechada en pacientes provenientes de áreas endémicas con factores de riesgo para el desarrollo de la enfermedad; en el Ecuador se desconoce su incidencia real. En los infantes inmunocompetentes suele tratarse de un proceso autolimitado, mientras que en el paciente inmunocomprometido suele ser potencialmente letal de no ser diagnosticada y tratada a tiempo.

Palabras claves: Histoplasmosis, Trastornos de la nutrición del niño, Enfermedades del sistema inmune.

Introduction

The first description of histoplasmosis was made by Samuel Darling in 1905 while conducting a study of systemic leishmaniasis; In the autopsy of a Panama Canal worker, this patient presented visceromegaly and multiple lung lesions, in the histological sections he discovered intracellular bodies similar to the amastigotes of Leishmania, although he noticed that the cells were surrounded by a translucent halo similar to a capsule[1].

In particular, histoplasmosis is considered a deep mycosis caused by Histoplasma capsulatum, a dysmorphic fungus found in soils contaminated with bird and bat guano. Three varieties of this species are recognized: Histoplasma capsulatum variety capsulatum, which is worldwide in distribution; Histoplasma capsulatum variety duboisii or African histoplasma and Histoplasma capsulatum variety farciminosum, an equine pathogen[2].

Histoplasmosis is a mycosis with a cosmopolitan distribution. In fact, cases have been reported on all continents except Antarctica, but it is endemic in the Americas region. Although its diagnosis is more frequent in this region, cases have also been reported in countries of Southeast Asia and South-Central Africa. It is estimated that it affects 40 million people and it is estimated that 200 thousand new cases are diagnosed each year; 15,600 new cases[3-5] are registered in the Americas region each year.

In Ecuador during 2018, 23 cases of histoplasmosis were reported, 4 of these in children under 18 years of age, according to figures reported in the health statistics yearbook[6]. Patients with disseminated histoplasmosis frequently suffer from pathologies that alter their immune capacity against intracellular pathogens; Conditions predisposing to disseminated histoplasmosis include HIV infection, primary immunodeficiency, use of immunosuppressive medications, anti-rejection therapies in solid organ transplant recipients, tumor necrosis factor (TNF) -alpha inhibitor therapies, extreme ages of the life[7].

It should be noted that nutrition is an important component for the development and maintenance of the immune response, malnourished patients have a higher risk of contracting opportunistic infections due to their compromised immune defense mechanism[8].

Presentation of the case

This is a 2-year-6-month-old female patient, the product of the fifth gestation of a 30-year-old mother with inadequate prenatal control, obtained at 36 weeks of gestation by eutocic delivery, with a birth weight of 2,200 g, height of 45cm and Apgar 8/9 at the minute of birth. In particular, the patient has a history of delay in the acquisition of expected maturation patterns for age, a consequence of agenesis of the corpus callosum.

It should be noted that it comes from a rural area in the province of Los Ríos, whose family was dedicated to raising poultry. The patient is admitted due to a clinical picture of one year of evolution characterized by abdominal distension (Figure 1), muco-bloody diarrheal stools and skin lesions.

The physical examination draws attention to the presence of multiple semi-moist crusted skin lesions on the scalp and neck, umbilicated whitish papules, crateriform nodule with central crust on the left shoulder, scaly micro papules and micro pustules on the trunk (Figure 2), with great abdominal distension, perimeter 56 cm at the expense of visceromegaly, liver 14 cm, spleen 11 cm, large reducible umbilical hernia, and moderate malnutrition deficit of 39% weight < 1P, ZS -3.

Laboratory results revealed normochromic normocytic anemia (hemoglobin 5.5g / dl),

(hypoalbuminemia 1.4mg / dl), which required management with blood components and blood products. Primary immunodeficiency studies were negative, human immunodeficiency virus (HIV) non-reactive, the rheumatological profile and antiphospholipid antibodies were negative. Histoplasma capsulatum yeasts were documented in the peripheral blood smear and blood culture. Furthermore, the biopsy of the crateriform lesion in the left shoulder ruled out malignancy and also revealed the presence of Histoplasma capsulatum.

Amphotericin B deoxycholate 1mg / kg was administered to the patient as treatment, requiring treatment for 7 weeks until a cumulative dose of 35mg / kg was reached. He subsequently received itraconazole therapy, observing remission of the crateriform skin lesion, partial remission of hepatosplenomegaly (liver and spleen, both in 10 cm), weight gain compared to his initial weight, although he maintained a deficit of 18%, weight < 1P, ZS-2.

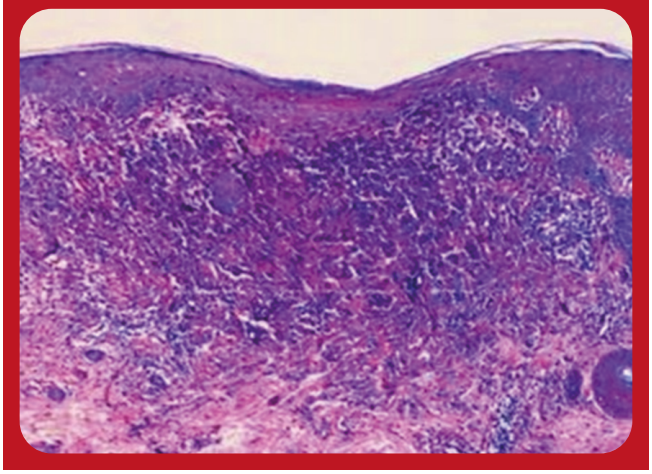
After 84 days of hospitalization, the patient is discharged, at the time of discharge she abandoned the medical follow-up and treatment, after five weeks she presented clinical deterioration, was hospitalized due to septic shock and died after 24 hours.

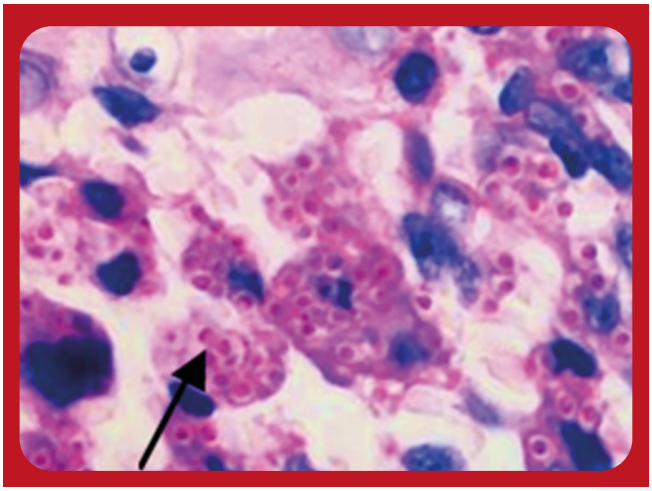
Figure 1. Globular abdomen at the expense of large hepatosplenomegaly and reducible umbilical hernia

Figure 2. Skin lesions

Source: *A. Moist crusty lesions on the scalp and neck. B Scaly micro-papules and micro-pustules on the trunk. C. Crateriform nodule with central crust on the left shoulder.*

Figure 3. Biopsy of chest skin lesion.





A. (PAS) staining, focal thinning of the epidermis, dense inflammatory infiltrate in the superficial and middle dermis, mononucleated and multinucleated lymphocytes and histiocytes.

B. Macrophages with abundant capsulated yeast-like fungal elements consistent with Histoplasma capsulatum.

Discussion

Histoplasma capsulatum is an endemic fungal agent in Ecuador, as a result of the climatic conditions that facilitate its growth[3]. The infection occurs by inhalation of microconidia, which are the infecting form of Histoplasma capsulatum, within the alveolus it proliferates in the form of yeast, they are phagocytosed by macrophages, producing an ineffective inflammatory reaction. Infected macrophages spread infection through lymphatic vessels to adjacent lymph nodes and from there hematogenous spread to the entire reticuloendothelial system occurs[7,9].

Although transmission is respiratory, there are reports of vertical transmission associated with the use of anti-tumor necrosis factor (anti-TNF) therapies.[10]. Symptoms appear between 3 to 17 days after infection with an average of 10 days, this depends on the size of the inoculum and the virulence of the fungus and the immune status of the host. In immunocompetent patients the infection usually has a benign course, but in immunosuppressed patients and in children it presents in a disseminated form caused by the continuous replication of Histoplasma capsulatum in infected organs. Indeed, fever, weight loss, and hepatosplenomegaly are the most common symptoms. While gastrointestinal symptoms occur in 10% of cases, skin involvement occurs in 10 to 15% of cases and central nervous system in 5-20% of cases [7,11].

Disseminated disease is manifest in immunocompromised patients. In the clinical context of the patient described in this study, pathologies that compromised her immune status were ruled out: primary immunodeficiencies, HIV, oncohematological diseases, immunological diseases, as well as other infections. With the diagnosis of moderate malnutrition based on the expected weight deficit for age, it was established that the patient had secondary immunodeficiency of nutritional cause.

Protein-caloric malnutrition is described as the most frequent secondary immunodeficiency in the world, the severity is directly related to the degree of hypoproteinemia that affects innate and adaptive immunity, producing lower production and functionality of T lymphocytes. Micronutrients weaken the mucosal barrier, producing greater susceptibility to infection [12-14].

The culture is still considered the gold standard for diagnosis, its limitation is time, since the fungus grows slowly and takes between 6 to 12 weeks to obtain results, in the histopathology the fungus is directly observed using Wright's stains, Giemsa and periodic acid Schiff (PAS), in addition to serological tests for early diagnosis [5,11].

Treatment is indicated in all patients with disseminated histoplasmosis. Indeed, amphotericin B is recommended, in lipid form amphotericin B at doses of 3 to 5 mg / kg / day, and in deoxycholate amphotericin B at doses of 0.7 to 1.0 mg / kg / day for one or two weeks, followed by itraconazole at doses of 2.5 to 5 mg / kg every 12 hours until completing 3 months of treatment in immunocompetent patients and 12 months in immunosuppressed patients [5, 11,12].

The patient described in this case presented immunological compromise due to her state of severe malnutrition, she presented common clinical manifestations in addition to gastrointestinal affection and skin lesions, in which Histoplasma capsulatum was directly observed with the stain (PAS), she received recommended treatment based on amphotericin B and itraconazole.

Conclusions

In the clinical case of a patient with histoplasmosis the diagnostic spectrum of the malnourished patient or one who presents some pathology that compromises his immunological status, with signs or symptoms compatible with the disease, must be taken into account. Nutritional status is an important component of the immune response, nutritional deficits increase the risk of severe infectious processes. Despite the advent of serologic testing, culture is still considered the gold standard for diagnosis. Early diagnosis, timely treatment, and adequate follow-up improve the patient's prognosis.

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