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Disseminated coccidioidomycosis with atypical presentation in an immunocompetent patient in Chiapas: clinical case

Coccidioidomicosis diseminada con presentación atípica en paciente inmunocompetente en Chiapas: caso clínico

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ABSTRACT. Coccidioidomycosis is an underdiagnosed infectious disease worldwide, caused by fungi from the *Coccidioides spp*. family. These fungi are typically found in alkaline, sandy soils of warm and arid regions of the western hemisphere, such as northern Mexico. However, due to migratory displacement, cases of coccidioidomycosis have been documented in non-endemic areas. The primary site of involvement is the lungs; pleural effusion is rare. Disseminated coccidioidomycosis affects 1% of infected patients and is associated with more severe outcomes. We present the case of a 28-year-old male from Chiapas, who has a history of residing in Baja California, without immunocompromising conditions, referred to our unit with atypical disseminated coccidioidomycosis characterized by pulmonary consolidations, lymphadenopathy, subcutaneous abscesses, and pleural effusion.

Keywords: disseminated coccidioidomycosis, coccidioidomycosis in immunocompetent, coccidioidomycosis in non-prevalence region.

RESUMEN. La coccidioidomicosis es una enfermedad infecciosa infradiagnosticada a nivel mundial, causada por hongos de la familia *Coccidioides spp*; habitualmente se encuentran en suelos alcalinos y arenosos de regiones cálidas y áridas del hemisferio occidental, como en el norte de México; sin embargo, debido al desplazamiento migratorio se han documentado casos de coccidioidomicosis en regiones no endémicas. El principal sitio de afección son los pulmones; el derrame pleural es poco frecuente. La coccidioidomicosis diseminada afecta al 1% de los pacientes infectados y está asociada con resultados más graves. Se presenta el caso de un masculino de 28 años originario de Chiapas con historia de haber radicado en Baja California, sin inmunocompromiso, referido a nuestra unidad con coccidioidomicosis diseminada de evolución atípica asociada, caracterizada por consolidaciones pulmonares, adenomegalias, abscesos subcutáneos y derrame pleural.

Palabras clave: coccidioidomicosis diseminada, coccidioidomicosis en inmunocompetentes, coccidioidomicosis en regiones no prevalentes.

INTRODUCTION

Coccidioidomycosis (CM) is an infection caused by dimorphic fungi of the family of *Coccidioides spp, first* described by Alejandro Posadas in 1892. They are usually found in alkaline and sandy soils of warm and arid regions of the Western Hemisphere. They thrive in areas with very hot summers and winters without severe temperature drops and, in addition, with low annual rainfall.[1] It is considered a under-diagnosed disease in desert regions of the New World due to its non-specific symptoms, similar clinical findings with other infectious and non infectious diseases, lack of reliable and affordable laboratory tests that allow a timely diagnosis and, in addition, limited existence of updated epidemiological information in Latin America.[2]

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Worldwide endemic areas have been stablished in Mexico, Central America (Guatemala, Honduras) and South America (Argentina, Bolivia, Brazil, Colombia, Paraguay and Venezuela), where genetic studies have shown that the predominant species is *C. posadasii*.[3] In United States, by 2022, according to the Centers for Diseases Control and Prevention (CDC), a total of 17,612 cases were recorded; between 10,000 and 20,000 cases of coccidioidomycosis are reported annually, mainly in Arizona and California, with an annual average of 200 deaths associated with coccidioidomycosis from 1999 to 2021.[4]

Coccidioidomycosis is one of the most prevalente systemic mycoses in Mexico; until 1994, approximately 1,500 cases were reported annually, with the states of Nuevo León, Tamaulipas, Chihuahua, Baja California and Sonora reporting the highest number of cases. As of 1995, coccidioidomycosis was removed from the national epidemiological registry for reportable diseases, therefore the current clinical burden of the disease in Mexico is unknown.[5]

The 60% of infections are asymptomatic, 40% have clinical manifestations similar to the common cold or pneumonia, and, only 1% develop disseminated disease, which can affect any area of the body. Disseminated coccidioidomycosis can be in a single site or in multiple sites, cases of osteomyelitis in pelvic bones, synovitis in knee joint, mediastinal lymphadenopathy, peritonitis and meningitis, infection of soft tissues, intramuscular infection and subcutaneous abscesses have been described.[6] The ethnicity (African, Asian and Hispanic ancestry), immunocompromised states (cancer, organ transplant, corticosteroid therapy, chemotherapy, HIV infection) and some genetic alterations are risk factors for disseminated coccidioidomycosis.[7]

PRESENTATION OF THE CASE

28 year-old male patient, originally from Frontera Comalapa, Chiapas; farmer, without chronic degenerative diseases. History of residence in Tijuana, Baja California, for a year for work reasons, where he worked in an electronics factory.

Current condition started four months prior to hospitalization, with temperature rises, preceded by shivers and followed by diaphoresis, without schedule predominance; occasional dry cough, mMRC 3 dyspnea, nausea and unintentional loss of approximately 15 kg. One month later he reports growth of the left supraclavicular lymph node, in addition, increased volume in the right costal and left dorsal region. External study protocol: chest X-ray with identification of left pleural effusion, left basal consolidation and cavitated node in the same region are identified, so left thoracentesis is performed with the extraction of 1,000 mL liquid and bronchoscopy with bronchial biopsy that reports chronic non-specific inflammation. Diagnostic definition is not achieved so multiple antimicrobial schemes based on clindamycin, cephalosporins and aminopenicillin are initiated, without showing clinical improvement. They decide to start treatment for tuberculosis in intensive phase with four drugs, without favorable clinical evolution, so they make reference to our institution, where we decided to suspend antibiotics and tuberculosis treatment.

External laboratory/imaging studies. Bronchial mucosa biopsy report by fibrobronchoscopy: Bronchial mucosa biopsy report by fibrobronchoscopy: respiratory mucosa with chronic non-specific inflammation; cytopathological broncho alveolar lavage (BAL) with moderate inflammatory reaction, with neutrophilic and lymphocytic characteristics, in addition to reactive mesothelial cells. BAL culture: positive for *Klebsiella spp*, negative for *Mycobacterium tuberculosis*; cytopathological pleural fluid with moderate inflammatory reaction, neutrophilic and lymphocytic, reactive mesothelial cells; pleural fluid cytochemical: glucose 70 mg/dL, lactic dehydrogenase (DHL) 158 U/L, proteins 6.7 g/dL, leukocytes 15-20 cel/mm^3, lymphocytes 95%, Gram staining: negative, adenosine deaminase (ADA) determination 28 U/L. Rapid test for HIV: non-reactive.

Institutional laboratory tests. Hemoglobin 9.9 g/dL, hematocrit 32, mean corpuscular volume (MCV) 80 fL, mean corpuscular hemoglobin (MCH): 31.4 pg, leukocytes 13,190/mm^3, segmented 85%, platelets 1'158,000/mm^3, procalcitonin < 0.5 ng/mL. Expectoration culture: negative. Gram stain and cotton blue stain of left thoracic subcutaneous abscess drainage fluid: identification of macrosiphonated, branched septate hyphae with no apparent forms of reproduction. Direct potassium hydroxide (KOH) examination of left thoracic subcutaneous abscess drainage, double membrane spherules suggestive of *Coccidioides spp*. are identified. Left thoracic subcutaneous abscess drainage culture: development of *Coccidioides spp*; determination of serum IgG and IgM anticoccidioides antibodies: both positive. Portable chest X-Ray: left pleural effusion. Simple computed axial tomography of the chest: left pleural effusion, cervical and mediastinal nodal conglomerates, as well as areas of posterior and left lateral-basal consolidations *(Figure 1)*. Left cervical nodal biopsy for histopathological analysis with identification of giant cells and spherules with endospores inside *(Figure 2)*.

Therefore, it was decided to start treatment with amphotericin B deoxycholate in the intensive phase; with clinical improvement and without eventualities, thus determining hospital discharge. However, two weeks later, the patient presents again with temperature rise, in addition to an increase in volume at the proximal level of the right forearm accompanied by an increase in local temperature and mild erythema. It was decided

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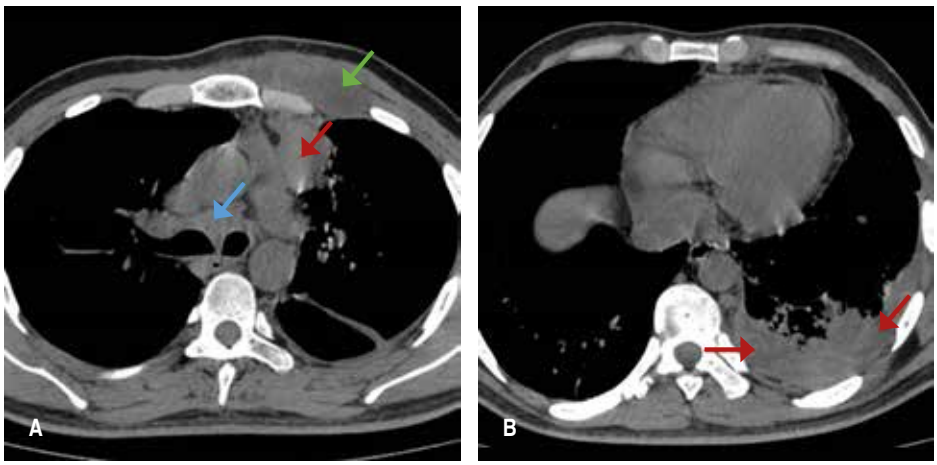

Figure 1:

Simple computed axial tomography of the chest. **A)** Mediastinal window, axial section: left lung consolidation; heterogeneous image suggestive of collection with soft tissue involvement (green arrow) without conditioning erosion of bone structures; mediastinal adenomegalies (blue arrow). **B)** Mediastinal window, axial section: in the left pleural space, pleural effusion is identified (red arrows) that conditions passive atelectasis.

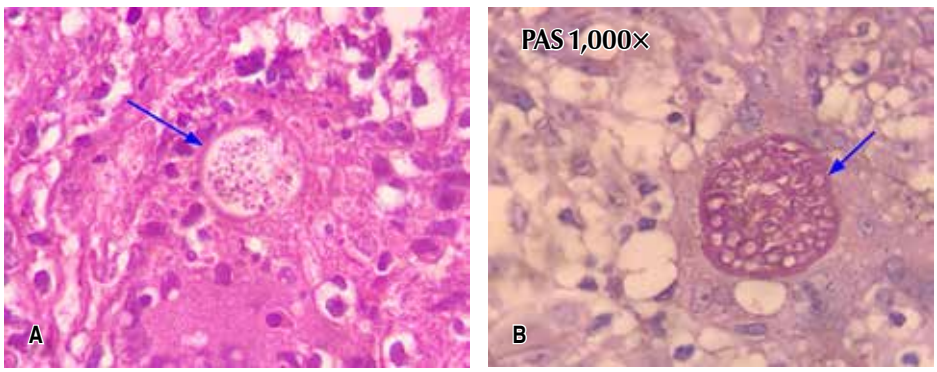

Figure 2:

Histological sections of lung abscess biopsy. Histopathological study of lung abscess: **A)** Hematoxylin and eosin staining: giant cells and spherules with thick walls of 50 µm in diameter are visualized. **B)** Periodic acid Schiff (PAS) staining: endospores are visualized within spherules.

to readmit him and start treatment with liposomal amphotericin B at a dose of 4 mg/kg every 24 hours. Patient with clinical improvement, without temperature increase and with decreased volume in injury, so hospital discharge was decided, with maintenance treatment with itraconazole for follow-up in the Outpatient Clinic area. One year after treatment, the report of IgM anticoccidioides antibodies is negative, so treatment suspension and definitive discharge from the service are decided.

DISCUSSION

Coccidioides spp. are fungi that commonly inhabit arid soils in the border states of the southern United States and northern Mexico, where soil and climate conditions favor the survival of this microorganism. The incidence of coccidioidomycosis has increased significantly in the last two decades in non-endemic regions, most of these cases are imported by patients after traveling or being exposed in endemic areas.[8] Travelers and people on the move who visit or transit to endemic regions determine a high risk of exposure to various microorganisms that are not prevalent in their localities of origin. Our patient had a residence history for one year in Tijuana, Baja California, due to the search for better working conditions, which constitutes his exposure to a region at high risk of infection by *Coccidioides spp*.

Coccidioidomycosis in its disseminated form is uncommon; however, it occurs regularly in subjects in a state of immunocompromise.[7] Pleural effusion in patients with coccidioidomycosis is detected in approximately 5 to 15% of cases; it is a frequent manifestation in pulmonary forms of the infection and it is very rarely observed in patients with disseminated coccidioidomycosis.[9] Immunocompetent patients may be able to «localize» the infection in the lungs by mounting a vigorous inflammatory response, resulting in increased vascular permeability of the pleura due to pro-inflammatory cytokines, resulting in the formation of pleural effusion. Patients with a disseminated form of the disease are less likely to generate an intense inflammatory response in the lungs, which results in less pleural inflammation and formation of pleural effusion.[10] We consider that in the case of our patient -despite not having identified any immunocompromising factor-, since he was not previously exposed to spores of the fungus

Coccidioides spp., he did not have an immunological memory that could have limited the dissemination of the infectious process.

Sample culture continues to be the gold standard for the diagnosis of coccidioidomycosis, followed by histopathological and cytological analysis; however, in addition to being directly dependent on the quality of the sample, this procedure requires a biosecurity level of the laboratory category 3, which conditions a limited availability in public hospitals in Mexico. Our hospital lacks a microbiology laboratory with this requirement, so the culture was performed in a surrogate manner. The identification of macrosiphonated septate hyphae in patients with coccidioidomycosis is a rare microbiological finding; however, there are isolated reports of this finding in disseminated infections associated with spherules with endospores inside.

CONCLUSIONS

The incidence of coccidioidomycosis has increased in recent times in places of low prevalence in relation to a phenomenon of global population mobility. Coccidioidomycosis is a diagnostic challenge in immunocompetent patients due to atypical presentation in its disseminated form.

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REFERENCES

1. Brown J, Benedict K, Park BJ, Thompson GR 3rd. Coccidioidomycosis: epidemiology. Clin Epidemiol. 2013;5:185-197. doi: 10.2147/clep.s34434.
2. Gastélum-Cano JM, Dautt-Castro M, García-Galaz A, Felix-Murray K, Rascón-Careaga A, Cano-Rangel MA, *et al.* The clinical laboratory evolution in coccidioidomycosis detection: future perspectives. J Mycol Med. 2021;31(3):101159. doi: 10.1016/j.mycmed.2021.101159.
3. Williams SL, Chiller T. Update on the epidemiology, diagnosis, and treatment of coccidioidomycosis. J Fungi (Basel). 2022;8(7):666. doi: 10.3390/jof8070666.
4. Facts and stats about Valley fever. CDC. Valley fever (Coccidioidomycosis). 2024. Available from: https://www.cdc.gov/valley-fever/php/statistics/index.html
5. Laniado-Laborín R, Arathoon EG, Canteros C, Muñiz-Salazar R, Rendon A. Coccidioidomycosis in Latin America. Med Mycol. 2019;57(Supplement_1): S46-S55. doi: 10.1093/mmy/myy037.
6. Johnson RH, Sharma R, Kuran R, Fong I, Heidari A. Coccidioidomycosis: a review. J Investig Med. 2021;69(2):316-323. doi: 10.1136/jim-2020-001655. Erratum in: J Investig Med. 2021;69(8):1486. doi: 10.1136/jim-2020-001655corr1.
7. Odio CD, Marciano BE, Galgiani JN, Holland SM. Risk factors for disseminated coccidioidomycosis, United States. Emerg Infect Dis. 2017;23(2):308-311. doi: 10.3201/eid2302.160505.
8. Diaz JH. Travel-related risk factors for coccidioidomycosis. J Travel Med. 2018;25(1). doi: 10.1093/jtm/tay027.
9. Light RW, Girard WM, Jenkinson SG, George RB. Parapneumonic effusions. Am J Med. 1980;69(4):507-512. doi: 10.1016/0002-9343(80)90460-x.
10. Thompson GR 3rd, Sharma S, Bays DJ, Pruitt R, Engelthaler DM, Bowers J, *et al.* Coccidioidomycosis: adenosine deaminase levels, serologic parameters, culture results, and polymerase chain reaction testing in pleural fluid. Chest. 2013;143(3):776-781. doi: 10.1378/chest.12-1312.