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Vertebral coccidioidomycosis with mechanical instability treated solely with antifungals: A case report

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ABSTRACT

Surgical treatment of vertebral coccidioidomycosis presents a challenge, with an unpredictable course and uncertain results. We present a 52-year-old man with disseminated infection due to coccidioidomycosis in the thoracolumbar spine, with vertebral instability, and deferral surgical treatment due to SARS-CoV-2 contingency. Treatment with itraconazole was initiated, followed by liposomal amphotericin B and fluconazole due to a relapse. The patient was discharged long-term with voriconazole. The axial pain improved without neurological deficits. Surgical treatment was not required. 2012 Elsevier Ltd. All rights reserved.

1. Introduction

Coccidioidomycosis, known as San Joaquin Valley fever, is caused by Coccidioides spp. Transmission occurs by inhalation of aerosolized arthrospores in the soil of endemic areas of southwestern United States, northern Mexico, and Central and South America. The infection tends to be self-limiting and often presents with fever, fatigue, rash, headache, night sweats, arthralgia, myalgia, or flu-like syndrome [1–3].

Dissemination is rare (0.5–1%); however, vertebral involvement is common and severe when accompanied by discitis, vertebral erosion, or neurological compromise, which also requires antifungal treatment. Surgical management is typically required in cases of mechanical instability, neurological compression, or paravertebral propagation [4]. Such procedures range from simple debridement to implant stabilization [5].

Although sole management with antifungals is not initially recommended for vertebral coccidioidomycosis with mechanical instability [6,7], there are reports of cases of vertebral lysis that received medical treatment without surgical instrumentation. A clinical case of coccidioidomycosis successfully treated with antifungals without the need for surgical intervention is presented.

2. Case presentation

A 52-year-old male, a México resident, arrived for consultation originally from Chiapas, who had worked in the railroad profession for 27 years with occupational exposure to coal smoke. The patient's medical history included type 2 diabetes mellitus (DM2; since four years) and hospitalization for possible community-acquired pneumonia (CAP) that required management with in-hospital antibiotics which was classified as day 0, and the patient was discharged. On day 38, he was admitted to the hospital for dry, non-cyanosing cough and dyspnea that had not subsided, weight loss of eight kg in the last five months, yellow expectoration with evolution to hemoptysis, and fever of 39 °C. Laboratory studies at day 39 showed leukocytosis (11,000/mm3) with neutrophilia, normochromic normocytic anemia, increased C-Reactive Protein (CRP) of 114 mg/L; tests for acid-fast bacilli and enzyme-linked immunosorbent assay for human immunodeficiency virus were negative; chest X-ray showed marked bilateral alveolar infiltrate in the lung bases (Fig. 1a); chest computed tomography (CT) revealed nodular

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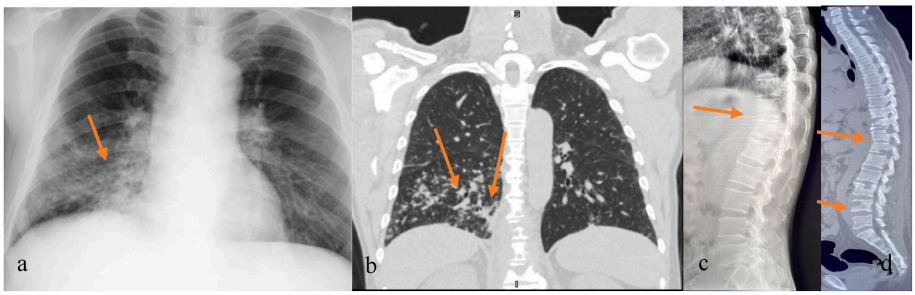

Fig. 1. Chest X-ray with accentuated bilateral alveolar infiltrate in lung bases (a). Axial tomography of the chest showing nodular lesions with a tendency to consolidate in the right middle and lower lobes, pulmonary bronchiectasis, and right basal pleural thickening (b). Plain lateral radiograph of the lumbar spine with kyphosis and non-evident lesions (c). Tomographic with thoracolumbar kyphosis, punched-out lytic lesions (T9-L5), 50 % loss of bone mass at T10-T12 (d).

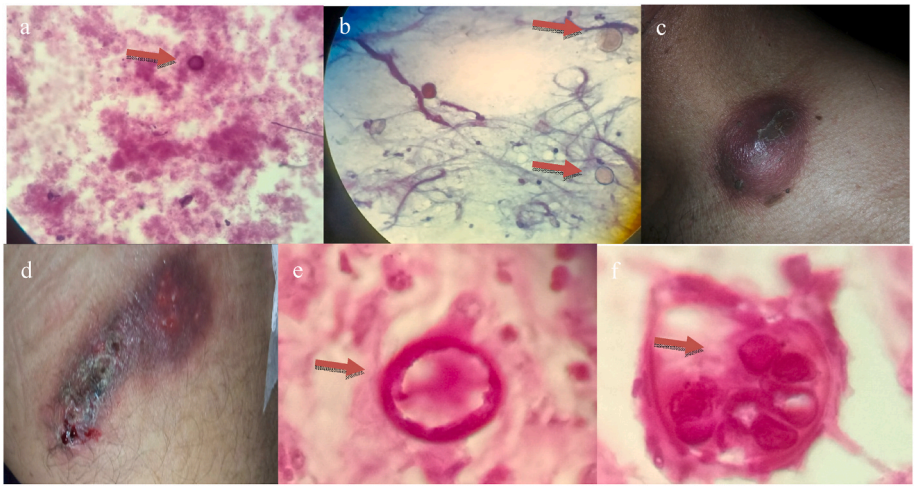

Fig. 2. A cytology sample H&E Harris staining, showing empty spherules (a–b). Lymphadenopathy with erythematous-violaceous exophytic neoformation, dark brown hematic crust, violaceous erythema, pustules, scabs on the neck and lumbar region. Lymph node sample PAS staining, with large spherules containing endospores inside, consistent with coccidioidomycosis (c–d). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

lesions with consolidation in the right middle and lower lobes, with pulmonary bronchiectasis and right basal pleural thickening (Fig. 1b); plain radiography of the thoracolumbar spine (Fig. 1c) revealed thoracolumbar kyphosis with no other lesions; therefore, disseminated infection was ruled out. A cytology sample was obtained by bronchoscopy on day 45 and revealed positive spherules for *Coccidioides* spp., as confirmed by hematoxylin and eosin (H&E) Harris staining (Fig. 2a–b). Thus, the diagnosis was made based on histopathology with no culture or susceptibility testing. On day 47, management with oral itraconazole 100 mg/day was started and continued for 16 months and suspended based on chest X-ray and clinical improvement. On day 660, six months after the end of treatment, the patient presented with localized dermatoses and lymphadenopathy in the neck, axillary, inguinal, and lumbar regions (Fig. 2c–d). Histological examination of a lymph node biopsy, on day 661, was performed with H&E and Periodic Acid-Schiff (PAS) revealed a chronic granulomatous inflammatory process with large spherules that contained endospores inside, which was consistent with *Coccidioides* spp. (Fig. 2e–f). The patient was hospitalized on day 667 and treated with 25 mg and 800 mg/day intravenous liposomal amphotericin B and fluconazole respectively. On day 670 it was decided to start with 200 mg oral voriconazole/12 h. During the hospital stay, SARS-CoV-2 coinfection was identified on day 671, and on day 674, the patient developed intermittent paresthesia in the lower extremities over the L2-L3 dermatome. A CT scan of the thoracolumbar spine on day 675 revealed 20° thoracolumbar kyphosis, punched-out lytic lesions of T9-L5, and loss of 50 % of the bone mass from T10-T12 (Fig. 1d). The patient continued to experience paresthesia, axial pain, and thoracic and lumbar tenderness, and was evaluated by the spinal surgery department on day 676. Physical examination revealed constant lumbar pain, without radiation, bilateral limp gait, support with a cane, bilateral toes-heels present, preserved lower extremity strength and sensitivity, normal tendon reflexes, absent neural tension or upper motor neuron signs, tenderness to thoracolumbar paravertebral palpation, bilateral sacroiliac predominance, thoracolumbar kyphosis, and a negative Adams sign. The patient was admitted to the orthopedics hospital and on day 677, and magnetic resonance imaging (MRI) of the thoracolumbar spine showed well-defined hyperintense lesions without mass effects and osteolytic lesions in the T9-L5 vertebral bodies (Fig. 3). The patient was diagnosed with potential vertebral instability, and surgery was considered for transpedicular vertebral stabilization and posterolateral arthrodesis. However, surgery could not be scheduled and was deferred because of the health contingency caused by the COVID-19. Medical treatment with voriconazole 200 mg/12 h was continued along with follow-up consultations until surgery could be scheduled. On day 857, another MRI scan revealed a favorable evolution with partial remission of the osteolytic lesions (Fig. 4). Therefore, orthopedic assessments and imaging studies were scheduled every six months, and on day 1037, a new MRI showed that almost all lesions had resolved (Fig. 5), with mild axial pain, without neurological deficits, remission of skin lesions, and walking without a cane. A decision was made to continue antifungal treatment in the long-term.

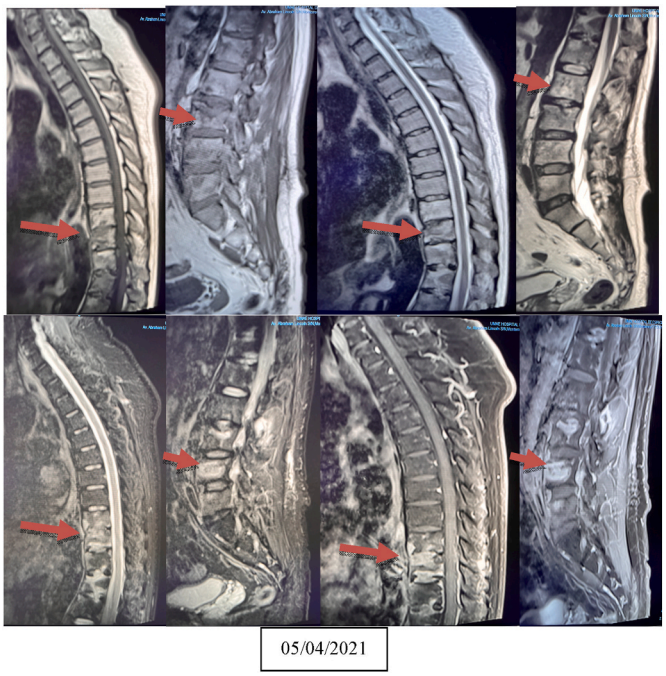

Fig. 3. Thoracic and lumbar Nuclear Magnetic Resonance image in T1, T2, Short Tau Inversion Recovery sequences and T1 sequence contrasted with Gadolinium, with well-defined hyperintense lesions without mass effect in T9-L5 vertebral bodies.

3. Discussion

The case discussed here presented initially with a pulmonary infection, which was not recognized and treated as a CAP. After 1 month the patient represented with a chronic pulmonary infection caused by *Coccidioides* spp. requiring antifungal treatment, with a relapse after stopping the itraconazole resulting in disseminated disease including the skin, lymphatic tissue, and thoracolumbar spine. Similar clinical pictures have been reported previously in 11 patients; 54 % presented with fever, chills, cough, chest pain, weight loss, pneumonia, axial pain, and pulmonary hilar adenopathy due to hematogenous dissemination to the spine with multilevel involvement [8]. Although it is an infection with uncertain behavior, clinical and radiological vertebral involvement must be intentionally studied to rule out or confirm dissemination because a delay in diagnosis could increase bone destruction [3,4,7]. However, in this case, recurrence was diagnosed by lymph node biopsy as only later clinical signs and symptoms became apparent and the spinal surgeon was consulted. Similarly, dissemination can put the lives of patients at risk, although mortality is low, as reported by only 31 (0.67 %) identified coccidioidomycosis as the cause of death [9].

Better outcomes have been reported with the combination of antifungal therapy and surgery in patients with bone disease, especially when located in the spine, due to residual vertebral deformity and its consequences, often implying multiple surgeries [10]. In this case, surgical treatment was preferred, but due to the SARS-CoV-2 health contingency, it was postponed, during which time the evolution of the disease with antifungals was favorable, despite the spinal deformity, and it was considered an adequate outcome. Antifungal treatment alone and in combination with spinal surgery (drainage, debridement, and fusion) has a success rate of 58 % and 86 %, respectively [3]. Nevertheless, if only spinal debridement and drainage are performed, the evolution may be complicated by increased instability due to aggressive debridement of soft tissue, which may prevent adequate healing and require fusion of vertebral bodies [11]. Thus, surgical treatment should always be considered as a complement to medical treatment and indicated to stabilize the spine and prevent neurological deficits, pain, and deformities [1,5]. In this case, thoracolumbar involvement predisposed the patient to instability requiring surgery, unlike a single thoracic condition that, as a rigid, stable region, can be treated with corset and antifungal therapy with good results [12]. Therefore, treatment success

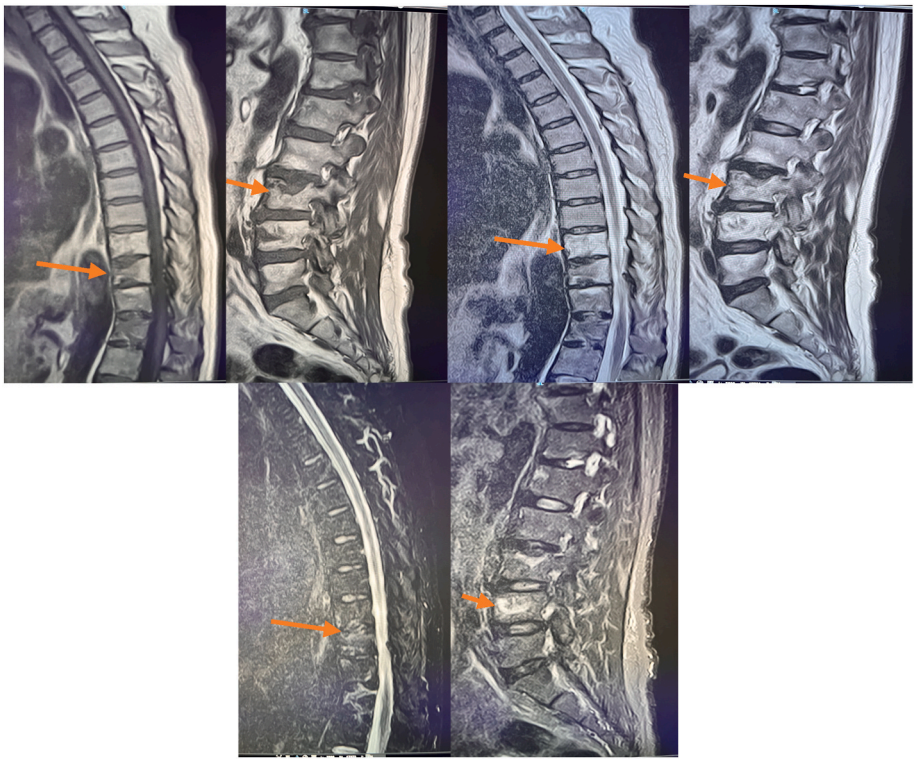

Fig. 4. Thoracic and lumbar Nuclear Magnetic Resonance image in T1, T2 and Short Tau Inversion Recovery sequences, still with osteolytic lesions in T9-L5 vertebral bodies in the process of remission.

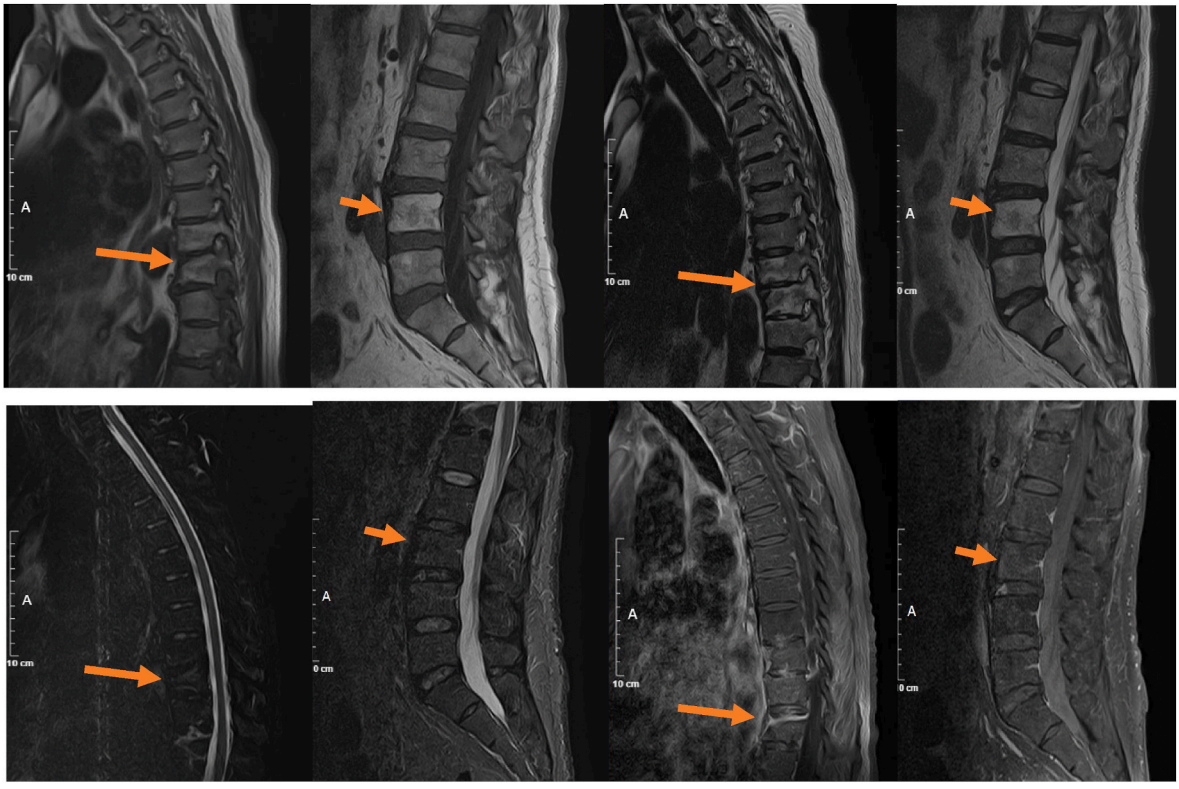

Fig. 5. Thoracic and lumbar Nuclear Magnetic Resonance image in T1, T2, Short Tau Inversion Recovery sequences and T1 sequence contrasted with Gadolinium, osteolytic lesions in T9-L5 vertebral bodies near full remission, but with persistent kyphosis.

based solely on antifungals in this case was considered possible, but not a given. The patient presented with treatable pain and thoracic kyphosis with no progress in neurological deficits. We believe that surgery could be indicated only when areas affected by bone infection with instability could be chosen as crucial points for fixation, limited vertebral fusion, and instrumentation and allow evolution with antifungal treatment at the least affected levels. The criteria for traumatic vertebral fractures [13] could support or guide surgical indications in these cases.

Ethical Form

Please note that this journal requires full disclosure of all sources of funding and potential conflicts of interest. The journal also requires a declaration that the author(s) have obtained written and signed consent to publish the case report/case series from the patient(s) or legal guardian(s).

The statements on funding, conflict of interest and consent need to be submitted via our Ethical Form that can be downloaded from the submission site www.ees.elsevier.com/mmcr. **Please note that your manuscript will not be considered for publication until the signed Ethical Form has been received.**

Funding source

There are none.

Consent

Written informed consent was obtained from the patient or legal guardian(s) for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Declaration of competing interest

There are none.

Acknowledgements

There are none.

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