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Case report

A Case of Osteomyelitis of the toe caused by Coccidioidomycosis in a 17 year-old with Diabetes Insipidus

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A B S T R A C T

We report a case of a 17-year-old male who presented with pain in his right first toe. His pain and swelling had worsened and x-rays of his foot revealed erosive changes of the great toe distal phalanx suggesting possible osteomyelitis. His co-morbidities were morbid obesity and diabetes insipidus. He was admitted to the hospital, blood cultures were drawn, and he was started on vancomycin for presumed bacterial osteomyelitis. He underwent incision and drainage of the fluctuant abscess of the toe, where a culture of the wound was taken. Preliminary results grew fungi. Being located in an endemic area, he was started on anti-fungal treatment for presumed disseminated coccidioidomycosis; culture was positive for *Coccidiodes immitis*. He also had serology positive for coccidioidomycosis titers. He had uneventful hospital stay and was discharged on long-term oral antifungal therapy.

Introduction

We present a case of a 17 year old boy with coccidiomycosis osteomyelitis of the right first toe. We discuss the epidemiology of disease caused by *Coccidioides immitis*, the patient's risk factors and hypothesize how these risk factors interacted.

This young man's case serves to illustrate the importance of considering a fungal etiology and the role of comorbid conditions on coccidiomycosis.

Case presentation

A 17 year-old male presented to the Emergency Department (ED) at our California Central Valley community hospital with pain and swelling of his right first toe. The pain had started two weeks prior to presentation; the swelling and redness had been present for only one week. His only significant past medical history was diabetes insipidus (DI) diagnosed at the age of 3. It was well controlled with desmopressin injections. Otherwise he was morbidly obese with a BMI of 51. He had gone to a local Urgent Care center where they noticed an ingrown toe nail, and supposed the infection was due that, removed part of the nail and discharged him on oral trimethoprim/sulfamethoxazol. During the next few days the pain, swelling, and redness increased. He returned to the Urgent Care center where he was administered ceftriaxone 1 g intramuscularly and was referred to the emergency department (ED) for x-rays, which revealed erosive changes of the right great toe distal phalanx, suggestive of osteomyelitis [Fig. 1].

Initial vital signs were all normal. Laboratory studies showed an elevated erythrocyte sedimentation rate (ESR) of 130, although the complete blood count was only minimally abnormal with a white cell count of 12,260 cells/microliter. He also had an elevated C-reactive protein (CRP) at 133.0 mg/L. The patient was admitted to the hospital. After blood cultures were drawn, he was started on vancomycin. A magnetic resonance imagining (MRI) scan with contrast showed acute osteomyelitis of the toe [Fig. 2].

On hospital day two he was taken to the operating room for partial distal hallux amputation; wound samples were sent for culture. He suffered no operative complications. On hospital day three, wound culture showed fungi. Coccidiomycosis was considered the most likely fungal infection, given that the patient had been born and raised in the Central Valley of California. He was started on 400 mg of fluconazole by mouth, twice daily. Following the surgery, his white count trended down to 8250, ESR down to 89, and CRP to 104.7. Blood serology and coccidioidomycosis titers were sent to an outside lab, at UC Davis medical center. The DNA probe came back positive for *Coccidioides immitis* on day five of hospital admission. Immunodiffusion was positive for IgG and IgM Complement fixation titer was 1:64, raising concern for dissemination. Aerobic culture grew *Coccidioides immitis*. The patient was discharged home five days after admission on fluconazole 800 mg by mouth daily. He continued to follow up with the infectious disease clinic and remained on long-term azole therapy to treat coccidiomycosis osteomyelitis.

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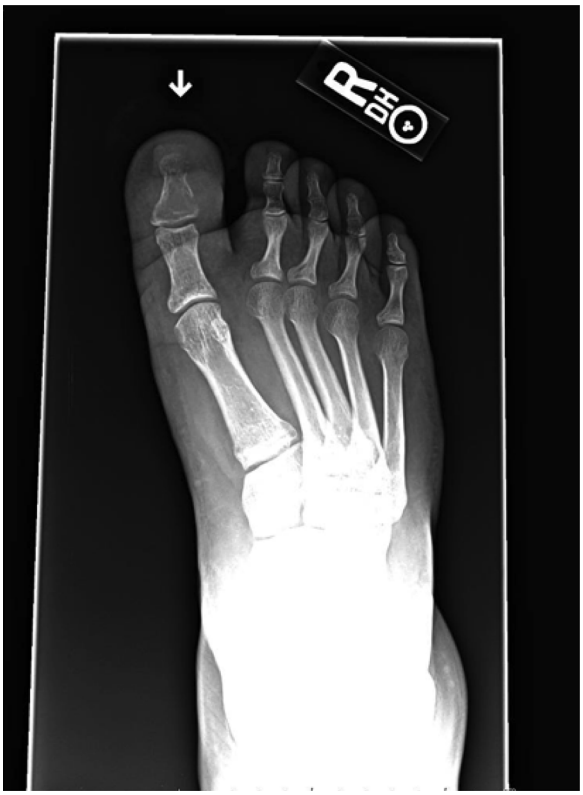

Fig. 1. X-ray of Right foot: Erosive changes of the great toe distal phalanx suggesting osteomyelitis.

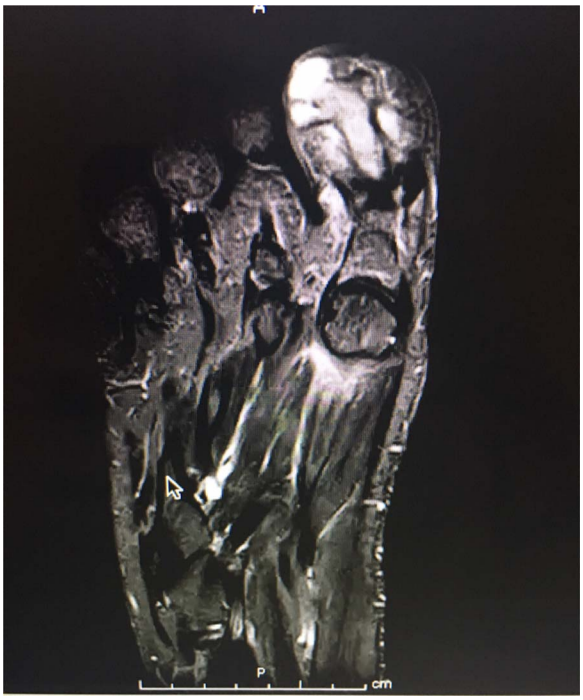

Fig. 2. MRI of Right foot with and without contrast: There is abnormal marrow signal intensity throughout the distal phalanx of the great toe. This is T1 hypointense with enhancement and STIR hyperintense. Findings compatible with acute osteomyelitis.

Discussion

Coccidiomycosis, also known as Valley Fever, is named after the San Joaquin (Central Valley) of California. It is caused by *Coccidiodes immitis*, a fungus endemic to the Southwestern United States, Mexico, and parts of Central and South America [1–3]. People are exposed to the organism by inhaling microscopic spores, usually from soil [4]. Inhalation of the spores from soil-dwelling, dimorphic fungi *C. immitis* usually is asymptomatic, but if symptomatic, most commonly causes pulmonary symptoms [5]. Pulmonary coccidioidomycosis is commonly misdiagnosed as bacterial community acquired pneumonia [3]. Clinical examination along with a thorough history is vital in many cases to determine diagnosis. There are no pathognomonic chest x-ray findings to indicate an infection with *C. immitis*.

Most people living in the Central Valley show serological evidence of past infection, however the majority remain asymptomatic or have had a mild, self-limiting respiratory disease [6,7]. Of those who become symptomatic, 60% have had a respiratory infection, usually pneumonia or bronchitis [8]. Most cases resolve spontaneously. Only 3–5% of patients develop chronic respiratory infection [8]. Almost all the morbidity and mortality associated with coccidioidomycosis is due to the chronic manifestations rather than to the acute respiratory infections [8].

Hematogenous spread of coccidioidomycosis is uncommon. The estimated incidence of dissemination is 1% of all infected individuals [9,10]. Extra-pulmonary manifestations such as skin, brain, or bone involvement are rare but can be fatal [11]. Of these extra-pulmonary manifestations, some 10–30% have osseous involvement [12,13]. Immunocompromised people have a higher chance of developing severe or disseminated coccidioidomycosis. Disseminated disease can cause meningitis, osteomyelitis, arthritis, and other soft-tissue infections. When the musculoskeletal system is involved, coccidioidomycosis prefers the axial skeleton, with joint involvement as the next most common target [11]. It has been hypothesized that at least some coccidioidomycosis bone infections arise through extension from adjacent soft tissues rather than from hematogenous spread [14].

The osteomyelitis that develops often affects the distal aspects of bones or bony prominences [9]. The most common radiographic finding with bony involvement includes osteolytic lesions, either with punched-out, well-circumscribed borders or demonstrating a permeative (or moth-eaten) appearance [10]. MRI, along with CT scan, has been shown to be helpful in evaluating the extent of soft tissue damage and bone erosion, along with determining any abscess formation [10].

Obesity, especially morbid obesity (BMI $\geq 35\ kg/m^2$), may be associated with immune suppression possibly due to the suppression of autophagy [15]. Furthermore, dendritic cells, which are key immune response cells, are significantly decreased in obesity [16]. With a BMI of 51, this patient may have been at higher risk. Diabetes Insipidus (DI) is a disease characterized by excessive thirst due to secretion of dilute urine. There are two main types. Central DI is caused by a pituitary deficiency of antidiuretic hormone (ADH). Nephrogenic DI results when the nephron is insensitive to ADH [17]. DI, by itself, is not an immunosuppressing disease; however there is one case report of DI in a patient with common variable immunodeficiency [18], although it is unclear whether there is a link between the two diseases. We found no case reports or studies mentioning osteomyelitis occurring in patients with diabetes insipidus.

Primary cutaneous coccidioidomycosis was also considered as the patient did not show any respiratory symptoms. However, it seemed unlikely as primary cutaneous infection is extremely rare, with about 25 cases previously reported in literature since 1926 [19]. Primary cutaneous infection results from direct traumatic inoculation of the organism into the skin by an external source and typically manifests as a painless, indurated nodule with ulceration [19]. This patient did not have this type of presentation. Diagnostic criteria for primary cutaneous coccidioidomycosis included: absence of pulmonary disease, clear evidence of traumatic inoculation, incubation period of 1 to 3 weeks, a chancriform lesion with a painless, ulcerated nodule or plaque, a negative or low complement fixation reaction, and spontaneous healing after some weeks [19,20]. Our case did not fit all of these criteria.

In summary, we present this case of a young man who presented like

a typical case of bacterial osteomyelitis, which, due to his co-morbidity of obesity, was initially assumed to be bacterial. He was ultimately diagnosed with coccidioidomycosis osteomyelitis, was treated appropriately, and discharged home after an uneventful short stay at the hospital.

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Consent

Written informed consent was obtained from the patient 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.

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