Case report

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

Ahmer Khalid⁎, Daniel J. Boken, Christine A. Nelson, Vicken Y. Totten

Kaweah Delta Health Care District, 400 West Mineral King Avenue, Visalia, CA 93291, United States

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/sulfamethozaxol. 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.
Coccidioidomycosis, also known as Valley Fever, is named after the San Joaquin (Central Valley) of California. It is caused by *Coccidioides 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 ≥ 35 kg/m²), 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.

**Funding**

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

**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.

**References**

[1] Hector RF, Laniado-Laborin R. Coccidioidomycosis—a fungal disease of the Americas. PLoS Med 2005;2(1):e2. http://dx.doi.org/10.1371/journal.pmed.0020002.

[2] Nguyen C, Barker BM, Hoover S, Nix DE, Ampel NM, Frelinger, et al. Recent advances in our understanding of the environmental, epidemiological, immunological, and clinical dimensions of coccidioidomycosis. Clin Microbiol Rev 2013;26(3):505–25. http://dx.doi.org/10.1128/CMR.00005-13.

[3] Rosenstein NE, Emery KW, Werner SB, Kao A, Johnson R, Rogers D, et al. Risk factors for severe pulmonary and disseminated coccidioidomycosis: Kern county, California, 1995–1996. Clin Infect Dis 2001;32(5):708–15. http://dx.doi.org/10.1086/319205.

[4] Malo J, Luraschi-Monjagatta C, Wolk DM, Thompson R, Hage CA, Knox KS. Update on the diagnosis of pulmonary coccidioidomycosis. Ann Am Thoracic Soc 2014;11(2):243–53. http://dx.doi.org/10.1513/AnnalsATS.201308-2865R.

[5] Fisher MC, Kornig GJ, White TJ, Taylor JW. Molecular and phenotypic description of Coccidioides posadasii sp. nov., previously recognized as the non-California population of Coccidioides immitis. Mycologia 2002;94(1):73–84.

[6] Borchers Andrea T, Gerdsbwin ME. Gerdsbwin the immune response in coccidioidomycosis. Autoimmun Rev 2010;10(2):94–102.

[7] Galgiani JN, Ampel NM, Blair JE, Catanzaro A, Johnson RH, Stevens DA, Williams PL. Coccidioidomycosis. Clin Infect Dis 2005;41(9):1217–23. http://dx.doi.org/10.1086/496991.

[8] Twong M, Thompson G. Coccidioidomycosis: recent updates. Semin Respir Crit Care Med 2015;36(05):746–55. http://dx.doi.org/10.1055/s-0035-1562900.

[9] Berli JU, Campbell WN, Katz RD. Coccidioidomycosis causing Osseomyelitis of the hand in an Immunocompetent patient. Hand 2014;10(3):562–4. http://dx.doi.org/10.1007/s11552-014-9696-9.

[10] Ellerbrook L, Laks S. Coccidioidomycosis osteomyelitis of the knee in a 23-year-old diabetic patient. Radiol Case Rep 2015;10(1):1034. http://dx.doi.org/10.2484/rcr.v10i1.1034.

[11] Megahan JP, Graves DS, Palmer PE, Stadnik RC, Dublin AB. Classic and contemporary imaging of coccidioidomycosis. AJR Am J Roentgenol 1981;136(2):393–404.

[12] Ho L, Schnall S, Schiller F, Holton P. Metacarpal coccidioidal osteomyelitis. Am J Orthop . 2011;40(1):34–6.

[13] Cortner JW, Schwartzmann JR. Bone lesions in disseminated coccidioidomycosis. Ariz Med 1957;14(7):401–4.

[14] Carter Ray A. Infectious granulomas of bones and joints, with special reference to coccidiodal granuloma. Radiology 1934;23(1):1–16.

[15] Joven Jorge, Guirro M, Marine-casadé R, Rodríguez-gallego E, Menéndez JA. Autophagy is an inflammation-related defensive mechanism against disease. Adv Exp Med Biol 2014;824:43–59.

[16] O’shea D, Corrigan M, Dunne MR, Jackson R, Woods C, Gaooatswe G, et al. Changes in human dendritic cell number and function in severe obesity may contribute to increased susceptibility to viral infection. Int J Obes 2015;39(1):1510–3.

[17] Rockenbauer D, Bichet D. Pathophysiology, diagnosis and management of nephrogenic diabetes insipidus. Nat Rev Nephrol 2015;11(10):576–88.

[18] Megias MC, Matei AM, Gonzalez Albarran O, Perez Lopez G. Partial central diabetes insipidus in patient with common variable immunodeficiency. Case Reports 2012;2012(July (1)). http://dx.doi.org/10.1136/bcr11.2011.5067. bcr1120115067–bcr1120115067.

[19] Garcia SGO, Alainis JCS, Flores MG, Gonzalez SEG, Cabrera LV, Candiani JO. Coccidioidomycosis and the skin: a comprehensive review. An Bras Dermatol 2015;90(2):610–9. http://dx.doi.org/10.1590/abd1806-4841-20153805.

[20] Wilson JW, Smith CE, Plunkett OA. Primary cutaneous coccidioidomycosis; the criteria for diagnosis and a report of a case. Calif Med 1953;79:233–9.