Coccidioidomycosis causing osteomyelitis of the hand in an immunocompetent patient

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Abstract Coccidioidomycosis osteomyelitis is a rare entity considered even more rare when identified in the immunocompetent patient. In non-endemic areas, the diagnosis of a fungus-causing osteomyelitis is often delayed or overlooked. This results in delayed or inappropriate treatment. We present the case of a 35-year-old immunocompetent male immigrant from India who was ultimately diagnosed as having *Coccidioidomycosis immitis* osteomyelitis of his ring finger metacarpal. His initial surgery included drainage and bacterial cultures only. When he failed to improve, he presented for a second opinion. The patient's origin and travel history coupled with the appearance of rapid bone destruction on plain radiographs prompted a second operation for tissue biopsy and culture for bacteria, fungus, and mycobacteria cultures. This case highlights the importance of a thorough clinical history in deriving an appropriate differential diagnosis prior to surgical intervention.

Keywords Coccidioides immitis · Coccidioidomycosis · Immunocompetent · Metacarpal · Osteomyelitis

Introduction

Coccidioides immitis is a fungus endemic to the American Southwest, Mexico, and portions of South America [12]. Many who have been exposed to the organism via inhalation of aerosolized spores remain asymptomatic or have only mild respiratory symptoms that resolve without specific treatment [13]. Hematogenous spread is relatively uncommon at an

estimated incidence of 1 % of all infected individuals [24]. At that rate, approximately 1500 Americans per year are affected by the disseminated organism which can affect any organ but appears to have a predilection for skin, soft tissue, meninges, joints, and bones [10, 21]. In patients with disseminated coccidioidomycosis, 10–30 % can have osseous involvement [13].

Given the low prevalence of infection in non-endemic areas and the rarity of hematogenous spread, the diagnosis of coccidioidomycosis as a cause of osteomyelitis is often delayed or missed. Correct diagnosis requires a high index of suspicion that can only come from a thorough history [8].

We present a case of an immunocompetent patient residing in a non-endemic area who was ultimately diagnosed with *C. immitis* osteomyelitis of the ring finger metacarpal. His risk of exposure was determined by a travel and occupation history.

Case Report

A 35-year-old male native of India who has been mostly living and working in the Eastern United States for 10 years presented with several months of hand pain. He spent 10 months living in Arizona about 9 months before presentation. He resided about 10 miles outside of Phoenix and pursued no outdoor activities. The only recognized environmental exposure was waiting every morning for transportation at an outdoor bus stop where he lived. He has a past medical history of pulmonary tuberculosis as a child in India that, per his report, was successfully treated with oral antibiotics. Three months prior to presentation to our clinic, and about 9 months after returning to Baltimore, he developed swelling, warmth, redness, and discomfort on the central dorsal aspect of his right hand. He felt that this may have been related to blunt trauma sustained when boarding a plane in Arizona destined for

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Chicago. Serial radiographs demonstrated a progressively destructive lytic bone lesion at the base of his ring finger metacarpal (Fig. 1). The rapid progression and recent onset raised suspicion for an infectious process. His initial treating surgeon had performed an open biopsy (negative for malignancy) and bacterial cultures (negative for aerobic or anaerobic growth).

He failed to improve after his biopsy and presented for a second opinion. He was taken back to the operating room for a repeat exploration, biopsy, and culture. Though immunocompetent, his history of recent work in the American Southwest and prior infection with tuberculosis prompted cultures to be sent for fungal and mycobacterial etiologies. Operative cultures grew out as “mold” with a final speciation of *Coccidioides posadasii*/*C. immitis*. Pathologic review established the presence of non-necrotizing granulomas on hematoxylin and eosin stains and fungal elements on silver stain. Importantly, in the process of evaluation, chest radiograph and contrast brain magnetic resonance imaging were obtained and were normal. About 4 weeks after the second hand surgery, while on antifungal therapy, he described increasing pain and swelling of his posterior right thigh. Upon reflection, he noted that he had discomfort in this area for several months. An incision and drainage were scheduled, but the abscess spontaneously drained. This abscess also yielded coccidioidomycosis. His disseminated coccidioidomycosis was treated with itraconazole 400 mg orally twice a day for 3 months and then 200 mg twice a day for 6 months. After surgical debridement and on this regimen, all symptoms and signs of infection resolved. He required no formal reconstruction of his metacarpal.

Discussion

C. immitis is a dimorphic fungus that infects approximately 150,000 Americans each year [4, 18]. It grows in a mycelial

Fig. 1 Radiograph demonstrating destructive lytic process involving ring finger metacarpal

state in soil and is endemic to particular regions of the American Southwest such as, Southern California, Texas, New Mexico, and Arizona; Mexico; and pockets of South America [23]. In nutrient-depleted conditions, the organism protects itself by shedding its hyphae and transforming into resistant spores called arthroconidia. When aerosolized by soil disruption, the potentially infectious arthroconidia can be inhaled. Once within a susceptible host, the organism has a dimorphic life cycle between parasitic spherules and offspring endospores. There is no conversion to mycelia within the infected host which means that the disease is not contagious [23]. Where rare human-to-human transmission may be possible in the presence of purulence in a moist environment such as a cast or prolonged occlusive dressing [21], it is estimated that close to 60 % of infected patients are subclinical and do not require any therapy [4, 21, 23]. There are no pathognomonic chest X-ray findings to indicate an infection with *C. immitis*. If symptoms do arise in the infected patient, they usually manifest as those of a nonspecific upper respiratory tract infection. At less than 1 % of all infections, disseminated coccidioidomycosis is quite uncommon [16, 23]. Though more common in immunocompromised patients, the disseminated form of the disease can also be found in the immunocompetent patient. Epidemiologic reports suggest that the disseminated form of the disease usually occurs within a year of acute infection and is more likely in pregnant women and those of African, Filipino, and Hispanic descent [17]. When present, the disseminated organism can affect any organ but appears to have a predilection for skin, soft tissue, meninges, joints, and bones [10, 21]. In those patients with disseminated coccidioidomycosis, 10–30 % can have osseous involvement [5, 10]. Reported areas of bone infection include the vertebral bodies, ribs, acromion, radius, carpus, metacarpals, patella, malleoli, and metatarsals [8, 20, 22]. The osteomyelitis that can develop often involves the distal aspects of bones or bony prominences [6, 15] and frequently presents with associated local superficial findings including abscess and sinus tracts [1, 22].

Diagnosing *C. immitis* infection first requires a high index of suspicion. As such, the importance of a thorough history cannot be over stated. In non-endemic areas, lack of suspicion is well documented and results in missed or delayed treatment [8]. The gold standard for diagnosis is culture and/or serological testing. On the appropriate culture medium, the endospores will undergo change to their mycelia form. The laboratory must be alerted when cultures that may grow and cause coccidiomycosis are delivered because the organism growing on media is a biosafety level 3 pathogen. Histologically, spherules with endospores can be appreciated and are pathognomonic for *C. immitis*. An antibody titer can be useful to dynamically follow the disease during treatment. An exception to this is meningeal infection that can present without elevation of IgG. There exist no clear guidelines for screening

or imaging organ systems once a patient is diagnosed with disseminated coccidioidomycoses.

The treatment of disseminated *C. immitis* is particularly challenging and involves a prolonged course of antifungal therapy [23]. Secondary to toxicity concerns, intravenous amphotericin B has largely been replaced by oral therapy with azoles (itraconazole, voriconazole, fluconazole) or liposomal amphotericin B [6, 7, 19, 23]. Of the above, itraconazole is the preferred azole as it has demonstrated a trend towards increased effectiveness and a decreased infection relapse rate in a head-to-head comparison with ketoconazole [11].

Patients with meningeal involvement may require lifelong suppression therapy as relapse can be deadly and relapse rates can be as high as 78 % [9].

Surgical debridement to decrease necrotic tissue burden and infectious bioburden is an integral part of the treatment [2, 14]. This is quite different than in disseminated tuberculosis where debridement is rarely indicated. For the reasons detailed above, even after surgical debridement, involvement of an infectious disease specialist is of paramount importance.

Development of a live vaccine against *C. immitis* has been successful in animal models and is currently under active research [3, 6].

When presented with an immunocompromised patient, most hand surgeons readily consider a broad range of infectious agents as potential causes. However, in non-endemic areas, fungal infections are often missed as part of this differential diagnosis. When a fungal infection is suspected, the hand surgeon should be aware of the possibility of disseminated disease and should consider other sites of concurrent infection. A thorough history including country of origin, residence, and travel is the key to early diagnosis and appropriate treatment.

Conflict of Interest Jens U. Berli declares that he has no conflicts of interest.

Wayne N. Campbell declares that he has no conflicts of interest.

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All authors have (1) reviewed the final version of the manuscript, (2) believe that it represents valid work, (3) approve it for publication, (4) certify that none of the material in the manuscript has been previously published and is included in another manuscript or currently under consideration for publication elsewhere, (5) certify that this article has not been accepted for publication elsewhere nor have any rights or interests in the manuscript been assigned to any third party and (6) the data upon which the manuscript is based, and will be able to produce it if the editor of *Hand* requests it.

Statement of Human and Animal Rights A statement of human and animal rights is not applicable to this paper because this is not a research study, and there was no human or animal experimentation.

Statement of Informed Consent Because this is a case report with no identifiable patient information, no informed consent was needed.

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