Acta Scientific Orthopaedics (ISSN: 2581-8635)

Volume 3 Issue 3 March 2020

Case Report

Tibial Osteomyelitis: A Case Report of Hyalohyphomycosis

Jahanavi M Ramakrishna[1], Claudia R Libertin[1]*, Courtney E Sherman[2] and Glenn G Shi[2]

[1]*Division of Infectious Diseases, Mayo Clinic, Fl, USA*

[2]*Department of Orthopedic Surgery, Mayo Clinic, Fl, USA*

***Corresponding Author:** Claudia R Libertin, Division of Infectious Diseases, Mayo Clinic, Fl, USA.

DOI: 10.31080/ASOR.2020.03.0151

Received: February 19, 2020

Published: February 24, 2020

Abstract

Microascus sp. has rarely been associated with invasive infections, and never reported as causing osteomyelitis. This report describes a rare case of tibial osteomyelitis due to hyalophomycosis in an immunocompetent patient with several comorbidities. Using advanced imaging and various microbiologic diagnostic techniques, *Microascus* was identified as the causative agent. The patient was managed with surgical debridement, delayed closure and antifungal pharmacotherapy. *Microascus* usually only progresses to invasive infection in immunocompromised patients and has yet to be reported as a cause of osteomyelitis.

Keywords: *Microascus*, Osteomyelitis, Hyalohyphomycosis

Introduction

Hyalohyphomycosis is a term describing a fungal infection caused by molds whose basic tissue form is hyaline hyphal elements that may be branched or unbranched and without pigment in their wall [1]. Hyalohyphomycosis typically includes species such as *Fusarium*, *Penicillium*, *Scedosporium* and other rarer entities such as *Microascus*. These organisms are commonly found in soil, air, and in plant litter, wood, compost and animal remains. Acquisition in humans has been identified as primarily from respiratory or integumentary sources [2]. Serious localized infections are extremely rare in otherwise healthy individuals. These hyalohyphomycoses with deep localized or disseminated infections typically occur in immunocompromised hosts, such as those with hematologic malignancies or organ transplantations [3].

Scopulariopsis (*Microascus*) species, one of the hyalohyphomycoses, are common causes of non-invasive infections, including onychomycosis and keratitis [4,5]. These fungi belong to the ascomycete family Microascaceae [2]. Invasive disease from this particular organism, though uncommon, has been reported in both immunocompetent and immunosuppressed patients and include infections such as endocarditis, sinusitis, brain abscess, deep cutaneous, and localized pulmonary and disseminated disease [6].

We describe a rare case of *Microascus sp* tibial osteomyelitis, which was successfully treated with multiple surgical debridements and two prolonged courses of voriconazole. This was a hyalohyphomycosis caused by one of the rarer molds *Microascus* species. It meets the criteria for proven invasive fungal disease caused by molds as described by the consensus group of the European Organization for Research and Treatment of Cancer/Invasive fungal Infections Cooperative Group and the National Institute of Allergy and Infectious Diseases Mycoses Study Group (EORTC/MSG) [7]. Hyphae elements were noted on the surgical histopathology, the pathogen grew in culture, and *Microascus sp* was identified by molecular sequencing.

Case Report

The patient presented to our hospital with history of several months of left lower leg pain. Comorbidities included hypertension, type II Diabetes Mellitus, peripheral arterial disease and prior right below knee amputation due to bacterial osteomyelitis. Clinical evaluation showed to gross deformities or sinus tracks. Radiographs of the left ankle revealed a mixed lytic and sclerotic lobulated lesion (Figure 1). MRI of the left leg showed evidence of distal lytic lesions on the anterior aspect of the tibia, which was suggestive of micro abscesses (Figure 2). A CT guided biopsy's histopathology revealed acute inflammation and hemosiderin-laden macrophages, most consistent with osteomyelitis. Bacterial, fungal and AFB cultures from the CT-guided biopsy had no growth. He then underwent an open biopsy of the left distal tibial lesion, combined with irrigation and debridement of the distal tibia including grafting with anti-

biotic-eluding cement (Figure 3). The only cultures that showed growth were the fungal cultures which grew the *Microascus* sp organism. The histopathology demonstrated areas of bone necrosis and granulomatous inflammation. Hyphae with branching at 45- and 90- degrees on Grocott's methenamine silver stain were noted. Based on microscopic morphology from lactophenyl cotton blue tape preparation (40x) after 16 days of growth on Brain Heart Infusion agar media at 30 degrees C septate hyphae were seen terminating in flask-shaped annellides. Narrow, cylindrical annellated zones with gradual tapering terminate in conidiogenous cells were noted in small brush-like groups, or occasional single conidia. Conidia are obovoidal with truncate bases, mostly rough walled (Figure 4). Sequencing was done on the D2 region of the fungal 28S ribosome. This yielded a final identification of *Microascus* sp. with homology of 99.3% as compared to the reference database. Sensitivities were performed (U.T. Health Science Center San Antonio, 7703 Floyd Curl Drive, Department Of Pathology, Fungus Laboratory San Antonio, TX 78229 - 3900): posaconazole was 0.125 mcg/ml, voriconazole was 4 mcg/ml, amphotericin B was < 0.03 mcg/ml. The patient was treated with voriconazole 400 mg daily for 3 months with therapeutic levels.

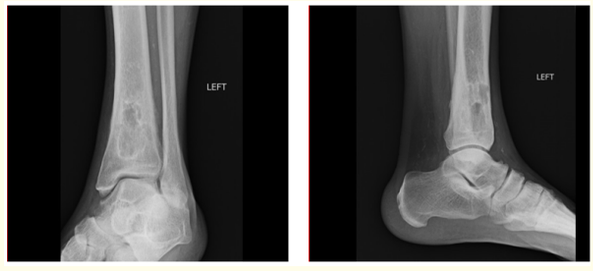

Figure 1: Preoperative AP and Lateral x-ray: AP and lateral x-rays of the left ankle demonstrate the lesion which has a mixed lytic and sclerotic lobulated appearance.

Figure 2: Preoperative MRI and MRI 2: The distal tibial lesion is seen on the sagittal MRI images to be intramedullary. The sections of the lesion are suspicious for micro abscesses.

Figure 3: Intra operative photograph: Intraoperative photograph shows direct anterior approach to the lesion, open biopsy. The patient subsequently underwent irrigation debridement and grafting.

Figure 4: Lactophenol cotton blue tape preparation of Microascus sp. (40X) after 16 days of growth on Brain Heart Infusion (BHI) agar media at 30 degrees C. Septate hyphae terminate in flask-shaped annellides. Narrow, cylindrical annellated zones with gradual tapering terminate in conidiogenous cells, noted in small brush-like groups, or occasional single conidia. Conidia are obovoidal with truncate bases, mostly rough walled.

Within 2 - 3 months of completing the voriconazole course, the patient developed soreness at the anterior aspect of the distal lower leg with wound drainage. A pustule had formed at that site after stopping voriconazole. An MRI showed rim-enhancing lesions of the anterior distal tibia. An anterior draining sinus tract was connected to the bone graft at the site of a draining ulcer. The tract coursed through an area of subcutaneous phlegmonous changes. Surgical debridement was performed to bone with application of a vacuum assisted closure (VAC) application. Three consecutive surgical debridement and curettage procedures were performed over a span of 8 days, one that included use of amphotericin eluding cement to place in the cavities. IV vancomycin and caspofungin was

started pending operative bacterial, fungal, and AFB cultures. Amphotericin B was avoided due to the patient's renal insufficiency. All cultures were without growth after 30 days. Histopathology showed acellular debris associated with acute inflammation and hemosiderin-laden macrophages along with scant fragments of bone. Grocott's methenamine silver stain did not show fungal elements. The patient received 4 months of a planned 6-month course of voriconazole with excellent wound healing and bone repair. The patient self-terminated voriconazole against medical advice unrelated to side effects. A 6 month visit post completion of the voriconazole course of therapy revealed bone healing (Figure 5) radiographically and clinically (Figure 6).

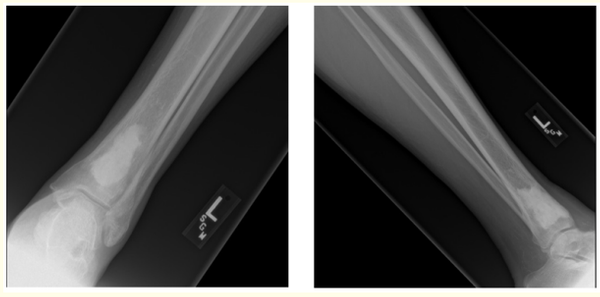

Figure 5: Postoperative AP/lateral x-rays: Final follow-up x-rays AP and lateral of the ankle shows progressive incorporation of the bone graft without radiolucency to suggest recurrence of the infection.

Figure 6: Clinical picture of the patient's left ankle showing the incision has been well healed without evidence of clinical infection.

Discussion

This case of *Microascus sp* tibial osteomyelitis is extremely rare. This likely is the first case reported. The hyalohyphomycosis opportunistic pathogen typically reported to involve bone has been *Fusarium* sp, but not this rarer organism [2]. A deep scopulariopsosis infection has been described involving the fascial planes and tendons of an ankle; but, the patient was not immunocompromised and no bone involvement was noted [8]. This case of *Microascus sp* tibial osteomyelitis progressed over several months in a diabetic patient who had no hematologic malignancy, known immunosuppression or clear site of entry for infection. The open biopsy showed inflammatory responses of granulomatous necrotic areas of bone and micro abscesses typical of hyalohyphomycosis. Branching septate hyphae were seen; but angioinvasive disease was not noted. Aggressive debridement combined with voriconazole therapy 400 mg daily for 3 months was initially given with a good response. However, the patient relapsed within 2 months with an inflammatory process (though no pathogen was identified). Repeat cultures (bacterial, fungal, and mycobacterial) did not grow the organism after the second set of debridements of the tibia. Voriconazole was continued for 4 months with an excellent clinical response. Patient reported no pain at the surgical site at the final clinical follow up at 10 months following the final debridement procedure. The inflammatory markers ESR and CRP normalized. Final ankle radiographs show incorporation of the bone graft without radiographic evidence of osteomyelitis.

Key in identifying this organism is the presence of hyphae elements in the surgical histopathology. Although microscopic analysis of tissue may not distinguish among the various mold pathogens, finding distinctive fungal elements especially the presence of conidia or ascomata may provide valuable information in the identification. Molecular sequencing was used to provide a rapid and accurate identification of this uncommon opportunistic pathogen, *Microascus* sp.

There are close to 40 accepted species of *Scopulariopsis* and *Microascus* [7]. Due to the prior practice of dual naming system of fungi, Iwen., *et al.* reviewed prior infections caused by both *Scopulariopsis* and *Microascus* species (a teleomorph) in 2012 [9]. Only 33 cases of infections from these organisms were found. Thirty-four percent or 11 of those patients had hematologic malignancies; the other 21 had complications of solid organ transplant, intravenous drug abuse, heart disease or chronic granulomatous disease. Dissemination occurred. In four of the cases blood cultures grew the fungi. Twenty-one of the cases showed hyphae elements in the tissue as noted in our case. In addition, 8 of the cases described blood vessel invasion [9]. As in this case, culture identification methodology can be quite difficult due to micromorphological characteristics that are not distinguishing between related species. Among the 33 prior reported cases of deep *Scopulariopsis* and *Microascus* infections, four recent ones described used genomic sequencing methods to confirm the species identification. Two of the 33 cases involved necrotic bone related to invasive sinonasal infections

[10,11]. No case of *Microascus* osteomyelitis has been reported until date.

In summary, this is a rare case of *Microascus* sp tibial osteomyelitis. Clinical suspicion confirmed by advanced imaging and pathology lead to the diagnosis. Following debridement, delayed closure and antifungal medical management the patient healed and returned to baseline function.

Bibliography

1. Abbott Sean P., *et al*. "Microascus Brevicaulis Sp. Nov., the Teleomorph of Scopulariopsis Brevicaulis, Supports Placement of Scopulariopsis with the Microascaceae". *Mycologia* 90.2 (1998): 297.

2. Ajello L. "Hyalohyphomycosis and Phaeohyphomycosis: Two Global Disease Entities of Public Health Importance". *European Journal of Epidemiology* 2.4 (1986): 243-251.

3. Beltrame A., *et al*. "A Fatal Case of Invasive Fungal Sinusitis by Scopulariopsis Acremonium in a Bone Marrow Transplant Recipient". *International Journal of Infectious Diseases* 13.6 (2009): e488-e492.

4. Bonifaz Alexandro., *et al*. "Onychomycosis by Molds. Report of 78 Cases". *European Journal of Dermatology* 17.1 (2007): 70-72.

5. De Pauw Ben., *et al*. "Revised Definitions of Invasive Fungal Disease from the European Organization for Research and Treatment of Cancer/Invasive Fungal Infections Cooperative Group and the National Institute of Allergy and Infectious Diseases Mycoses Study Group (EORTC/MSG) Consensus Group". *Clinical Infectious Diseases* 46.12 (2008): 1813-1821.

6. Iwen PC., *et al*. "Utilization of the Internal Transcribed Spacer Regions as Molecular Targets to Detect and Identify Human Fungal Pathogens". *Medical Mycology* 40.1 (2002): 87-109.

7. Iwen Peter C., *et al*. "Invasive Scopulariopsis Brevicaulis Infection in an Immunocompromised Patient and Review of Prior Cases Caused by Scopulariopsis and Microascus Species". *Medical Mycology* 50.6 (2012): 561-569.

8. Kriesel JD., *et al*. "Invasive Sinonasal Disease Due to Scopulariopsis Candida: Case Report and Review of Scopulariopsosis". *Clinical Infectious Diseases* 19.2 (1994): 317-319.

9. Neglia Joseph P., *et al*. "Invasive Scopulariopsis in the Immunocompromised Host". *The American Journal of Medicine* 83.6 (1987): 1163-1166.

10. Ragge NK., *et al*. "A Case of Fungal Keratitis Caused by Scopulariopsis Brevicaulis: Treatment with Antifungal Agents and Penetrating Keratoplasty". *British Journal of Ophthalmology* 74.9 (1990): 561-562.

11. Sekhon AS., *et al*. "Deep Scopulariopsosis: A Case Report and Sensitivity Studies". *Journal of Clinical Pathology* 27.10 (1974): 837-843.