Pathologic Quiz Case

Unremitting Ulcer in a Scuba Diver

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A 34-year-old woman presented in September 1998 with spontaneous pain and swelling of the right index finger at the proximal palmar interphalangeal crease. There was no associated history of trauma, with the exception of a bee sting in the same area that had occurred in 1996. The patient’s hobbies included scuba diving and maintaining an aquarium. On examination of her finger, a discrete mass was noted, and a clinical diagnosis of giant cell tumor of the tendon sheath was made. Surgical exploration of the nodule was consistent with an infectious process, and tissue was sent for bacterial, fungal, and mycobacterial cultures, including *Mycobacterium marinum* and *Mycobacterium haemophilum*. All cultures were recorded as negative for growth. The patient failed to respond to various antimicrobial therapies, which included azithromycin dihydrate and vancomycin, and the surgical wound did not heal spontaneously. Several subsequent attempts at debridement and surgical closure of the chronically open and draining wound failed, while repeat cultures of the drainage were positive for *Streptococcus agalactiae* but negative for mycobacteria.

The patient was referred to the Henry Ford Hospital, Detroit, Mich, in early November 1999 for reevaluation. A radiograph of the lesion showed soft tissue swelling with intact bone along the entire index finger. There was no joint space narrowing at the proximal interphalangeal joint or any other joint of the right hand. Ultrasound of the lesion could not rule out the presence of a foreign body, but magnetic resonance imaging highlighted a soft tissue abnormality consistent with granulation tissue. A provisional diagnosis of a foreign body infection with the possibility of a marine or aquarium-associated microorganism was considered. Excision of the flexor tenosynovium was performed.

The microbiologic testing of the tissue included Gram stain with aerobic and anaerobic bacterial cultures, acid-fast bacilli smear, mycobacterial culture, fungal smear, and fungal cultures. Once again, all microbiological results were negative.

Histopathologic examination of the specimen revealed necrotizing granulomatous inflammation of the subcutaneous tissue (Figure, A). The hematoxylin-eosin–stained sections demonstrated spherical organisms of varying size with central basophilia located within the necrotic granuloma (Figure, A).

The organisms were stained with Gomori methenamine silver (Figure, B and D) and mucicarmine (Figure, C) stains, which highlighted the internal septation and double-layer cell wall.

The biopsy revealed predominantly fibrous tissue with prominent chronic inflammation and a focus of necrotizing granulomatous inflammation containing numerous nonbudding cells, ranging in size from 3 to 30 μm in diameter. On hematoxylin-eosin–stained sections, the organisms had a hyaline appearance with variable degrees of central basophilia. Staining with Gomori methenamine silver and periodic acid–Schiff demonstrated internal septation and multiple endospores (2–4 μm). A mucicarmine stain of the tissue was focally positive, but no capsular material was identified surrounding the organisms.

What is your diagnosis?
Prototheca species are aerobic, achlorophyllous, algae-like, unicellular organisms. The primary cell or sphere is known as the *theca*, and the appearance of the autosporeulating theca has been termed mulberry-like endosporeulation,\(^3\) morula,\(^4\) and frambusiform.\(^5\) Prototheca were first recognized as human pathogens in 1964.\(^6\) To date, 7 species of *Prototheca* have been identified, but only 2 have been associated with human disease, namely, *Prototheca wickerhamii* and *Prototheca zopfi*.

*Prototheca* species are widely distributed in the environment and have been isolated from water, sewage, and soil, but fewer than 100 cases of human infection have been reported in the literature.\(^6\) Trauma and contaminated water are the most common vectors of infection,\(^7\) while the face and exposed extremities are the usual sites of cutaneous protothecosis. Protothecosis has been reported in both immunocompromised and immunocompetent individuals, and clinical presentations of infection include focal or disseminated, chronic cutaneous/subcutaneous infection,\(^5\) bursitis,\(^8\) and, rarely, systemic infection. Soft tissue infections favor the olecranon bursa, sites of trauma, or surgical wounds exposed to soil or water (eg, hand tendon repair). The cutaneous lesion may vary in appearance, depending on the immune status of the individual. Immunocompromised patients typically present with vesiculobullous and ulcerative lesions, purulent discharge, and crusting. In contrast, immunocompetent individuals usually develop lesions that range from slightly erythematous nodules and papules to eczematous plaques with or without associated cellulitis.\(^9\) Gradual enlargement of the lesions typically occurs over weeks to months, with no tendency for spontaneous resolution.\(^10\)

The diagnosis of protothecosis is generally made by direct identification of the organism in histologic sections or by culture of the organism from infected tissue. The cells of *P. wickerhamii* are round in comparison to the oval or cylindrical shapes of *P. zopfi*. Both species reproduce by internal septation, resulting in the formation of sporangia. Each sporangium contains up to 20 endospores that are released on rupture. The sporangia of *P. wickerhamii* (3–13 μm) are smaller than those of *P. zopfi* (14–16 μm). The latter species produces sporangia less frequently. Organisms that morphologically mimic *Prototheca* include those capable of forming endosporeulating spherules, such as *Coccioidoides immitis*, *Rhinosporidium seeberi*, and *Chlorella* species. *Coccioidoides immitis* and *R. seeberi* form sporangia 2 to 10 times larger than protothecal sporangia.\(^2\) Lesions produced by *Chlorella* species are reported to be green on gross examination. Moreover, they contain a greater amount of periodic acid-Schiff-positive, diastase-sensitive granules than do *Prototheca* species, owing to the starch present within the cytoplasm.\(^3\)

Nonsporeulating organisms mimicking *Prototheca* species include *Cryptococcus neoformans*, *Blastomyces dermatitidis*, and *Paracoccidioides brasiliensis*.\(^2\) *Cryptococcus neoformans* is an encapsulated budding yeast, whereas *B. dermatitidis* produces broad-based budding yeast cells and *P. brasiliensis* forms multiple buds on a single yeast cell.\(^3\)

In general, protothecosis does not resolve spontaneously.\(^10\) The drug of choice for systemic or disseminated protothecosis is Amphotericin B, while the role of imidazole is unclear. Focal cutaneous or subcutaneous infection can be treated with surgical excision with or without Amphotericin B. Our patient was treated surgically without recurrence to date.

### References