Case Report

Disseminated *Prototheca wickerhamii* Infection with Arthritis and Tenosynovitis

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ABSTRACT. Achloric algae of the *Prototheca* species are a rare cause of infection in humans. These infections are usually localized to the skin, olecranon bursae, and tendon sheaths of the hands and wrists. Our patient with acquired immunodeficiency syndrome and a chronic *Prototheca wickerhamii* skin infection of the hand developed tenosynovitis and arthritis of his ankle in the setting of a documented algemia. This is the first reported case of protothecal arthritis and tenosynovitis resulting from hematogenous dissemination. The reported musculoskeletal manifestations of protothecal infections are reviewed. (J Rheumatol 2004;31:1861–5)

Key Indexing Terms:
PROTOTHECA ALGAE TENOSYNOVITIS
INFECTIOUS ARTHRITIS ACQUIRED IMMUNODEFICIENCY SYNDROME

Prototheca are achloric algae that can be a rare cause of infection in humans. Infections are generally localized to exposed skin of the face and distal extremities, olecranon bursae, and tendon sheaths of the hands and wrists. They occur in both immunocompetent and immunocompromised hosts. Systemic protothecosis with visceral and meningeal involvement occurs rarely in immunocompromised individuals. We describe a man with acquired immunodeficiency syndrome (AIDS) and a chronic *Prototheca wickerhamii* skin infection of the hand who subsequently developed arthritis and tenosynovitis of his ankle in the setting of a documented algemia. This is the first reported case of protothecal arthritis and tenosynovitis arising as a result of hematogenous dissemination.

CASE REPORT

A 49-year-old man with advanced AIDS was admitted to the hospital with drug-induced pancreatitis. A nonhealing wound had developed on his left thumb 28 months prior to this hospitalization. Four months after its onset, a physician described a firm, 1 cm nodule with serous drainage and obtained a culture that grew *P. wickerhamii*. The patient had an aquarium that he regularly cleaned without wearing gloves. He was treated with oral itraconazole and topical amphotericin for 6 weeks and then with intravenous amphotericin B for 2 weeks because of lack of response to the initial regimen. The drainage resolved but the nodule persisted. A biopsy of the nodule, obtained 9 months prior to hospitalization, showed granulomatous inflammation with ovoid basophilic bodies both in and around histiocytes (Figure 1). A culture grew *P. wickerhamii*. Oral itraconazole was resumed. Within 3 weeks of this biopsy, the patient inadvertently stepped in a hole and forcibly dorsiflexed his left ankle; swelling of the ankle persisted for over 2 months, prompting an intraarticular injection of dexamethasone. Five months prior to hospitalization, the patient developed several subcutaneous nodules in his left lower extremity, despite ongoing itraconazole therapy. He was treated with intravenous amphotericin for 14 days for presumed disseminated protothecosis; the nodules decreased in size. Chronic oral tetracycline therapy was started at the completion of the amphotericin. Two weeks prior to hospitalization, the patient developed tender subcutaneous nodules on the right anterior leg and the dorsum of his left foot.

During the second week of his hospitalization, he developed fever and swelling of the left ankle. Physical examination at that time demonstrated multiple verrucous plaques on the left thumb, some of which were ulcerated (Figure 2). Subcutaneous nodules were present in the left forearm, right calf, right peroneus tendons, and extensor digitorum longus tendon sheath of the left ankle (Figure 3). The left ankle was diffusely swollen, warm, and tender. Fluid samples aspirated from the extensor digitorum longus tendon sheath and from the left ankle joint each grew *P. wickerhamii*. Numerous intracellular ovoid organisms that stained with Gomori methenamine silver were present in the fluid aspirated from the tendon. The scant amount of fluid obtained from the ankle joint was insufficient for cell count. On the day that the ankle was aspirated, a blood culture planted 2 weeks earlier was reported as growing *P. wickerhamii*.

He was treated with intravenous amphotericin B but failed to respond. His mental status deteriorated. The cerebrospinal fluid white blood count was 811/mm^3 with 88% neutrophils, glucose was 39 mg/dl, and protein was 243 mg/dl. Culture of the cerebrospinal fluid was sterile. The patient died on the 27th hospital day.

DISCUSSION

The genus *Prototheca* includes 3 species of unicellular, spheric algae that lack chlorophyll and are thus unable to produce energy from photosynthesis. They exist as saprophytes in a natural habitat that includes fresh and marine water, slime flux of trees, fish tanks, vegetable surfaces, and sewage. These organisms reproduce asexually by the formation of internal autospores, each identical to the parent cell.

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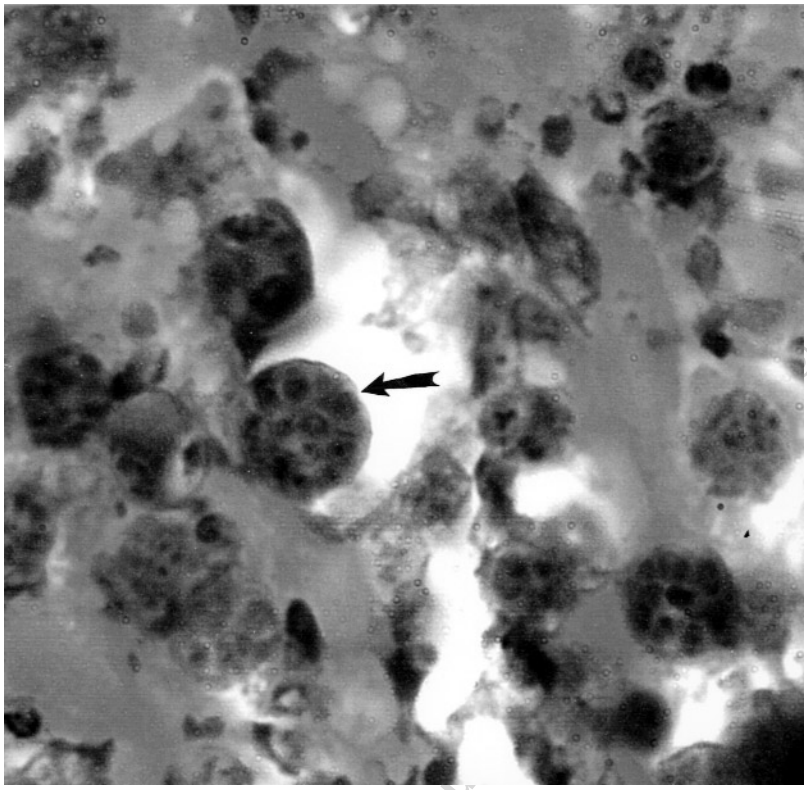

Figure 1. Left thumb lesion. Several sporangia in the morula form (arrow) are seen within this granulomatous infiltrate (hematoxylin and eosin stain, magnification 100×).

Figure 2. Left thumb. Verrucous plaques with focal ulceration are evident.

Figure 3. Left lower leg. Multiple subcutaneous nodules are evident along the lateral aspect of the lower leg. Cytologic examination of fluid aspirated from the swollen extensor digitorum longus tendon sheath (arrow) showed numerous intracellular ovoid organisms that stained with Gomori methenamine silver.

Of the 3 protothecal species, *P. wickerhamii*, *P. zopfii*, and *P. stagnora*, only the first 2 are known to cause human infection. *P. wickerhamii* is the more common etiologic agent and can be readily recognized by the presence of a characteristic morula in histologic sections. The morula is a cell with symmetrically arranged endospores resembling a daisy or soccer ball that is visualized best with Gomori methenamine silver or periodic acid-Schiff stains.

Protothecal infections in humans are of 3 basic forms: cutaneous, musculoskeletal, and disseminated. The skin lesions are almost always on exposed areas, such as the distal extremities and face. Postoperative wounds in these areas are particularly susceptible to infection. In patients with a serious underlying illness or immunosuppression, the skin lesions are vesiculobullous, ulcerative, or nodular[1]. In patients with intact immune systems, the lesions are usually plaques or papules, often eczematous. Development of these infections can usually be traced to contact with dirty water, fish tanks, or soil. Most cases have been reported from tropical areas of the world, including the southeastern United States.

Prototheca species grow rapidly on standard laboratory media; visible colonies are usually evident within 7 days. Prior or ongoing treatment with amphotericin may hinder recovery of the organism, as it most likely did with the culture of our patient's cerebrospinal fluid. The organisms can be identified by their morphology as well as with immunofluorescent staining methods and biochemical assimilation assays.

Twenty-three patients with involvement of the musculoskeletal system from protothecosis have been reported (Table 1). Olecranon bursitis is the most common type of involvement, having been reported in 18 patients to date[2]. In most of these cases, the bursitis is preceded by local nonpenetrating trauma or a previous corticosteroid injection. Infection of the tendon sheaths in the hands and wrists has been reported in 5 patients, all in surgical or accidental wounds; 2 patients' infections could be traced to cleaning an aquarium. Our patient is unique in that he developed tenosynovitis and arthritis of the ankle in the setting of a documented algemia. His initial infection was a nonhealing nodule of the left thumb. A sporotrichoid type of lymphangitic spread was not noted in his left arm. Infection of the patient's ankle joint may have been facilitated by the prior intraarticular injection of dexamethasone.

Table 1. Reported cases of musculoskeletal involvement in human protothecal infections.

Reference	Age/Sex	Musculoskeletal Involvement	Organism	Comorbid Conditions	Antecedent Events/ Possible Sources of Infection	Treatment
7	63 M	Olecranon bursa	Prototheca species by morphology			Excision
7	62 M	Olecranon bursa	Prototheca species by morphology		Trauma to elbow	Excision
8	58 M	Olecranon bursa	*P. wickerhamii*		Nonpenetrating trauma; bursal steroid injections	Excision
8, 9	36 F	Olecranon bursa	Prototheca species by morphology			Excision
8, 9	60 M	Olecranon bursa	Prototheca species by morphology			
10	42 M	Olecranon bursa	*P. wickerhamii*		Automobile accident preceded bursitis	Excision
10	65 M	Olecranon bursa	*P. wickerhamii*		Automobile accident preceded bursitis	Excision
11	39 M	Olecranon bursa	*P. wickerhamii*		Penetrating trauma; sewage exposure	Excision
2	72 M	Olecranon bursa	Prototheca species by morphology		Bursal steroid injections	Excision
12	65 M	Olecranon bursa	*P. wickerhamii*	Alcohol abuse	Presumed trauma	Excision
9	48 M	Olecranon bursa	*P. wickerhamii*			Excision
9	70 M	Olecranon bursa	*P. wickerhamii*	Felty's syndrome, splenectomy	Bird bath	Unknown
13	74 M	Olecranon bursa	Prototheca species by morphology		Trauma	Excision
14	72 M	Olecranon bursa	Prototheca species by morphology			Excision
15	52 F	Olecranon bursa	*P. wickerhamii*	Mixed connective tissue disease; immunoblastic lymphoma	Gardening on hands and knees	Intrabursal amphotericin
16	68 M	Olecranon bursa	*P. zopfii*		Bursal steroid injection	Excision
17	45 M	Olecranon bursa				Excision
18	51 M	Olecranon bursa	*P. wickerhamii*	Alcohol abuse; metastatic lung carcinoma; corticosteroid therapy	Automobile accident	Doxycycline; intrabursal amphotericin; excision
19	62 F	Tenosynovium of hand (surgical site)	*P. wickerhamii*		Post-surgical infection	Synovectomies and IV amphotericin
10	18 F	Ganglion excision site	*P. wickerhamii*		Steroid injection; cleaned aquarium	
7	43 M	Wrist ganglion excision site	Prototheca species by morphology		Surgical wound infection; patient cleaned fish tank repeatedly following the surgery	
20	46 F	Wrist tendons	*P. wickerhamii*	Alcoholic liver disease	Surgical wound	Oral ketoconazole
21	24 F	Extensor tendon of hand	Prototheca species by morphology		Hand trauma from broken glass	Excision, and tetracycline
This report	49 M	Ankle joint and tenosynovium	*P. wickerhamii*	AIDS	Cleaning aquarium	IV amphotericin

Cases of disseminated protothecosis have included meningitis, peritonitis, hepatic abscesses, and urinary tract infection[3,4]. Most have occurred in immunocompromised patients, including those treated with immunosuppressive agents and those with longstanding indwelling intravascular catheters and endotracheal tubes. To our knowledge, there is only one prior report of systemic protothecosis in a patient with AIDS[5]. Our patient developed meningitis during his terminal illness that was most likely a result of the disseminated protothecal infection.

Protothecal infections of the olecranon bursa and surgical wound sites are not self-healing and have generally required surgical excision for cure. Prolonged therapy with oral imidazole antifungal agents may be used for limited cuta-

neous infections[6]. Disseminated infections require systemic antifungal therapy with intravenous amphotericin B. There is a synergistic effect between intravenous amphotericin B and oral tetracycline, and some authors have recommended the routine use of this combination in disseminated infections[1].

As illustrated by our patient, the clinical spectrum of protothecal infection is broader than previously reported. This algal infection must be considered as a potential cause of subcutaneous nodules, acute tenosynovitis, and acute arthritis in immunocompromised patients.

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