SKIN

BRIEF ARTICLE

Cutaneous *Acanthamoeba* Infection Presenting with Granulomatous Vasculitis

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ABSTRACT

Cutaneous acanthamoebiasis is a rare diagnosis that carries a mortality rate of over 70%.[2] This disease predominantly affects immunocompromised individuals, though infections have been reported in immunocompetent individuals.[2] We report a fatal case of cutaneous *Acanthamoeba* infection in a patient with granulomatous vasculitis on biopsy, initially thought to be antineutrophil cytoplasmic antibody (ANCA)-negative vasculitis. The patient primarily presented with ulcerating nasal lesions, which subsequently developed into widespread cutaneous lesions. Diagnosis was made months after presentation when amebae were identified during histopathological examination of biopsies obtained repeatedly after the patient failed to improve on standard therapies for ANCA-negative vasculitis. Treatment was unsuccessful, and the patient died due to complications of widespread *Acanthamoeba* infection. Cutaneous acanthamoebiasis should be considered in the differential diagnosis of granulomatous vasculitis that fails to improve on standard therapies. Early detection and treatment may improve outcomes and reduce mortality in this highly fatal infection.

INTRODUCTION

Free-living amebae from the *Acanthamoeba* genus are common in soil, water and dust. They exist as trophozoites in favorable conditions and as cysts in nutrient poor conditions.[1] Cutaneous acanthamoebiasis due to *Acanthamoeba* is extremely rare, predominantly occurring in immunosuppressed individuals.[2] Disseminated *Acanthamoeba* infection carries a poor prognosis, with mortality over 70%, and 100% in patients with central nervous system (CNS) involvement.[2] CNS involvement is thought to occur from hematogenous spread after cutaneous or nasal exposure.[1] Therapeutics for *Acanthamoeba* infection are poorly studied and numerous antimicrobial agents have been employed with varying response.[2,3] We describe a fatal case of invasive *Acanthamoeba* infection.

CASE REPORT

A 52-year-old woman with type 2 diabetes mellitus and recurrent marginal zone lymphoma in remission presented with erythematous and subcutaneous nodules on her right upper arm and both legs. Her lymphoma diagnosis was 25 years prior to her skin lesions and recurred five and 17 years after her diagnosis. She initially received radiation, then 6 cycles of cyclophosphamide, vincristine and prednisolone for her first recurrence, and 6 cycles of rituximab with bendamustine (R-bendamustine) for her second recurrence. Biopsy of the nodules showed granulomatous dermatitis, concerning for sarcoidosis, without identifiable organisms. Blood counts, electrolytes and inflammatory markers a few months earlier were unremarkable. Full body computed tomography one year prior showed no hilar adenopathy. Concurrently, she was treated by otolaryngology for nasal septal abscesses with *Aspergillus* and septal perforation. After seven months, she developed an erythematous infiltrative plaque with overlying yellow crust on the nose encompassing nasal tip, nasal side walls, right medial cheek, and right upper cutaneous lip (**Figure 1**). Both lower extremities had violaceous, indurated nodules and plaques. She received intralesional triamcinolone and oral minocycline. A month later, due to lesion progression and concern for vasculitis, she was started on hydroxychloroquine and methotrexate. Within three weeks the nasal lesion extended to the medial cheeks bilaterally and upper cutaneous lip. Two lesions on her lower extremities became ulcerated with gray borders. She was admitted and treated with prednisone and an increased dose of methotrexate.

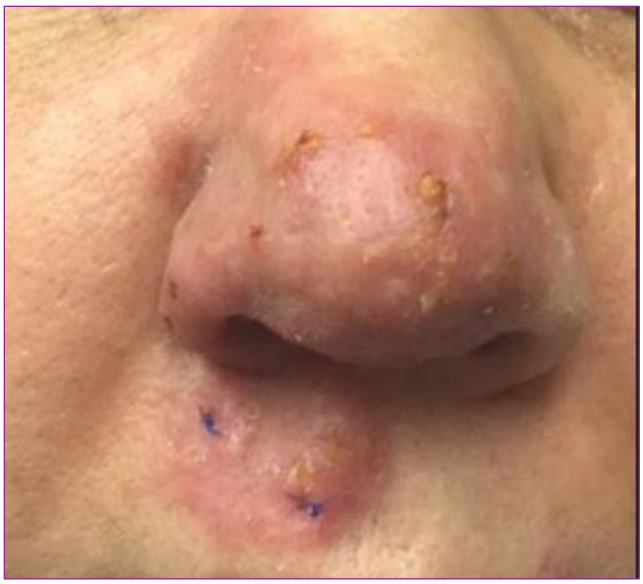

Figure 1. Erythematous infiltrative plaque with overlying yellow crust on the nose and upper lip.

Shortly after discharge, she required another admission after the lesion progressed to erosions with plaques of thick yellow-brown crust encompassing the entire nose, medial cheeks, upper cutaneous and mucosal lip. She received pulse-dose steroids and intravenous cyclophosphamide. One month later was re-admitted when the lesion coalesced, creating a dry, brown plaque of the central face with necrotic nasal cartilage. She received oral cyclophosphamide and prednisone. Repeat testing for HIV, tuberculosis, antinuclear antibodies, antineutrophil cytoplasmic antibody (ANCA), acid-fast bacterial culture and smear, and fungal studies were negative. Repeat biopsies showed small vessel vasculitis with necrosis, granulomatous inflammation, and arteritis which continued to be interpreted as ANCA-negative granulomatosis with polyangiitis. Tissue cultures grew pan-sensitive methicillin-susceptible *Staphylococcus aureus,* subsequently treated with intravenous vancomycin. She received intravenous immunoglobulin intermittently for low immunoglobulin levels, initially concerning for common variable immunodeficiency, though later thought

unlikely. Despite continued treatment with pulse-dose steroids and cyclophosphamide, a month later her facial lesion evolved to a dry necrotic eschar replacing the entire nose and medial cheeks. Her upper lip was mostly lost with underlying dental structures exposed (**Figure 2**). Scattered nodules with eschar and deep ulceration developed on her chest and extremities.

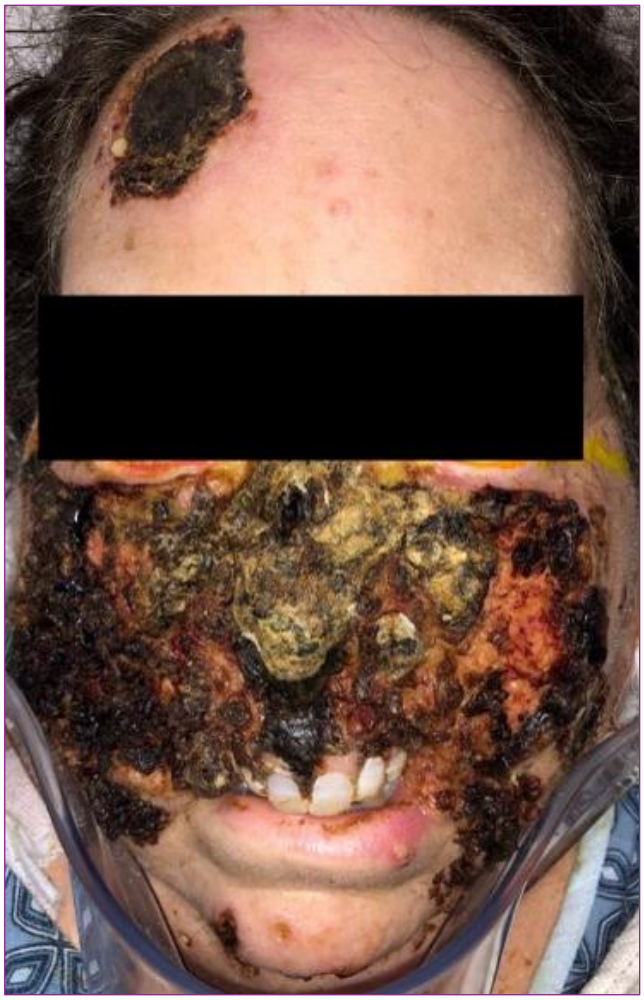

Figure 2. Dry necrotic eschar encompassing the nose, medial cheeks, and upper lip.

The patient became febrile, tachycardic and was treated for presumed sepsis. Repeat deep tissue biopsy and review of previous biopsies showed very rare, large, rounded mononucleated cells with vacuolated cytoplasm and centrally located nuclei with a dense, slightly eosinophilic structure in the nucleoplasm suspicious for trophozoites. These findings suggested tissue invasive acanthamoebiasis, confirmed by the Centers for Disease Control and Prevention (CDC) via immunohistochemistry assay to be *Acanthamoeba* species (**Figure 3**). Brain imaging showed no evidence of CNS involvement. Immunosuppressive medications and antibiotics were stopped. Despite treatment with miltefosine, fluconazole, oral and topical sulfadiazine, pentamidine, flucytosine, and topical ketoconazole, the patient developed sepsis, kidney failure, and respiratory failure and died 15 months after initial presentation.

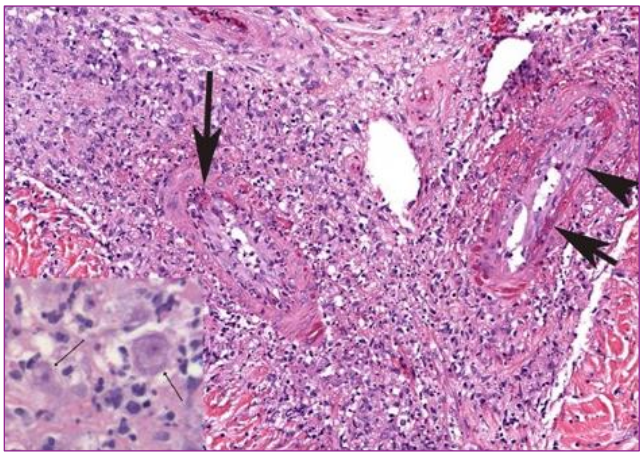

Figure 3. Large, rounded mononucleated cells with vacuolated cytoplasm and centrally located nuclei with a dense, slightly eosinophilic structure in the nucleoplasm suspicious for trophozoites.

DISCUSSION

The diagnosis of acanthamoebiasis requires a high index of suspicion, given its rarity and ability to mimic other pathologies.[1,2,4] Lesions of *Acanthamoeba* infection are usually described as erythematous or violaceous intradermal or subcutaneous nodules.[2] These lesions typically enlarge, ulcerate, developing into necrotic eschar, as illustrated here. Pathology often shows nonspecific granulomatous inflammation and previously reported cases were initially mistaken for

fungal infections and vasculitides.[1,2,4] *Acanthamoeba* species may infect the CNS causing granulomatous amoebic encephalitis, which shows necrotizing or granulomatous response on pathologic examination.[5] Granulomatous vasculitis is often associated with ANCA vasculitis, and less commonly other etiologies such as lymphomatoid granulomatosis, rheumatoid vasculitis, or herpes simplex virus.[7] Given the severity of *Acanthamoeba* infection, cutaneous acanthamoebiasis should be considered in the differential diagnosis of granulomatous vasculitis that fails to improve on standard therapies and with clinical history suggestive of exposure. While histopathology is crucial to diagnosis, more sensitive molecular analysis of tissue with polymerase chain reaction (PCR) (available through the CDC or Mayo Medical Laboratories), may allow earlier detection.[3,8,9] This real-time PCR assay is able to detect one amoeba per sample.[10] Early diagnosis of *Acanthamoeba* infection is essential for appropriate management that may reduce likelihood of death.[4,8]

Historically, cutaneous *Acanthamoeba* infections have almost exclusively been seen in immunocompromised individuals.[2,11] While this patient was not on immunosuppression initially, she had diabetes mellitus which increases the risk of skin infections.[12] The patient's exposure was thought to be from swimming in a fresh water lake or through nasal lavage with well water. Management of cutaneous *Acanthamoeba* infection is not well studied and no consensus on optimal pharmacologic therapy exists.[2,4] Previously reported cases were treated with various antimicrobial agents with variable effect.[2–4,8,9,11] Treatment with flucytosine and miltefosine has been associated with better responses, although rarely curative.[2,3] As illustrated here, the toxic effects of these antimicrobial agents must be considered during treatment.

CONCLUSION

Acanthamoeba infection is a rare cause of cutaneous lesions that may mimic granulomatous inflammatory diseases including vasculitis. Given its high potential mortality, patients with worsening lesions despite conventional therapies and granulomatous vasculitis on pathology should be further evaluated for amoebiasis either by meticulous histopathology or by PCR.

Disclaimer: The findings and conclusions in this report are those of the authors, and do not necessarily represent the official positions of the Centers for Disease Control and Prevention.

Conflict of Interest Disclosures: None

Funding: None

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