A case of primary cutaneous malakoplakia in a cardiac transplant recipient

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INTRODUCTION

Malakoplakia is a rare, acquired, chronic, granulomatous, inflammatory disease first described by Michaelis and Gutmann in 1902.[1] Cutaneous malakoplakia is even less common and tends to occur in the perianal and genital regions.[2] We present a case of a cardiac transplant patient with primary cutaneous malakoplakia occurring in a previously unreported cutaneous distribution.

CASE REPORT

A 69-year-old man with a history of orthotopic cardiac transplant for ischemic cardiomyopathy was seen by the dermatology department for painful, subcutaneous nodules of the right lower extremity 4 months after his transplant. Eighteen days after his transplant, he had chills, right leg pain, and swelling. Evaluation for deep vein thrombosis was negative; however, blood cultures found *Escherichia coli* resistant to ampicillin, tetracycline, levofloxacin, and trimethoprim-sulfamethoxazole. The source was thought to be a previously removed right groin hemodialysis catheter. He was treated with intravenous ceftriaxone for 14 days, and complete recovery ensued.

Four months after transplantation, he again had right leg redness and swelling diagnosed as cellulitis. Doxycycline was initially prescribed; however, his symptoms persisted, and blood cultures again grew *E coli* with the same sensitivities. He received ceftriaxone and cephalexin for 14 days, but a few days after completing this therapy, painful subcutaneous nodules developed on the right thigh and leg. Tissue culture isolated *E coli*. The dermatology department was consulted with concern for ecthyma gangrenosum.

Physical examination found numerous 2- to 8-mm subcutaneous nodules with no epidermal changes extending from the posterolateral distal right thigh onto the lower leg. The distal right shin had a 4- × 2-cm firm subcutaneous nodule with an overlying violaceous hue (Fig 1, *A* and 1, *B*). No inguinal lymphadenopathy was appreciated. Computed tomography of his right leg found multiple small hyperdense nodules within the subcutaneous fat. Punch biopsies of 2 different lesions on the right leg were performed and sent for histopathologic examination and tissue culture.

Histopathologic examination found a dermal nodule consisting of confluent sheets of histiocytes containing abundant granular amphophilic cytoplasm admixed with an inflammatory infiltrate and scattered collection of neutrophils (Fig 2, *A*). Concentrically lamellar, basophilic, intracytoplasmic histiocytic inclusions stained positively for calcium on a von Kossa stain (Fig 2, *B*), positively on periodic acid—Schiff stain, and occasionally positive on iron stain. A Grocott methenamine silver, Gram, and Fite stain were negative for fungal, bacterial, and mycobacterial organisms, respectively. *E coli* was isolated from the tissue culture.

Together these findings were consistent with malakoplakia. Surgical excision of the largest lesion was performed, and intravenous ceftriaxone was initiated and continued for a total of 11 weeks. By week 10, he had complete resolution of his lesions.

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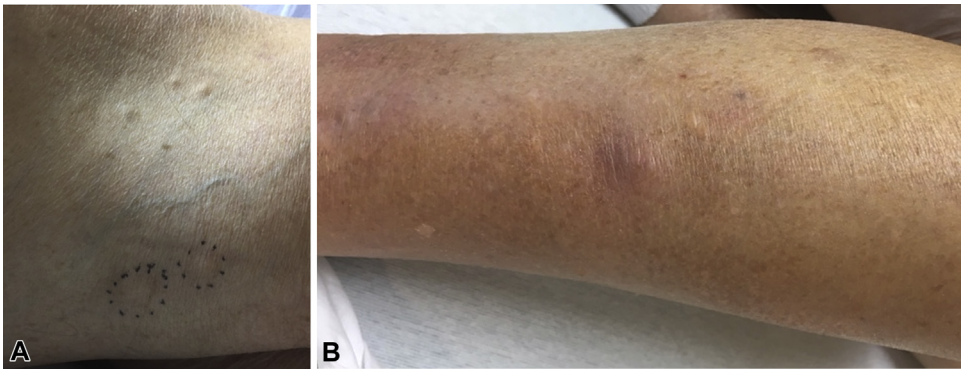

Fig 1. **A**, Right leg with several 2- to 8-mm subcutaneous nodules with no epidermal changes. **B**, Distal right shin with a 4- × 2-cm firm tender subcutaneous nodule with an overlying violaceous hue.

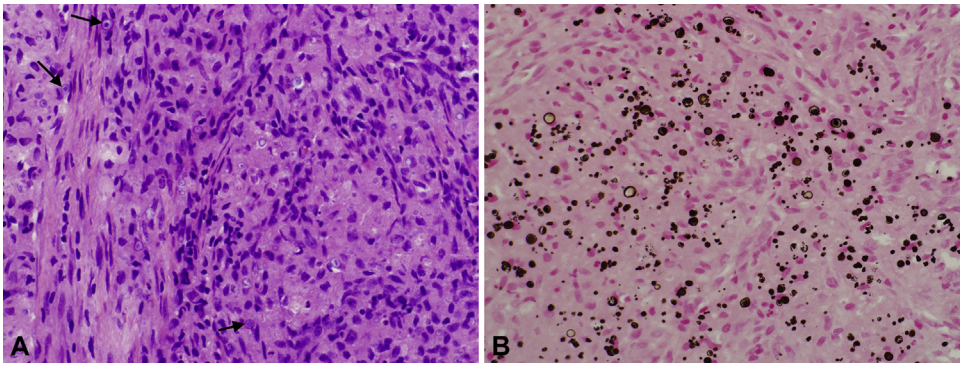

Fig 2. **A**, Dermal nodule with confluent sheets of histiocytes containing abundant granular amphophilic cytoplasm (*arrows*) admixed with an inflammatory infiltrate and scattered collection of neutrophils. **B**, Histiocytic inclusions staining positively for calcium on a von Kossa stain.

Four months after discontinuing his therapy there was no evidence of recurrence.

DISCUSSION

Malakoplakia is a rare and chronic inflammatory condition typically associated with bacterial infections of the urinary tract, although a wide variety of organs have been reported.[1] Cutaneous malakoplakia is a rarer entity that has predilection for the perianal and genital regions.[2] Malakoplakia has been associated with immunosuppression such as HIV, connective tissue diseases, tuberculosis, sarcoidosis, and malignancy as well as developing in sites of surgical wounds and irradiated cancerous tissue.[2,3]

The clinical presentation of cutaneous disease is highly variable. Among the documented presentations are papules, plaques, nodules, ulcerative lesions, or fistulas. These presentations can mimic inflammatory, infectious, or infiltrative cutaneous disease, making the diagnosis on clinical grounds challenging.[1] Owing to the nonspecific presentation, histopathologic evaluation is vital to establish this diagnosis. The presence of sheets of foamy macrophages (von Hansemann) containing granular and concentrically lamellar intracytoplasmic inclusions (the Michaelis-Gutmann bodies) can establish the diagnosis. These are best seen by von Kossa stain because of a peripheral calcified zone surrounding a central sphere of calcium apatite. However, those bodies can also stain positive with periodic acid—Schiff and Perl's (iron) stains.[4]

The pathogenesis of malakoplakia is poorly understood, but is thought to be secondary to an acquired bactericidal defect in macrophages.[1,2,5] In vitro studies by Abdou et al[6] postulated that decreased guanosine monophosphate production in macrophages results in decreased lysosomal activity. Immunosuppression appears to be etiologic, and one study suggests that the macrophage dysfunction can be reversed after immunosuppression is discontinued.[3] Most of the cases of cutaneous malakoplakia occurring in transplant patients have

been in kidney transplant recipients. To our knowledge, only 2 other cases in heart transplant patients have been published.[4,7]

Gram-negative bacilli, most commonly *E coli*, are the most commonly associated organisms known to cause malakoplakia. However, other organisms, such as *Klebsiella*, *Mycobacterium tuberculosis*, and *Staphylococcus aureus* have also been reported.[4]

Successful treatment and high cure rates of malakoplakia have been reported with incision and drainage alone or with surgical excision in conjunction with quinolones and trimethoprim-sulfamethoxazole.[1,2] The higher cure rates with quinolones have been attributed to its intracellular penetration. Bethanechol, a cholinergic agonist, has also been proposed owing to its presumed ability to increase the intracellular cyclic guanosine monophosphate.[8]

There have been a few reports of cutaneous malakoplakia undergoing spontaneous regression in immunocompetent patients. On the other hand, malakoplakia can extend and relapse, despite medical and surgical treatment.[7]

To our knowledge, this is the first reported case with a distribution on the lower extremity. We hypothesize that this is secondary to hematogenous spread of *E coli* from a previous hemodialysis catheter. Also, our patient had complete resolution of most of his lesions under treatment with a cephalosporin. Although traditionally held to be more effective, this particular patient's *E coli* was resistant to fluoroquinolone. We thus support culturing the bacteria if possible to guide antibiotic usage. Furthermore, the excellent outcome of this case was achieved with surgical excision in combination with antibiotic therapy that was tailored to the resistance profile of the underlying bacterial pathogen.

CONCLUSION

Cutaneous malakoplakia is a rare chronic granulomatous inflammatory disorder, most commonly associated with gram-negative bacilli. It is rare in cardiac transplant patients. To our knowledge, this is only the third case of cutaneous malakoplakia in a cardiac transplant recipient and the first to report this distribution of lesions. In view of this case, cutaneous malakoplakia should be included in the differential diagnosis of infiltrative cutaneous lesions in immunosuppressed individuals. Accurate diagnosis of malakoplakia requires skin biopsy with histochemical stains as the initial step to appropriate treatment of these patients.

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