

Acute symmetric peripheral gangrene following a long-standing *Mycobacterium malmoense* infection: A very rare kinship



Frans Maruma, MBChB, DipHivMed, AAAM, MMed-Derm, FC Derm(SA),^a
Richard Carter, MBChB, MMed-Int Med, FCP (SA),^b Fatima Moosa, MBChB,^a Harriet Makuru, MBChB,^a and
Taahir Asmal, BOptom, MBChB^b
Bloemfontein, South Africa

Key words: arteritis; disseminated intravascular coagulation; hyperferritinemia; *Mycobacterium malmoense*; symmetric peripheral gangrene.

INTRODUCTION

Symmetric peripheral gangrene is a clinical entity characterized by symmetric distal ischemic damage in 2 or more sites in the absence of major vascular occlusive disease.¹ In his original description in 1891, Hutchinson² described the first case of symmetric peripheral gangrene in a 37-year-old man who had septic shock and gangrene of fingers, toes, and ear borders.³ The term *purpura fulminans* is reserved for cases in which there is additional or predominant nonacral necrosis.⁴ The postulated etiopathogenesis of symmetric peripheral gangrene includes vasoconstriction, hypotension, vascular obstruction, and endothelial damage. A low-flow state along with disseminated intravascular coagulation is often present.⁵ We present a case of symmetric peripheral gangrene after a long-standing infection caused by *Mycobacterium malmoense* in the absence of disseminated intravascular coagulation. To our knowledge, our case is the first one of symmetric peripheral gangrene associated with disseminated *M malmoense*.

CASE REPORT

A 27-year-old man presented with an acute onset of symmetric peripheral gangrene involving the nose, ear helices, and legs up to the knees (Figs 1 and 2). Minimal involvement of his scrotum and cheeks was also noted.

Further investigation revealed that the patient had a 2-year history of chronic sinusitis and recurrent self-healing lower limb ulcerations. During this time, he attended a primary care hospital, where a biopsy of a lesion on his left leg was performed. High-load acid-fast bacilli were demonstrated; however, the patient was lost to follow-up and thus never treated.

He then presented to our dermatology clinic 5 months later and was admitted for further evaluation and treatment. A multidisciplinary team consisting of dermatology, rheumatology, infectious disease, surgery, plastic surgery, and otorhinolaryngology was involved in his assessment and care.

On clinical examination, the patient had normal vital signs and overt cachexia. He had generalized significant lymphadenopathy. All peripheral pulses were palpable, equal, and regular. Systemic examination results, including those for the respiratory system, were unremarkable.

Noncontributory laboratory investigations performed included complete blood cell count, antineutrophil cytoplasmic antibody testing, iron studies, autoimmune markers, blood cultures, coagulation screen, and HIV and hepatitis studies. A fourth-generation enzyme-linked immunosorbent assay result was negative for HIV, testing result for hepatitis B and C was negative, and the autoimmune panel results, including those for cryoglobulin, were also negative. Inflammatory markers were significantly elevated, with a ferritin level of 7047 µg/L and

From the Department of Dermatology^a and Department of Internal Medicine,^b University of Free State, Faculty Health Science, Bloemfontein.

Funding sources: None.

Conflicts of interest: None disclosed.

Correspondence to: Frans Maruma, MBChB, DipHivMed, AAAM, MMed-Derm, FC Derm(SA), PO Box 339, University of Free State, Faculty of Health Sciences, Bloemfontein 9301, South Africa. E-mail: fransmaruma2@icloud.com or marumaf@ufs.ac.za.

JAAD Case Reports 2020;6:1088-90.

2352-5126

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<https://doi.org/10.1016/j.jdcr.2020.07.051>



Fig 1. Initial presentation (left) and after debridement and 4 weeks of antimicrobial therapy (right).



Fig 2. Lower legs: extensive gangrenous necrosis is evident up to the knee level.

c-reactive protein level of 150 mg/L. The albumin level was 17 g/L in the absence of liver dysfunction.

Radiologic studies included contrast computed tomography of the head and chest, which elucidated the extent of necrosis in and around the nose, involving the entire anterior part of the nasal septum

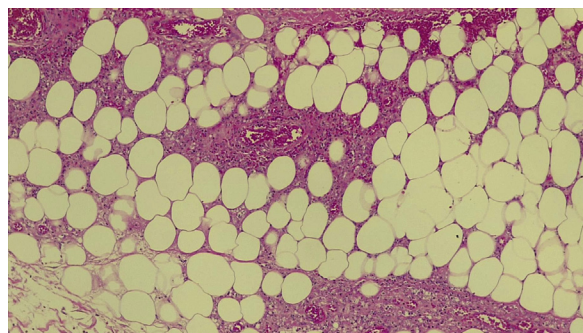


Fig 3. Biopsy of skin lesions (hematoxylin-eosin). Leukocytoclastic vasculitis of cutaneous vessels.

and stopping before reaching the cribriform plate. The lesion further extended anteriorly to involve the middle and lower conchae and also inferiorly to and including the hard palate. A computed tomographic aortogram demonstrated a normal aorta and normal main branches with no dilatations or coarctations and no thrombi. Echocardiogram result was normal.

One nasopharyngeal biopsy and 4 skin punch biopsies were performed at different sites, and all demonstrated leukocytoclastic vasculitis, with consistently positive Ziehl-Neelsen stain result, depicting a high bacterial load (Fig 3). Because results for a Fite stain and tuberculosis polymerase chain reaction were both negative, a mycobacteria other than tuberculosis polymerase chain reaction test was

performed and it was positive for *M malmoense*. The cultures after 42 days of incubation did not yield any growth.

Surgical management was instituted with deep debridement of the centofacial area, as well as the distal aspect of the lower extremities. The extensive necrosis warranted amputation of the toes of the right foot and nose. Antituberculous chemotherapy composed of rifampicin, azithromycin, levofloxacin, and ethambutol was initiated and the patient showed remarkable response (Figs 1 and 2). He was followed up nearly 12 months after initial diagnosis and treatment. The skin lesions on the face had healed completely with scarring and a hollow fistula was noted in situ at the nasoseptal area. There were no active vasculitic lesions present, and multistaged skin grafting, as well as reconstructive surgery of all defects, was commenced.

DISCUSSION

According to Patial et al,⁶ vasculitis can be associated with *M tuberculosis* infection. In our case, the tuberculosis gene expert and Fite stain results were both negative. Our patient had a positive polymerase chain reaction result for *M malmoense*, but with no growth in culture medium, probably because the organism is extremely slow growing, can take up to 8 weeks to grow in mycobacterial culture, and may require the growth medium to be supplemented with pyruvate and the pH to be acidified to facilitate growth.⁷

Nearly 80% of symmetric peripheral gangrene cases are related to sepsis with disseminated intravascular coagulation. Mycobacterial infections are a rare cause of the disease.⁵ Our case of the nontuberculous *M malmoense* infection represents an extremely rare cause in general but particularly in an immunocompetent host with the skin as a primary site of involvement. *M malmoense* was reported as a pathogenic, nonphotochromogenic mycobacterial species by Schroder and Juhlin in 1977,⁸ with the first case isolated in 1954 in Malmo, Sweden.^{9,10} The incidence of *M malmoense* infections has increased since 1980, especially in northern Europe, with a predilection for pulmonary involvement.⁷ In HIV-positive patients, hyperferritinemia of greater than 1000 ng/mL is a common finding, and 1 study

demonstrated that ferritin at greater than 10,000 ng/mL was mainly associated with tuberculosis in South Africa.¹¹ Our case patient was HIV negative and had ferritin levels of 7047 µg/L amid his disseminated nontuberculous *Mycobacterium* infection.

The absence of disseminated intravascular coagulation and the latent period of *M malmoense* infection before the onset of symmetric peripheral gangrene epitomize the perplexities of the poorly understood pathogenesis of symmetric peripheral gangrene. Both symmetric peripheral gangrene and cutaneous *M malmoense* infections are rare. Our case represents a further pathobiologic conundrum. Whether there are pathogen-related or immunogenetic factors to give impetus in this severe clinical presentation remains an obscurity.

In conclusion, clinicians should be aware of symmetric peripheral gangrene, particularly in areas where the *M malmoense* species are endemic. Further insight into the pathogenesis of symmetric peripheral gangrene is still required.

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