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Case Report

Atypical Mycobacterial Infection Complicating a Rare and Difficult to Treat Vasculopathy

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ABSTRACT

Livedoid vasculopathy (LV) is a chronic, recurrent, painful, and debilitating inflammatory skin disease that causes erythematous plaques and papules primarily on a patient's lower extremities (LE). The primary form of treatment is anti-coagulation and immunosuppression. In the presented case, our patient began experiencing LV symptoms soon after she self-treated a knee abscess secondary to a canine hair embedded in her skin. She was placed on a powerful immunosuppressive regimen that worked wonders for her disease symptoms but left her vulnerable to opportunistic infections, such as, the non-tuberculoid Runyon group, M. *abscessus/chelonae* complex. Should we as clinicians, place our patients in this kind of danger by means of treatment? We want to do what is best for our patients, but sometimes we may inadvertently harm our patients in the process.

Keywords: Livedoid vasculopathy; Atrophe blanche; Immunosuppression; Papules; Plaques; Erythematous; Mycobacteria; M. *chelonae/abscessus*; Abscess; Ulcer

INTRODUCTION

Livedoid Vasculopathy (LV) is a chronic, recurrent, ulcerative condition that can significantly impair the quality of life of a patient. It initially manifests as erythematous or purpuric plaques or papules that are painful and/or pruritic and are most commonly located bilaterally around the ankles. These lesions may ulcerate and then slowly heal over a period of 3 to 4 months, forming residual atrophic stellate white scars called atrophe blanche [1]. Atrophe blanche was first reported in 1929 by Milian, when he described a particular form of cutaneous atrophy that he believed was associated with either syphilis or tuberculosis. It seems that he was referring to the distinctive, painful, ulcerated lesions on the lower extremities associated with porcelain white, stellate scars. The term atrophe blanche was used by Degos and Nelson in the 1950s to describe patients with characteristic clinical lesions and histopathologic findings of fibrinous occlusion of dermal blood vessels [2]. There are many other forms of skin diseases which also heal with an atrophic scar such as Henoch-Schonlein purpura, venous stasis lesions, lesions from lupus, rheumatoid arthritis, and many more. This can lead to diagnostic confusion that can create difficulty in diagnosing LV.

Livedoid vasculopathy primarily occurs in young to middle-aged adults and is more common in females than in males. The pathogenesis of LV is nebulous, but is postulated to involve increased coagulation or impaired fibrinolysis that results in occlusion of dermal blood vessels with fibrin thrombi. The diagnosis is confirmed through a skin biopsy that demonstrates characteristic vascular abnormalities, including intraluminal thrombosis, endothelial proliferation, and sub-intimal hyaline degeneration. Livedoid vasculopathy may occur in association with thrombophilia and systemic rheumatic diseases. It may be beneficial to assess patients presenting with LV symptoms for underlying systemic conditions.

Pain management and wound care are central components of management. Smoking cessation and compression also may be beneficial. Therapies reported as beneficial include anti-platelet, anti-coagulant, fibrinolytic, immunomodulatory, immunosuppressive, and vasodilators. Recommended agents such as sulfasalazine may be associated with agranulocytosis, neutropenia, or myelosuppression. This can lead to serious infections including sepsis, pneumonia, CNS, and skin infections, which are serious conditions to monitor for during treatment with such deleterious agents.

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Patients are provided immunosuppressive agents to reduce their disease symptoms but are left defenseless against an innumerable list of opportunistic infections. One such organism that commonly infects immunosuppressed hosts is the *Mycobacterium abscessus/chelonae* complex, which is comprised of a group of rapidly growing, multidrug-resistant, nontuberculous mycobacteria that are responsible for a wide spectrum of skin and soft tissue diseases, central nervous system infections, bacteremia, ocular, and other infections [3].

M. abscessus complex skin infections have diverse presentations, including cutaneous nodules (usually tender), erythematous papules/pustules, and papular eruptions or abscesses. There are two major mechanisms for acquiring this infection. Direct contact with contaminated material or water through an opening in the skin or secondary involvement of the skin during disseminated disease. Our patient suffers from livedoid vasculopathy and was prescribed immunosuppressive medication to reduce her symptoms, which led to the formation of an abscess on her upper extremity that grew the *M. abscessus* complex on culture [4].

CASE

Our patient is a 64-year-old female with a past medical history of essential hypertension, type 2 diabetes mellitus, possible Henoch-Schonlein purpura, mitral valve prolapse with aortic stenosis, a past surgical history of a hysterectomy for uterine fibroids, and bilateral knee surgeries. Her primary care physician referred her to a dermatologist because she was experiencing pain and debilitation secondary to erythematous lesions on the lower extremities that eventually ulcerated and became brownish in color as they healed. She related the onset of the lower extremity lesions to when she grew an abscess on her left knee because some form of dog hair embedded into her skin. This led to a localized infection and abscess formation. She works as a dog groomer and the animals she works with occasionally scratch her.

She used over the counter topical antibiotics to treat the infection but did not endorse using oral antibiotics. She denied any constitutional symptoms including fever, chills, or fatigue at the time. She did state that the lesions are progressive and recurring. On physical examination, there was some mild diffusion actinic elastosis with mild irritant dermatitis of the hands bilaterally. Her lower extremities showed linear and serpiginous erythematous plaques with active peripheral borders and hyperpigmented "burnt out" centers. There was also some suggestion of cribriform scarring on the left lateral malleolus. Several non-palpable, erythematous macules that did not blanch completely with pressure were also present on her LE. The dermatologist performed punch biopsies of the lesions and referred the patient to a hematologist.

At the hematologist, numerous laboratory tests were performed on our patient to find a cause for her debilitating symptoms including, complete blood counts with differentials, complete metabolic panel, anti-phospholipid antibodies, anti-streptolysin O antibodies, complement protein levels, acute phase reactants, immune complex panels, coagulation studies, cryoglobulins, and hepatitis panels. Many other laboratory tests were also performed. All of which resulted within normal limits. Fortunately, protein C and S activities were performed, and the protein C activity was found to be elevated to 233, which was a significant finding. According to Vasudevan et al., activated protein C resistance is the more common inherited cause of thrombophilia associated with livedoid vasculopathy. A glutamine with arginine substitution at position 506 of factor V (factor V Leiden mutation) causes protein C resistance. This mutation impairs activation of coagulation factor V by activated protein C leading to an increased risk of deep vein thrombosis [2]. The pathology report revealed the diagnosis.

The findings were most consistent with a low-grade vasculitis. Mild thickening of blood vessels with focal fibrinous change were suggestive of a low-grade vasculitis. There were also overlying venous stasis changes present in the specimen. The dermatopathologist suggested the possibility of a livedoid vasculitis or coagulopathy, which became the working diagnosis for our patient. She was started on heparin to treat the coagulopathic aspect of the disease. She was also prescribed high dose prednisone, mycophenolate mofetil, and dapsone to reduce her inflammatory symptoms. The immunosuppressive effects of the corticosteroids helped reduce her symptoms, and provided improvement of our patient's quality of life, especially during episodes of disease "flare ups".

Over the course of treatment of this recurrent inflammatory skin condition, she developed an abscess on her right forearm that was tender to the touch. Our patient presented this to her dermatologist at her next follow-up appointment. She also informed her physician that she had an unintentional weight loss of over 25 pounds during the same period. The dermatologist appropriately decided to perform a punch biopsy of the abscess. The sections of the punch biopsy of skin demonstrated a compact hyperorthokeratotic stratum corneum with foci of parakeratosis. There was irregular psoriasiform hyperplasia of the vital epidermis. In the deep reticular dermis, near the sub cutis was a fairly well circumscribed area of suppurative and granulomatous inflammation that was surrounded by fibrosis and angiogenesis consistent with a scarring process.

Kinyoun, Gram, and Gomori-Methenamine silver (GMS) stains were also performed. The Kinyoun stain highlighted beaded rod-shaped mycobacteria present within some of the histiocytes. The gram stain highlighted scattered bacteria. The GMS was negative for fungal elements. This forearm lesion was re-biopsied and sent for culture that grew *Mycobacterium abscessus/chelonae*.

Infectious disease (ID) was consulted to help treat this bacterial infection before it disseminated and could lead to sepsis and systemic infections. Her immunosuppressive regiment could not be discontinued because there was risk of LV flare up. Due to the severity of the infection, the ID specialist decided to place the patient on a triple therapy regimen. They also ordered the placement of a peripherally inserted central catheter (PICC) to facilitate intravenous antibiotic therapy. She was placed on Azithromycin, Amikacin, and Imipenem for 6 months of therapy.

Our patient eventually beat the *M. abscessus* complex infection and continued treatment with her immunosuppressive regimen to help treat her vasculopathy symptoms. She is taking the same medications and following up with her dermatologist to this day. Recently she has been doing well, her LV is stable, and she has not had a recurrence of any opportunistic infections.

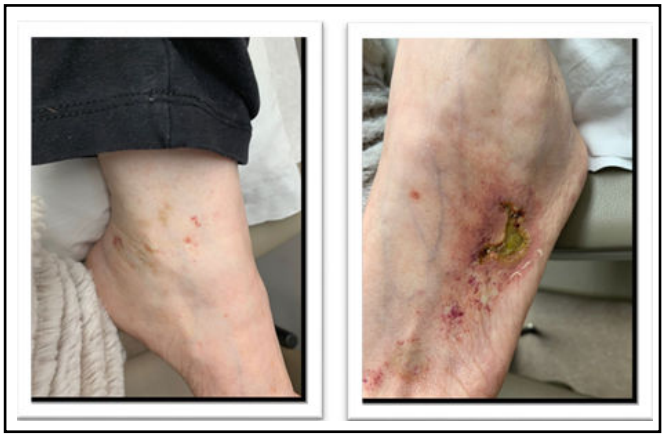

Figure 1: Patient's vasculitic lesions at varying stages, including a larger healing ulcer on the left dorsolateral foot.

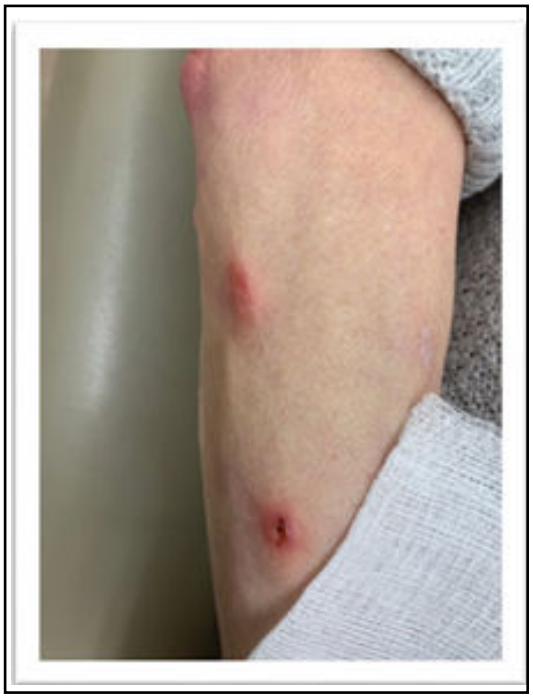

Figure 2: New nodular and painful lesion-right forearm.

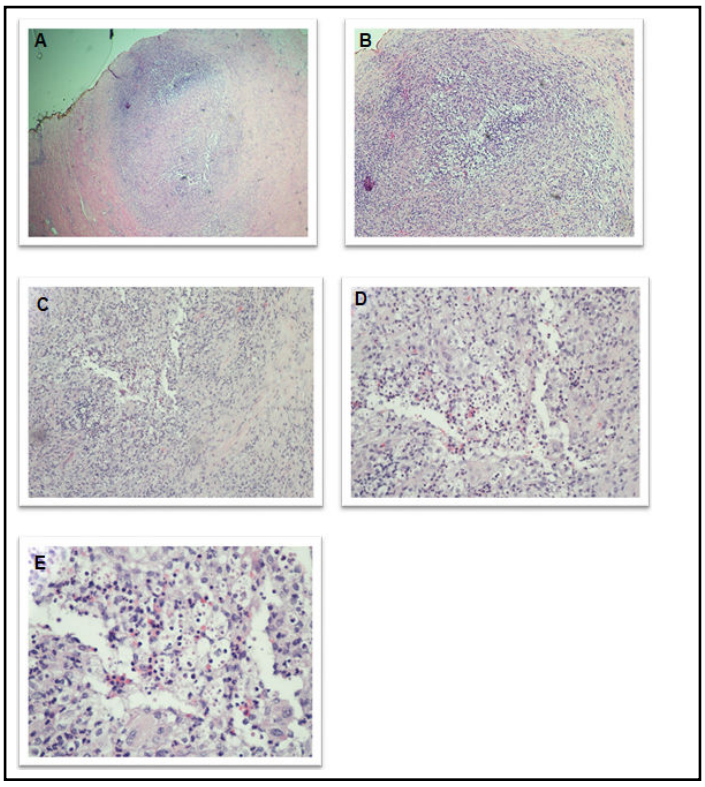

Figure 3: Histological Presentation with Hematoxylin and Eosin Stain. (A) Low power (4x) photo demonstrating a granuloma in the deep to mid reticular dermis. (B-E) Mid to high power (10x – 40x) photos of the granuloma showing mixed neutrophilic and lymphohistiocytic inflammatory response with prominent foamy histiocytes.

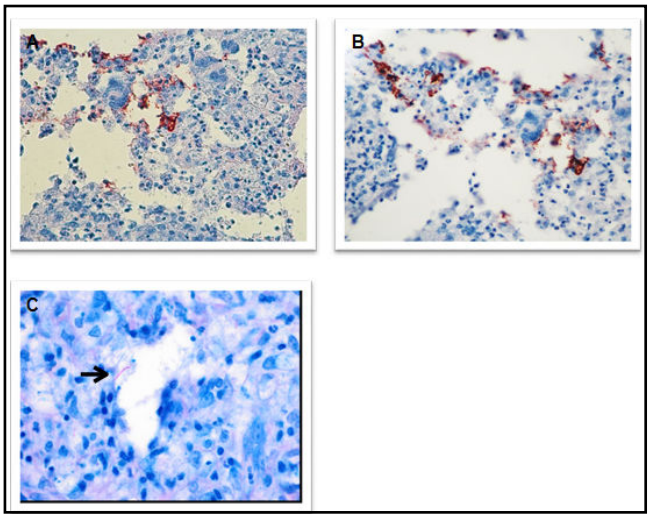

Figure 4: Kinyoun Stain. (A-C) Kinyoun stain for acid-fast bacteria (40x-60x) highlights beaded rod-shaped bacilli in a chain within a foamy macrophage.

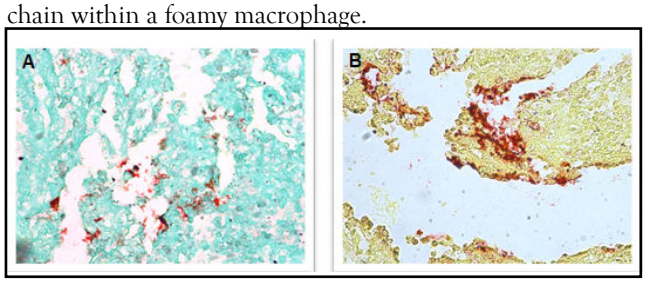

Figure 5: Gomori-Methenamine Silver. (A-B) GMS stain showing lack of fungal elements in affected tissue.

DISCUSSION

Livedoid vasculopathy is a rare cutaneous vasculopathy, initially considered a vasculitis, which presents clinically with painful cutaneous ulcerations that generally occur on the lower extremities. The lesions heal with fibrosis and appear clinically as an atrophe blanche lesion. The name atrophe blanche is nonspecific, is best reserved as a descriptor of clinical appearance, and should be avoided as an outright diagnosis. There are many causes of atrophe blanche and LV is just one [5]. LV, rheumatoid arthritis, scleroderma, lupus, and hematologic malignancies can produce similar appearing lesions leading to diagnostic confusion. This then leads to unnecessary treatments and side effects for the patient. Since the lesions [6] from LV resemble those from other pathologic entities, should clinician's biopsy every new lesion on a patient? Or should clinicians meticulously examine and describe each lesion, so that those lesions deviating from usual clinical appearances can be biopsied to rule out other etiologies? What can be done to prevent our patients from being defenseless against opportunistic infections? Immunosuppressive therapeutics are immensely important in the treatment of countless diseases other than LV, and are necessary drugs to have stocked in our pharmacies. They provide great benefit in cases where treatment options are not straight forward, but how can we prevent our already suffering patients from suffering from additional infectious diseases that are unrelated to their primary ailment, which required the use of immunosuppressive therapy in the first place? In a study performed by Kamiya et al., it was stated that infectious organisms co-evolve with immunosuppression. They found that immunosuppression increases the optimal parasite exploitation by creating more coinfections in which more competitive (and hence more virulent) strains are favored [7]. This phenomenom will continue occurring and there may be a point where no medications created by mankind will be effective against infectious organisms [8,9].

CONCLUSION

In our case, the patient presented with a new nodular lesion on the right forearm, which differed from the flat, ulcerated lesions on her lower extremities. There was a clear distinction between the lesion appearances, which prompted a biopsy leading to her diagnosis of a disseminated mycobacterial infection. The patient also has a history of other vasculitides such as HSP, which normally presents as palpable purpuric lesions in children, but in adults presents as bullae and ulcers which can look similar to LV. All vasculitides can present with similar looking lesions, thus it is important that the clinician examines the lesions in the proper clinical context to arrive at the correct diagnosis. Even chronic venous insufficiency can be associated with the atrophe blanche, and hence, health professionals need to be aware of the clinical presentation of atrophe blanche and the numerous etiologies which could be underlying this clinical lesion. Lesions which appear outside where the majority of the lesions are located, are in non-classical distributions for the entity, or are morphologically different, should be examined with high clinical suspicion of another diagnostic entity, as occurred in our case. In addition, we as clinicians who have been placed in a privileged position of being the caretakers of our fellow human should look to reduce the complications that can be caused by immunosuppressive medications.

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