CLINICAL VIGNETTE

Identifying the Etiology of Leg Ulcers is Key to Successful Treatment

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A 42-year-old woman was referred to rheumatology for further evaluation of lower extremity ulcers. She had been diagnosed with type 2 Diabetes Mellitus (DM) 5 years prior and for the most part had been poorly controlled. A year after diagnosis, she was diagnosed with osteomyelitis of the left great toe, treated with several rounds of oral antibiotics followed by intravenous antibiotics. After two years of treatment for chronic osteomyelitis she underwent debridement with first hallux arthroplasty. Shortly thereafter, she developed lower extremity ulcers which would occasionally become infected and treated with several rounds of antibiotics which would lead to some improvement but never fully resolved. Over the years, she also had a persistently elevated white blood cell count for which she was referred to hematology for evaluation. Hematology concluded that the variable leukocytosis reflected ongoing inflammatory stimulus from chronic foot infections for which she had been on intermittent antibiotics, without clear eradication of the infection. Due to the fact that the patient had recurrent lower extremity ulcers over the last two years, an Antinuclear Antibody (ANA) was checked which returned positive with a titer of 1:80 and the patient was referred to rheumatology for evaluation of a connective tissue disease as the cause for her ulcers.

On physical exam the patient was in no acute distress and vital signs were normal. Her cardiopulmonary exam was unremarkable. Her abdominal exam was normal. She did not have any oral ulcers, but her hair appeared to be thinning. Her joint exam was normal without evidence of synovitis, joint tenderness or deformities. Her skin exam was without malar rashes or palpable purpura. She did not have any digital ulcers or nail changes. Her lower extremities had multiple ulcerations of her anterior legs with pink edges ranging in size from 1 – 3cm. The ulcers appeared well demarcated without granulation tissue. There were also ulcers on her bilateral great toes without cyanosis.

Given the positive ANA and the fact that the wounds on her extremities were not healing, further serological testing was obtained which was essentially negative. Infectious labs included negative hepatitis B/C, HIV, RPR, QuantiFERON gold and Cocci IgM and IgG. Extensive rheumatologic testing was also unrevealing including dsDNA, RF, ANCA, SSA/SSB, Sm/RNP, TPO, C3/C4. Her antiphospholipid antibodies were normal (anti-cardiolipin, Beta 2 Glycoprotein and DRVVT).

She was evaluated by dermatology and biopsy of the right skin ulcer revealed superficial and deep, perivascular and interstitial, chronic lymphohistiocytic and plasmacytic inflammatory infiltrate involving the dermis and both the lobules and partially the septae of subcutaneous fibroadipose soft tissue, with few admixed neutrophils and rare eosinophils**.** There was no evidence of microorganisms on PAS and AFB stains and there was no evidence of vasculitis.

The patient underwent MR angiogram of the abdomen/pelvis with lower extremity run-off to evaluate for vasculitis which revealed drop off signal in the mid right Superficial Femoral Artery (SFA) with length of 10 mm which may represent thrombus versus a focal dissection. The flow was noted to reconstitute more distally within the distal right SFA and throughout the right lower extremity.

She was evaluated by interventional radiology and concurrently referred to vascular surgery and immediately scheduled for bilateral angiogram with right lower extremity angioplasty, atherectomy and stenting of the SFA. Unfortunately, she developed acute onset of severe lower extremity pain and was admitted to an outside hospital where she was diagnosed with compartment syndrome and underwent emergency fasciotomies and SFA thrombectomy. After a prolonged post-operative course with very tight glucose control the patient's ulcers healed.

Leg ulcers are common with an estimated prevalence of 1%-2% in adults.[1] About 70% of leg ulcers are caused by venous disease and about 20% are caused by arterial insufficiency.[2] There are also neuropathic ulcers which most commonly occur in diabetic patients.[2] Several risk factors have been identified for both venous and arterial ulcers. Risk factors for venous ulcers include age, female gender, family history of leg ulcers, previous leg injury, leg edema, prolonged standing and sedentary lifestyles. For arterial ulcers[2] risk factors include DM, Hypertension, obesity and smoking. Less common causes of ulcers include trauma, infection, vasculopathy, pyoderma gangrenosum, panniculitis, malignancy, and medications.[2] Regarding rheumatologic causes of leg ulcers, the clinical finding in cutaneous vessel vasculitis is palpable purpura which typically does not blanche when the skin is pressed and can lead to overlying necrotic vesicle or bulla which can then ulcerate.[3]

This case illustrates the importance of identifying the underlying etiology of the cause of the ulcers for successful treatment.

A comprehensive history can identify risk factors followed by a physical examination including examination of the wound. The appearance and location of the ulcers are important in categorizing the type of ulcer.[3] Venous ulcers occur primarily over the medial malleolus. These are associated with swelling, pigment deposition, venous dermatitis, and lipodermatosclerosis.[3] The leg swelling usually worsens throughout the day and improves with elevation of the legs. Venous ulcers are often shallow and contain granulation tissue with yellow fibrin.[3,4] Ultrasonography of the lower leg is used to identify venous reflux.[4]

In contrast, patients with arterial ulcers may report claudication.[2] Arterial ulcers are more common in the anterior leg and distal foot. These ulcers appear dry and well demarcated with a non-granulating necrotic base and are usually deeper. Patients may also have abnormal pedal pulses, coolness in only one leg or foot or a femoral bruit. Measurement of the ankle-brachial index (ABI) is a simple way to evaluate leg perfusion.[2] Computed tomographic angiography and magnetic resonance angiography may be useful if the diagnosis is not clear.[2]

Neuropathic ulcers are painless and occur over pressure points of the foot or heel. Ulcers usually appear well punched out and typically occur within a callus. On physical exam, patients may exhibit claw toes, Charcot arthropathy and dry, scaly feet.[2]

Venous ulcers occur when the veins dilate and retrograde blood flow lead to venous hypertension.[4] This pressure leads to leakage of fluid and protein which causes edema and extravasation of red cells with hermosiderin deposition and pigmentation.[5] Disruption of the endothelial cells leads to inflammation and expression of cytokines which destroy dermal tissues and leads to ulcer formation.[2] In contrast, arterial ulcers result from the lack of perfusion to the tissues which results in ischemia and necrosis, leading to ulceration. Arterial blood is compromised in patients with DM, vasculitis, and microthrombi with atherosclerosis, macrovascular and microvascular disease.

Promptly identifying the cause of ulcers is crucial for successful treatment. Treatment for venous ulcers include compression therapy with care to monitor degree of compression which can further impair arterial flow in severe cases.[1,5] Venous ablation appears to reduce recurrence and may facilitate healing.[1] Studies report 45% of venous ulcers are due to superficial vein reflux primarily in the superficial system which can be treated with sclerotherapy or venous ablation. Treatment of arterial ulcers is to restore local blood flow by revascularization.[2]

The most common causes of ulcers are arterial, venous and neuropathic ulcers. Though our patient had only had diabetes for 5 years, she had been poorly controlled. Promptly identifying the cause of lower extremity ulcers leads to successful treatment and less complications.[2] Although she had a positive ANA, a connective tissue disease was not identified, but will require ongoing monitoring.

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