SHORT COMMUNICATIONS

A 65-Year-Old Male with a Large Plaque of Retiform Purpura with Impending Necrosis on the Right Lower Abdomen

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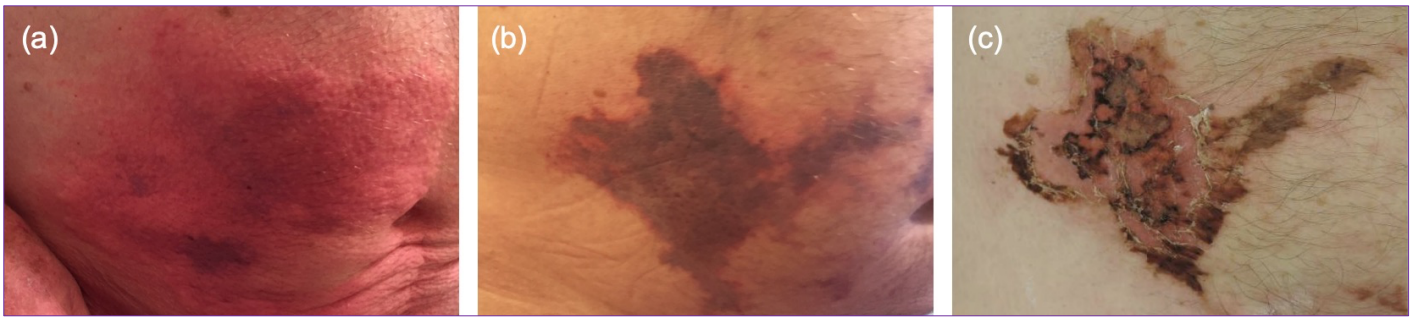
A 65-year-old male patient presented to dermatology as a referral from neurology clinic for concern of an injection site reaction. The patient had a history of multiple sclerosis treated for the past eight years with glatiramer acetate (GA) (Copaxone ®) 40 mg/mL via self-injection 3 times weekly to the thighs and abdomen. Three weeks prior to presentation, he experienced pain and erythema of the right lower abdomen immediately after an injection of GA. The patient had experienced a similar reaction of pain and swelling of his right thigh after a previous administration of GA five years before. On examination, he had a large plaque of retiform purpura with impending necrosis on the right lower abdomen, clinically diagnostic of Nicolau syndrome (Figure 1).

Nicolau Syndrome (NS) is a rare but highly distinctive adverse reaction to intramuscular, intra-articular, or subcutaneous injections which can lead to ischemic necrosis of the skin, muscle, and adipose tissue.[1,2] NS has been reported following injections of various medications, including nonsteroidal anti-inflammatory drugs, antibiotics, glucocorticoids, and anesthetics.[2,3] In this report, the patient experienced NS after self-injecting GA after approximately 8 years of prior GA therapy. There are other published reports of NS associated with GA, and reactions may occur years after starting GA.[1,2,4]

The clinical presentation of NS is intense pain at the injection site immediately after administration, erythema and reticular or livedoid purpuric changes within a few hours, and necrotic ulceration within a few days that can progress into a scar in a few weeks.[1,4] The pathophysiology of NS likely involves ischemic damage from a thromboembolic occlusion or direct vascular injury that subsequently leads to occlusion.[3] When diagnosing NS, it is also important to consider other vasculopathic conditions resulting from thrombotic or embolic occlusions. Relevant conditions to distinguish NS from are myxoma emboli, cholesterol emboli, necrotizing fasciitis, and calcific medial arteriolopathy (calciphylaxis).[3] Myxoma or cholesterol emboli would be more likely to cause livedo changes in the bilateral distal lower extremities rather than at an injection site.[3] Necrotizing fasciitis is more likely to present with a rapidly spreading, severely painful necrotic plaque in a febrile patient.[3] Biopsy may be necessary when the diagnosis is unclear but usually is not needed.

Figure 1. **(A)** Edematous, erythematous patch at the site of subcutaneous glatiramer acetate (GA) injection on the right lower abdomen, immediately following injection. **(B)** After one week, a large plaque of retiform purpura is seen. **(C)** After 20 days, the plaque is resolving with a dry necrotic slough.



Supportive management is the main treatment of NS and can include dressings, topical steroids, anticoagulation, analgesics, and antibiotics. In the present case, conservative wound management with topical mupirocin and dry dressings were utilized with slow resolution of the reaction. In extreme cases, surgical debridement may be indicated.[1,3,4] NS is mainly attributed to improper injection technique and the risk of recurrence is low, so it is not a contraindication for continuing therapy.[1,4] NS may be avoided by using Z-track injections, long needles, auto-injectors, performing aspirations prior to injection, and injecting in regions with less blood vessels.[3] Our patient did not resume glatiramer therapy and four months later, his multiple sclerosis remained stable.

In conclusion, we present a rare but distinct reaction to injected glatiramer known as Nicolau syndrome. This reaction as such is likely underrecognized, and we seek to highlight its classical presentation scenario.

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