Nicolau Syndrome: A Rare Entity with Significant Clinical Implications

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History

- A 42-year-old white female with a history of multiple sclerosis presented with two well-demarcated, purpuric plaques on the left hip.
- The lesions first appeared two days after the injection of Copaxone (glatiramer acetate) into the same location, starting as red plaques that gradually darkened to a purple hue and were accompanied by a burning sensation.
- Initially suspected to be infectious by an outside provider, the rash was treated with Cephalexin and Ciprofloxacin for two weeks, without improvement.
- The patient had been on Copaxone therapy, injecting three times per week for the past seven years without previous complications or history of similar lesions.

Examination

- Two well-demarcated purpuric plaques with erythematous borders and areas of vesiculation on the left hip.
- The larger plaque measures 6 cm at its widest diameter, while the smaller one measures 4 cm at its widest diameter.

Course and Therapy

- The diagnosis of Nicolau Syndrome (Embolia Cutis Medicamentosa) was favored due to the presence of a necrotic plaque on the left hip directly at the site of the Copaxone injection.
- The patient was started on triamcinolone 0.1% ointment for three weeks, after which she was instructed to transition to Vaseline. She was advised to use gentle wound care with antibacterial soap and to keep the lesion covered. Warm compresses were also recommended to promote vasodilation and healing.
- After three weeks, the initial plaques showed evidence of central fibrin deposition and the development of healthy pink granulation tissue. No new nodules had appeared during this period.
- The patient reported that she had consulted with a neurologist at the Cleveland Clinic and was switched from Copaxone injections to an oral DMARD for her MS.

Clinical Photos

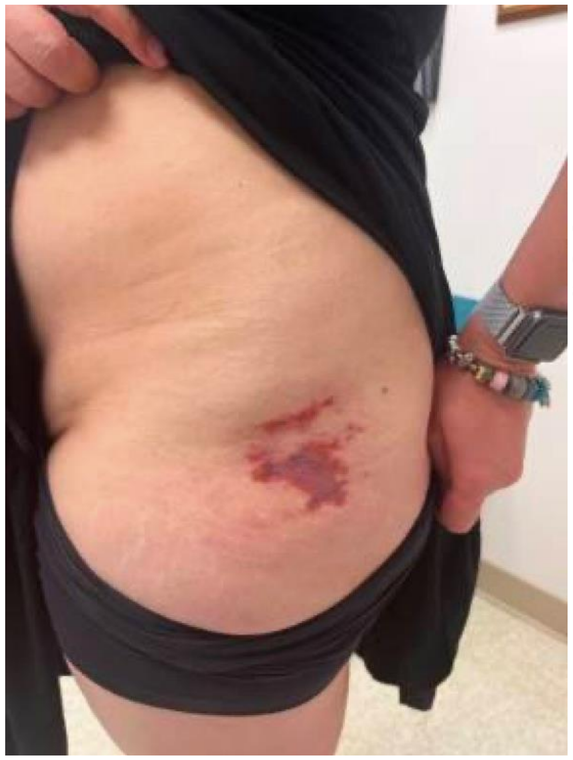

Figure 1: Initial presentation of two purpuric plaques with erythematous borders and areas of vesiculation on the left hip

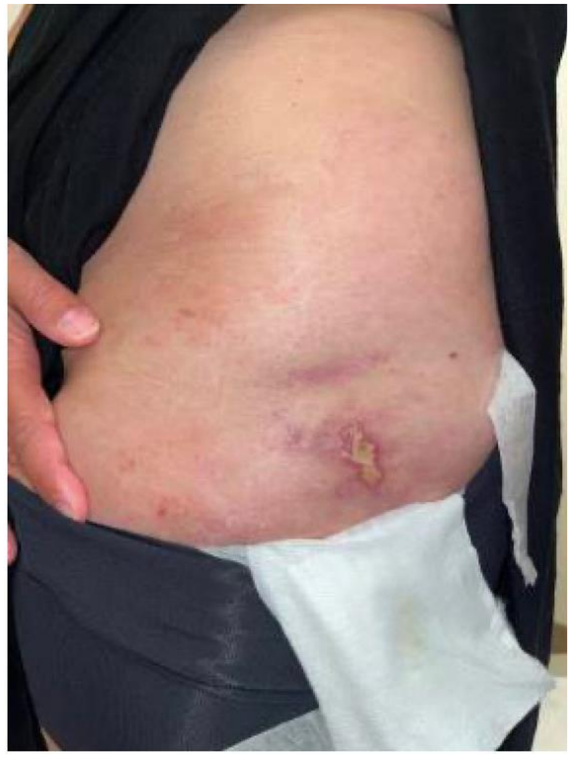

Figure 2: Four weeks later, an irregularly shaped ulceration at the site of the initial plaques, with central yellow fibrin deposition and peripheral healthy pink granulation tissue. No surrounding subcutaneous nodules are present, and the overall lesion size is reduced

Discussion

- Nicolau syndrome, also known as Embolia Cutis Medicamentosa, is a rare but severe complication that can follow intramuscular, intravenous, or subcutaneous injections of various medications.
- The exact pathophysiology is unclear but likely involves accidental intra-arterial injection or intravascular drug deposition, leading to vascular occlusion, ischemia, and tissue necrosis.
- In patients with multiple sclerosis treated with Glatiramer acetate (Copaxone) injection, Nicolau syndrome has been reported as a potential adverse effect. The mechanism by which Glatiramer acetate precipitates Nicolau syndrome is likely multifactorial, involving T-cell modulation, changes in local blood flow, and inflammatory responses at the injection site.
- Other injectables linked to Nicolau syndrome include NSAIDs (especially diclofenac), IM benzathine penicillin, local anesthetics such as lidocaine, and, less commonly, injectable vitamins including Vitamin K and cyanocobalamin.
- Clinically, Nicolau syndrome typically presents with sudden and intense pain at the injection site, followed by livedoid skin changes and progression to necrosis, as observed in our patient.
- Prompt recognition and intervention are critical to prevent extensive tissue damage. Treatment primarily involves supportive care with wound management, topical corticosteroids, and pain control.
- Early pharmacological interventions, such as vasodilators (nitroglycerin or nifedipine) to enhance blood flow, and anticoagulants (heparin) to prevent vascular occlusion, may also be considered.
- In severe cases, surgical debridement may be required for extensive necrosis.

References

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