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Case Report
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A Bullous Eruption Following Apixaban Administration in Patient with Porphyria Cutanea Tarda

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Introduction

Porphyria Cutanea Tarda (PCT) is a rare blood disorder caused by an enzymatic deficiency in the heme production pathway [1]. Pseudoporphyria is a related blistering skin condition that shares clinical and histopathologic features of PCT but lacks the enzyme deficiency associated with bullous formation [2]. Anticoagulants, mainly heparin, are known to cause various cutaneous eruptions such as skin necrosis, hematomas, and bullae [3]. Cutaneous reactions secondary to the initiation of newer direct oral anticoagulants (e.g., apixaban, rivaroxaban) have rarely been reported in the literature [4-7]. This case report describes an 83-year-old female with stable PCT who presented with acute bullous eruption after recent hospitalization and treatment for extensive bilateral Deep Venous Thromboses (DVT) with apixaban.

Case Presentation

An 83-year-old female with a 10-year history of PCT, in addition to Crohn's disease and hereditary hemochromatosis presented to her primary care physician with worsening eruption of bullae on her lower extremities. The patient had recently completed a 6-day hospital stay for extensive bilateral lower extremity DVTs and was started on a 7-day course of apixaban 10 mg oral BID. On day 4 of her hospital stay, she developed several large, painful, and edematous blisters with seeping serous fluid on her bilateral lower extremities.

A week and a half after hospital discharge, the patient presented to her primary care office in visible distress from her worsening and enlarging bullae, with the largest bulla measuring 10 cm × 20 cm. The patient even developed a new serous-filled blister during the visit. Emergency medical services were called, and the patient was taken to a local hospital for better pain control. Further workup revealed full-thickness skin loss with loose skin involving the entire medial aspect of the right calf, a large eschar separating from the deep soft tissues with exposed muscle on the left calf, and additional large serous-filled blisters (Figure 1, 2). The patient was transferred to a high-level burn center for intensive wound care management and surveillance.

During her hospital stay at the burn center, the patient underwent tangential excision and debridement of over 400 cm^2 of full-thickness lower extremity bullae on two separate occasions. Cultures sent from the wound fluid grew *E faecalis*, *Citrobacter farmeri*, and GPR's consistent with diphtheroids, for which the patient was placed on Zosyn. The pathology report of multiple incisional biopsy specimens revealed an entirely denuded epidermis with nonspecific dermal fibrosis and minimal dermal inflammation. Subcutaneous and deep vessel wall calcifications were noted with no evidence of vasculitis. PAS stain with diastase was noncontributory. The histopathologic features were compatible with but not specific for porphyria. Immunofluorescence was not performed due to patient preference but was recommended with a repeat biopsy if clinically indicated. The patient underwent two additional debridement procedures the following week with Kerecis fish-skin graft placement to the bilateral lower extremities. At the time of discharge, the patient's Kerecis grafts were dressed in Adaptic dressing and Aquaphor while her skin tears were dressed in Xeroform and Bacitracin. Three weeks post-op, patient had no complications and wounds were slowly healing with Kerecis grafts (Figure 3).

Discussion

Porphyria cutanea tarda is a photodermatosis characterized by fragile, hemorrhagic bullae and erosions with associated milia, hyperpigmentation, and hypertrichosis [8]. PCT typically develops in the 5th or 6th decade of life and risk factors include alcohol use, estrogen use, viral infections,

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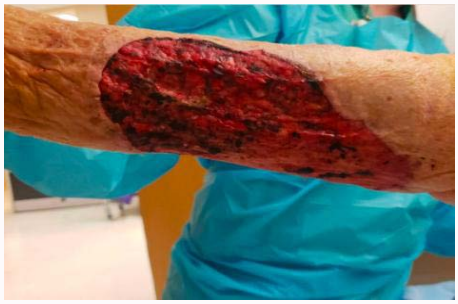

Figure 1: Large eschar on left calf exposing soft tissue at site of prior blister.

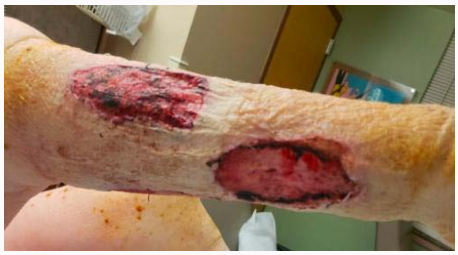

Figure 2: Eruptions right lateral anterior calf. Full-thickness skin loss with loose skin at site of prior blister formation.

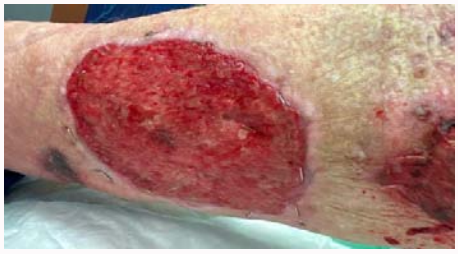

Figure 3: Healing Kerecis grafts 3 weeks postoperative.

smoking, and iron overload1. Treatment options include frequent therapeutic phlebotomies or low-dose oral hydroxychloroquine [9].

This study reports a rare case of painful bullae and eschar formation in a patient with a history of well-controlled PCT, Crohn's disease, hereditary hemochromatosis, and recent anticoagulant initiation. Due to the unusual nature of this patient's presentation along with a complex medical history, the etiology behind this eruption was not entirely understood. The differential for this patient included a PCT eruption, bullous hemorrhagic dermatosis, cutaneous Crohn's disease manifestation, autoimmune bullous skin disease, and other subepidermal bullous diseases (e.g., epidermolysis bullosa acquisita, bullous pemphigoid) [10].

We hypothesize that the combination of our patient's lower extremity edema secondary to bilateral DVTs, predisposition to subepidermal bullous formation due to PCT, and initiation of apixaban for DVT treatment contributed to her painful bullous eruption. The histopathologic features of uniformly absent epidermis, nonspecific dermal fibrosis, and minimal dermal inflammation all support the diagnosis of an atypical PCT eruption with the recent initiation of apixaban as a potential trigger. A more extensive dermatologic investigation in the outpatient setting, including a repeat biopsy with immunofluorescence, is necessary to elucidate if one of our patient's other comorbid conditions contributed to her reaction. Ultimately, our patient was successfully treated with IV antibiotics and fluids, surgical debridement, narcotics, and wound care management at a high-level burn unit.

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