

Enoxaparin-induced eruptive angiokeratomas

Michał Niedźwiedz¹, Agnieszka Żebrowska², Aleksandra Lesiak¹,
Joanna Narbutt¹, Małgorzata Skibińska¹

¹ Department of Dermatology, Pediatric Dermatology and Dermatological Oncology, Medical University of Lodz, Łódź, Poland

² Department of Dermatology and Venereology, Medical University of Lodz, Łódź, Poland

Enoxaparin is one of the medications used in the prophylaxis of thromboembolic complications. Its mechanism of action is based on binding to antithrombin and forming a complex that irreversibly inactivates clotting factor Xa. Among other indications, enoxaparin is used in the prevention of deep vein thrombosis and pulmonary embolism, in patients with atrial fibrillation hospitalized for mild or moderate COVID-19 pneumonia, and those after orthopedic surgeries.^{1,2} An extremely rare side effect of enoxaparin is the occurrence of eruptive angiokeratomas.

Patient 1, a 78-year-old man with type 2 diabetes mellitus, chronic kidney disease (stage G2), hypertension, persistent atrial fibrillation, and a history of an aortic bioprosthesis implantation, was admitted to the cardiology ward due to pneumonia in the course of SARS-CoV-2 infection and exacerbation of congestive heart failure. Until admission to the hospital, he had been treated with apixaban, which was then replaced by enoxaparin (40 mg subcutaneously once daily). After 8 days of therapy, black, painless, soft papules, and nodules with a diameter of 2 mm to

9 mm appeared on the upper limbs, mainly on the dorsa of the hands (FIGURE 1A and 1B). A few lesions were also present on the lower limbs. Dermoscopic examination of individual cutaneous lesions revealed well-demarcated, round, dark lacunae fused with a whitish veil. Upon request of the consulting dermatologist enoxaparin was stopped, the anticoagulant treatment was modified to apixaban, and the patient was admitted to the dermatology department. A punch biopsy sample was taken for histopathologic examination. Gradual resolution of the skin lesions after discontinuation of the enoxaparin treatment was observed within 10 days. Based on the clinical picture, a diagnosis of enoxaparin-induced eruptive angiokeratomas was proposed, which was confirmed by the results of the histopathologic examination (FIGURE 1C).

Patient 2 was a 64-year-old woman with a history of type 2 diabetes mellitus, hypertension, and chronic kidney disease. Due to a tibia fracture she required surgical treatment and thromboprophylaxis with 80 mg of subcutaneous enoxaparin. Ten days after the operation, skin lesions similar to those described above appeared on her upper

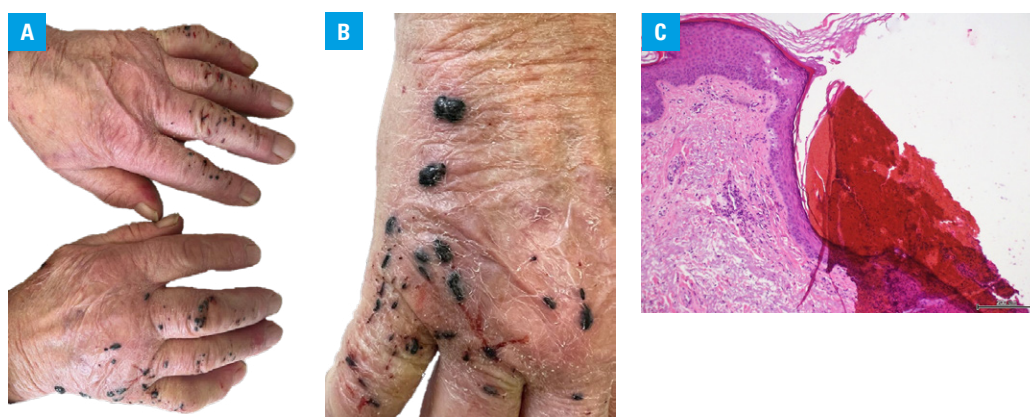


FIGURE 1 Clinical features of 2 patients with eruptive angiokeratomas; **A–C** – patient 1; clinical features of the skin lesions (**A, B**) and histopathologic analysis showing congested vessels (only in the papillary dermis) with epidermal acanthosis, hyperkeratosis, and papillomatosis (**C**, hematoxylin and eosin staining; magnification $\times 40$)

Correspondence to:
Michał Niedźwiedz, MD,
Department of Dermatology,
Pediatric Dermatology and
Dermatological Oncology,
Medical University of Lodz,
ul. Kniaziewicza 1/5,
91-347 Łódź, Poland,
phone: +48 42 651 10 72, email:
michal.niedzwiedz@umed.lodz.pl
Received: February 7, 2023.
Revision accepted: March 8, 2023.
Published online: March 14, 2023.
Pol Arch Intern Med. 2023;
133 (5): 16463
doi:10.20452/pamw.16463
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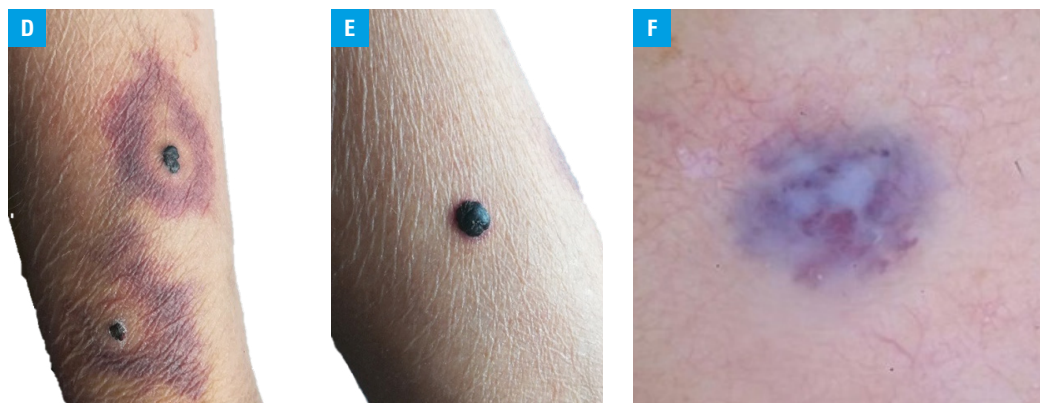


FIGURE 1 Clinical features of 2 patients with eruptive angiokeratomas; **D–F** – patient 2; clinical features of the skin lesions (**D, E**) and dermoscopic examination of a single lesion (**F**)

and lower extremities (**FIGURE 1D** and **1E**), with identical dermoscopic features (**FIGURE 1F**). A change of anticoagulant treatment was advised post consultation; however, the patient refused a biopsy and was lost to follow-up.

In the available literature, only 3 cases of eruptive angiokeratomas induced by enoxaparin were found.^{3–5} Angiokeratomas are benign vascular lesions with unknown exact etiopathogenesis.³ They may arise due to vasoconstriction, downregulation of angiogenic factors, and induction of apoptosis of capillary endothelial cells leading to local hyperkeratosis and acanthosis. In the case of enoxaparin-induced eruptive angiokeratomas, local injury or underlying malformations of the capillary blood vessels were also suggested as a possible explanation.³ Clinical and dermoscopic findings, if necessary followed by a biopsy and histopathologic examination, are the most important factors in the diagnostic process.³ Modification of anticoagulant therapy by discontinuation of enoxaparin and careful observation of the patient are the first-line management strategies in the event of eruptive angiokeratomas induced by enoxaparin.³ Physicians should consider this diagnosis when characteristic clinical signs occur shortly after starting enoxaparin treatment.

ARTICLE INFORMATION

ACKNOWLEDGMENTS None.

FUNDING This research was supported by statutory funds of the Medical University of Lodz (503/5-064-04/503–01).

CONFLICT OF INTEREST None declared.

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HOW TO CITE Niedźwiedz M, Żebrowska A, Lesiak A, et al. Enoxaparin-induced eruptive angiokeratomas. *Pol Arch Intern Med.* 2023; 133: 16463. doi:10.20452/pamw.16463

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