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Authors

Concha-Garzon, MJ
Sotomayor-Lopez, E
Solano-Lopez, G
[et al.](#)

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Letter

Bullous hemorrhagic dermatosis distant from the site of heparin injection.

M.J. Concha-Garzón¹, E. Sotomayor-López¹, G. Solano-López M.¹, J Fraga, D². De Argila¹.

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Servicio de Dermatología¹. Servicio de Anatomía patológica². Hospital Universitario de La Princesa. Madrid, Spain.

Correspondence:

María José Concha-Garzón
C/ Diego de León 62, CP 28006, Madrid, Spain
Telephone: +34915202433
Fax: +34915202435
E-mail: mjconchg@gmail.com

Abstract

Enoxaparin sodium is a heparin of low molecular weight with antithrombotic properties that acts by inhibiting factor Xa. We present a 59-year-old woman who developed heparin-related bullous hemorrhagic dermatosis, at sites distant from the injections, one month after starting treatment with enoxaparin.

Keywords: Bullous dermatosis, heparin, enoxaparin

Enoxaparin sodium is a heparin of low molecular weight with antithrombotic properties. It inhibits factor Xa by binding to antithrombin III [1]. Unlike with coumarin, reactions related to defects in the immunological system or deficiency in natural anticoagulants have not been described [2]. Adverse skin reactions observed with the greatest frequency are: hematomas at the injection site, cutaneous necrosis, contact dermatitis, and urticarial [1,2]. In 2006, hemorrhagic bullae occurring at sites distant from subcutaneous injections of heparin were described for the first time [3].

We present the case of a 59-year-old woman who presented with a 2 week history of asymptomatic blistering on the dorsum of the right hand and 1 week later on the dorsum of the left hand. The eruptions began as small vesicles that progressively grew. She had a personal history of a stage IV epidermoid carcinoma of the lung, which was treated with radiotherapy 1-month prior, and with cisplatin and docetaxel chemotherapy the day prior to the consultation. Also, she had been on treatment with enoxaparin sodium for about one month at a dose of 80 mg per day for a superior vena cava syndrome. On physical exam-she presented with blood-filled vesicles and blisters of 1-2cm diameter. These showed no inflammation at the base, but exhibited crusted surfaces and were distributed irregularly on the dorsum of the fingers of both hands (Figure 1). Her complete blood count showed slight thrombocytopenia (136.000 mil/mm³) and lymphocytosis (0.48 mil/mm³). A coagulation study showed no significant deviation except for a slight increase in fibrinogen (659 mg/dL).

Histological study of the blisters showed a hemorrhagic sub-epidermal blister with areas of erosion and focal necrosis of the overlying epithelium. There was acute and chronic inflammation in the papillary dermis. No signs of hemosiderin, amyloid material, vasculitis, nor thrombosis in the region of the vessels were observed. Puncture and emptying of the lesions was carried out and treatment was maintained with enoxaparin at the same dose. The lesions resolved spontaneously in 3-4 days without residual lesions nor subsequent new outbreaks.

Bullous hemorrhagic dermatosis distant from the site of heparin injection is a condition that exhibits blood-filled, taut blisters with an uninflamed base distributed distant from the area of injection of the drug. The lesions tend to appear within a few days or some weeks from the initiation of treatment [3-5]. This cutaneous reaction has been reported in association to treatment with low molecular weight heparin (dalteparin, tinzaparin) and unfractionated heparin (heparin calcium) [3-5].

It presents an unusual clinical picture, although it should be noted that it is often misdiagnosed owing to its benign and self-resolving nature.

The mechanisms implicated in the pathogenesis are unknown. Some authors postulate an idiosyncratic origin given the absence of thrombosis in the dermal capillaries, excluding a phenomenon related to the presence of anti-factor Xa antibodies [4]. On the other hand, in the cases discussed, the patients were found to be receiving therapeutic (non-prophylactic) doses of the drug. Therefore, it could be speculated that this condition is dose-dependent [3-5].

The most frequent histopathological finding is the presence of blood-filled intra-epidermic vesicles, sub-epidermal vesicles, or subcorneal blisters without associated vasculitis [5]. The prognosis is favorable with spontaneous remission and without necessity to suspend treatment.

In conclusion, although this is an unusual phenomenon, we believe that the understanding of this skin condition is important because necessary heparin treatment can be continued.

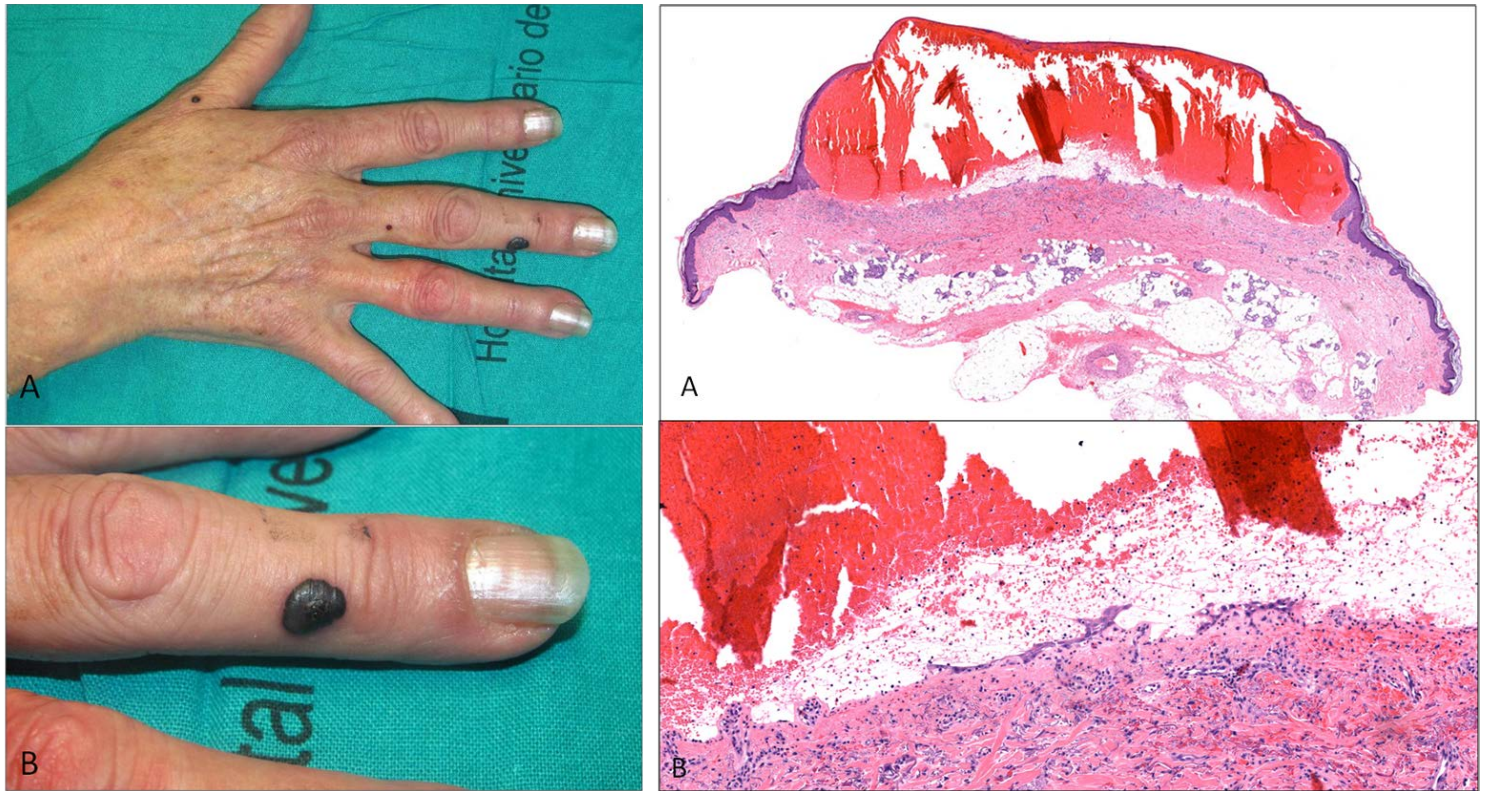


Figure 1. A and B: Blood-filled blisters and a non-inflamed base on the dorsum of right hand

Figure 2. A: Subepidermal blister (haematoxylin-eosin, 10x). B: Base of the blister with mild inflammation in the papillary dermis

References

1. Villanueva CA, Nájera L, Espinosa P, Borbujo J. Bullous hemorrhagic dermatosis at distant sites: a report of 2 new cases due to enoxaparin injection and a review of the literature. *Actas Dermosifiliogr.* 2012; 103:816-9. [PMID:22341878]
2. Harenberg J, Hoffmann U, Huhle G, Winkler M, Bayerl C. Cutaneous reactions to anticoagulants. Recognition and management. *Am J Clin Dermatol.* 2001; 2:69-75.[PMID:11705306]
3. Perrinaud A, Jacobi D, Machet MC, Grodet C, Gruel Y, Machet L. Bullous hemorrhagic dermatosis occurring at sites distant from subcutaneous injections of heparin: three cases. *J Am Acad Dermatol.* 2006; 54:S5-7.[PMID:16427995]
4. Beltraminelli H, Itin P, Cerroni L. Intraepidermal bullous haemorrhage during anticoagulation with low-molecular-weight heparin: two cases. *Br J Dermatol.* 2009; 161:191-3.[PMID:19416230]
5. Maldonado Cid P, Moreno Alonso de Celada R, Herranz Pinto P, Noguera Morel L, Feltes Ochoa R, Beato Merino MJ, Collantes Bellido E, López Rodríguez M, Casado Jiménez M. Bullous hemorrhagic dermatosis at sites distant from subcutaneous injections of heparin: a report of 5 cases. *J Am Acad Dermatol.* 2012; 67: e220-2. [PMID:23062924]