

Eosinophilic panniculitis after subcutaneous administration of sodium heparin

Sir,

Cutaneous side-effects of heparins are well-known. Among them, nodule development is uncommon. Usually, these nodules reveal calcinosis cutis on histological examination.

A 66-year-old woman presented with pruriginous lesions on her abdomen, 25 days after initiating oral acenocoumarol and subcutaneous enoxaparin for a pulmonary thromboembolism. On physical examination, multiple tender, poorly delimited, subcutaneous nodules at enoxaparin injection area were evident [Figure 1]. A biopsy and several complementary studies were performed. Hemogram, erythrocyte sedimentation rate, serum chemistry including alpha-1-antitrypsin, lipase, tryptase, angiotensin I-converting enzyme, rheumatoid factor, thyroid hormone function, autoimmunity studies, urinalysis, chest X-ray and purified protein derivative test were all normal, except for slight eosinophilia with normal white cell count. Cutaneous biopsy showed a mainly septal panniculitis [Figure 2]. The inflammatory infiltrate was predominantly composed of eosinophils, together with few lymphocytes and histiocytes, within the thickened septa and lobules [Figure 3]. In the dermis, scant perivascular and

interstitial inflammatory cell infiltrate composed predominantly of eosinophils was evident. Mild overlying spongiosis was also identified. A diagnosis of cutaneous drug reaction with eosinophilic panniculitis induced by heparin was made. Enoxaparin injections were discontinued, which resulted in cutaneous improvement. A positive patch test to enoxaparin confirmed this diagnosis.

The incidence of skin lesions induced by subcutaneous heparin is unknown. Urticaria, angioedema, ecchymosis, cutaneous necrosis, cutaneous induration and eczema-like lesions have been reported secondary to heparin administration. Delayed-type hypersensitivity reactions appear to be the most common mechanism to develop these cutaneous lesions. The presence of nodules or panniculitis caused by heparin has rarely been described.^[1] The majority of these patients presented with calcinosis cutis or subcutis on histological examination and only one case of eosinophilic panniculitis was reported. Most patients with nodules were receiving treatment with calcium non-fractionated heparins or low molecular weight heparins (LMWH) containing calcium salts. On the other hand, patients with calcinosis cutis following subcutaneous heparin injection usually



Figure 1: Subcutaneous nodules in areas of heparin injection (abdomen)

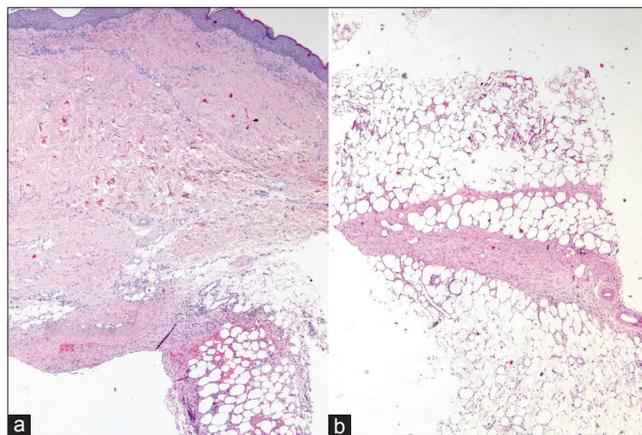


Figure 2: (a and b) Cutaneous drug reaction with eosinophilic panniculitis induced by heparin. Low power view showing inflammatory infiltrate in the upper dermis, thickened septa and lobules (H and E, x40)

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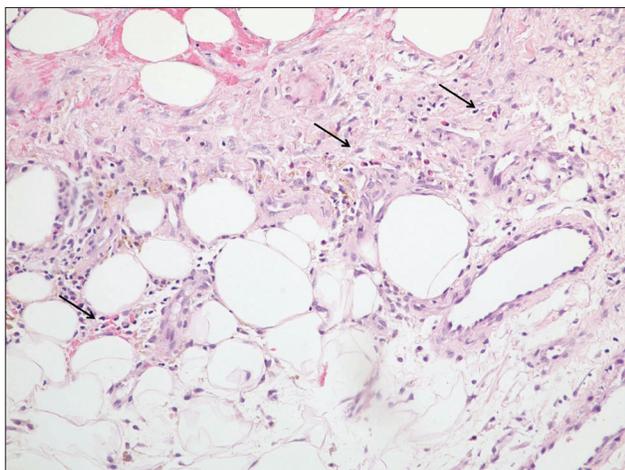


Figure 3: Detail of numerous eosinophils (arrows) in the inflammatory infiltrate in the septum (H and E, x200)

suffered from vitamin D, parathyroid hormone or calcium-phosphate disturbances.^[2] Nodules induced by sodium LMWH have also been found. Funt *et al.* observed nodules in 14 of 426 cancer patients following dalteparin (heparin with sodium salts) injection. These authors described the radiological characteristics of these nodules, but histological studies were not performed.^[3]

Regarding to acenocoumarol, the absence of reported cases of panniculitis caused by this drug as well as the involution of cutaneous lesions despite continuing with this treatment, helped us to exclude acenocoumarol as a possible cause of the lesions of our patient.

Eosinophilic panniculitis is a rare form of panniculitis characterized by septal and lobular involvement with eosinophilic infiltration. It is believed to be a reactive process that has been associated with a variety of systemic conditions such as gnathostomiasis, leukocytoclastic vasculitis and erythema nodosum.^[4] In rare instances, eosinophilic panniculitis has been observed as a local phenomenon induced by subcutaneous or intramuscular drug injections including apomorphine, specific immunotherapy, benzathine penicillin and calcium

heparin.^[1,5] Delayed-type hypersensitivity reactions have also been considered as the cause of these reactions.^[5]

CONCLUSION

To the best of our knowledge, this is the first case of eosinophilic panniculitis induced by administration of LMWH containing sodium salts.

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