

# Medicinal mishap

## Hypersensitivity skin reaction to enoxaparin

Prepared by **Huong Van Nguyen**, Geriatrician and endocrinologist, and **Alpana Marissa Antony**, General medicine registrar, Bankstown Hospital, Sydney

### Case

A 77-year-old man presented with a two-day history of a rash covering both calves. It was associated with mild swelling and a moderate amount of pain. He was systemically well and there were no signs of bruising, haematoma, heart failure, cellulitis or deep vein thrombosis of the legs. His abdominal examination revealed no swelling or rash.

The man had a history of gastro-oesophageal reflux disease, portal hypertension of unknown aetiology without liver failure, hypertension, dyslipidaemia, transient cerebral ischaemic events, right carotid artery stenting in 2008, and past surgery for small bowel obstruction. Four months earlier he had been started on warfarin following a pulmonary embolus. His other drugs were irbesartan 300 mg once daily, esomeprazole 20 mg once daily and atorvastatin 20 mg once daily. As the patient was due to have an elective gastroscopy, his warfarin was being withdrawn. Instead he had been given three injections of enoxaparin at therapeutic doses (over 1.5 days).

The international normalised ratio was normal at 1.1, the activated partial thromboplastin time was mildly raised at 36 seconds (normal range 25–32). Full blood count, C-reactive protein, liver function tests and estimated glomerular filtration rate were normal.

### Comment

The patient probably had an allergic drug reaction. This is because the lower limb rash appeared after enoxaparin was given and improved after it was stopped on two different occasions. The patient had a similar reaction when the drug was given on a previous occasion and there were no alternative causes for the rash.

Low molecular weight heparins have been known to cause type 1 and type 4 hypersensitivity reactions. These appear as local skin changes – usually at the injection sites.<sup>1–6</sup> Little has been published about hypersensitivity reactions remote to the site of injection.

The pathogenesis for heparin sensitivity is not fully understood, but is thought to be due to the heparins acting like a hapten by binding to dermal or subcutaneous structural proteins and triggering a delayed type 4 hypersensitivity reaction.<sup>5</sup> This case is interesting and unusual as there was a complete absence of rash at the site of subcutaneous injections. The recurrence of the rash in the lower legs similar to that following his first exposure to enoxaparin is likely due to a recall reaction. This phenomenon has also been observed in already sensitised patients having patch tests. They developed eczematous rashes at remote, previously affected sites.<sup>3</sup>

The mild elevations in activated partial thromboplastin time and prothrombin time on this occasion were likely due to the anticoagulant effect of enoxaparin. These values returned to normal after enoxaparin was withdrawn. These abnormalities were not thought to be part of drug allergy or liver dysfunction.

### Conclusion

Enoxaparin can cause delayed hypersensitivity reactions remote from the injection site. While the pathophysiology of these reactions is incompletely understood, clinicians should be vigilant to allow early detection of these problems.

### References

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*Conflict of interest: none declared*