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(CASE REPORT)

Enoxaparin-induced bullous hemorrhagic dermatosis in a patient with squamous cell carcinoma of tongue: A rare adverse drug reaction

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Abstract

Bullous hemorrhagic dermatosis (BHD) is a rare, self-limiting cutaneous adverse reaction associated with heparin and low-molecular-weight heparin therapy. It is characterized by the sudden onset of hemorrhagic bullae at sites distant from injection areas. We report a case of a 73-year-old male with squamous cell carcinoma of the right ventro-lateral border of the tongue and multiple cardiovascular comorbidities who developed hemorrhagic bullous lesions over the palms and soles following administration of subcutaneous enoxaparin. The lesions resolved completely after discontinuation of the drug, supporting the diagnosis of enoxaparin-induced bullous hemorrhagic dermatosis. This case highlights the importance of early recognition of this uncommon but benign adverse drug reaction to prevent unnecessary investigations and interventions.

Keywords: Enoxaparin; Bullous hemorrhagic dermatosis; Low molecular weight heparin; Adverse drug reaction; Squamous cell carcinoma tongue

1. Introduction

Low molecular weight heparins (LMWH), such as enoxaparin, are widely used for thromboprophylaxis and treatment of thromboembolic disorders due to their predictable pharmacokinetics and favourable safety profile. Cutaneous adverse reactions to LMWH are uncommon and typically include injection site reactions, urticaria, and delayed hypersensitivity reactions.

Bullous hemorrhagic dermatosis (BHD) is a rare dermatological adverse effect associated with unfractionated heparin and LMWH. It is characterized by painless, tense, hemorrhagic bullae occurring at sites distant from injection areas, without systemic bleeding or coagulation abnormalities. Because of its rarity and benign course, BHD is often underrecognized. We present a case of enoxaparin-induced BHD occurring in a post-operative oncology patient with multiple comorbidities.

2. Case presentation

A 73-year-old male patient was admitted with a chief complaint of a non-healing ulcer on the right side of the tongue for the past two years, which was gradually progressive, following an evaluation, biopsy suggested verrucous carcinoma. Surgical excision was performed, and histopathology showed no residual tumour. However, a progressively enlarging lesion developed on the same side of the tongue over the subsequent months, associated with slurring of speech for 18 months. There was no history of pain.

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The patient had multiple medical comorbidities, including coronary artery disease, aortic stenosis, tricuspid regurgitation, mild pulmonary arterial hypertension, hypertension, dyslipidemia, chronic obstructive pulmonary disease, hyperuricemia, and benign paroxysmal positional vertigo.

Clinical examination revealed an ulcero-proliferative lesion measuring approximately 5 × 4 cm on the right ventro-lateral surface of the tongue, crossing the midline, with a palpable right level IB lymph node. Imaging studies confirmed carcinoma of the tongue with regional lymphadenopathy.

The patient underwent wide local excision of the tongue lesion with bilateral selective neck dissection (levels I–IV), radial forearm/ALT flap reconstruction, and tracheostomy under general anaesthesia. Postoperatively, he was managed in the MICU.

During admission, the patient developed chest pain, for which a cardiology evaluation was done. Screening echocardiography revealed a suboptimal echo window, left ventricular ejection fraction of 55%, and diastolic dysfunction, Mild aortic regurgitation, mitral regurgitation and tricuspid regurgitation. In view of underlying coronary artery disease, the patient was started on subcutaneous enoxaparin 0.6 mL once daily.

After a few days of enoxaparin therapy, the patient developed severe itching over the palms and soles, followed by the appearance of tense, fluid-filled hemorrhagic bullae over these regions. The lesions were not present at the injection sites. There was no associated mucosal bleeding, thrombocytopenia, or coagulation abnormality.

Dermatology consultation was obtained, and a local examination of large tense and flaccid haemorrhagic blisters was diagnosed; enoxaparin-induced bullous hemorrhagic dermatosis was considered. Enoxaparin was immediately discontinued. Following withdrawal of the drug, the itching subsided, and no new lesions appeared. The existing bullae resolved spontaneously over the following days without scarring or sequelae. The patient's overall condition improved, and he was discharged in a stable state.

3. Discussion

Bullous hemorrhagic dermatosis is a rare adverse cutaneous reaction associated with heparin therapy, first described in 2006. It typically presents within days to weeks of initiation of therapy and manifests as painless hemorrhagic bullae on the extremities or trunk, often distant from injection sites.

The exact pathogenesis of BHD remains unclear. Proposed mechanisms include delayed hypersensitivity reactions, local vascular fragility, or idiosyncratic drug reactions rather than direct anticoagulant effects, as coagulation parameters are usually normal. Unlike heparin-induced thrombocytopenia, platelet counts remain unaffected.

In the present case, the temporal relationship between initiation of enoxaparin and development of hemorrhagic bullae, absence of systemic bleeding or laboratory abnormalities, and complete resolution after drug discontinuation strongly support the diagnosis of enoxaparin-induced BHD. Given the patient's multiple comorbidities and post-operative status, early recognition prevented unnecessary investigations and anxiety.

Most reported cases suggest that BHD is self-limiting and may resolve even without stopping anticoagulation. However, discontinuation or switching to an alternative anticoagulant is often preferred, especially in symptomatic patients.

Abbreviations

- BHD: Bullous hemorrhagic dermatosis
- LMWH : Low molecular weight heparin

4. Conclusion

Enoxaparin-induced bullous hemorrhagic dermatosis is a rare but benign adverse drug reaction that clinicians should be aware of, particularly in hospitalized patients receiving LMWH. Early recognition based on clinical presentation and temporal association with drug administration can prevent misdiagnosis and avoid unnecessary interventions. Prompt withdrawal of the offending agent leads to complete resolution in most cases.

Compliance with ethical standards

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Disclosure of conflict of interest

There is no conflict of interest.

Statement of Informed consent

The authors certify that they have obtained all appropriate patient consent forms. The patient has consented to the reporting of clinical information in the journal. The patient understands that his name and initials will not be published, and due efforts will be made to conceal his identity, but anonymity cannot be guaranteed.

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