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Case Report

Heparin-Induced Ecchymosis Following Intravenous Unfractionated Heparin Therapy: A Case Report

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ABSTRACT

Heparin is one of the most widely used anticoagulants for the prevention and treatment of thromboembolic disorders. Although bleeding complications and thrombocytopenia are well-recognized adverse effects, cutaneous manifestations such as ecchymosis are relatively uncommon and may be underreported in clinical practice. A 75-year-old female with a history of type 2 diabetes mellitus, systemic hypertension, chronic kidney disease, and Parkinson's disease presented with breathlessness, palpitations, and generalized weakness. She was diagnosed with accelerated hypertension, acute pulmonary edema, atrial fibrillation, and acute left ventricular failure. Following administration of intravenous unfractionated heparin (4000 IU), the patient developed a large, painless, non-blanching ecchymotic patch measuring more than 10 cm in diameter on the right forearm within five hours of exposure. There was no prior history of drug allergy or cutaneous adverse reactions. Based on the temporal relationship between drug administration and lesion development, a causality assessment was performed using the Naranjo Adverse Drug Reaction Probability Scale. The patient achieved a score of 8, indicating probable adverse drug reaction to heparin. The lesion was managed conservatively and monitored closely. During follow-up, no progression of the lesion was observed, and gradual resolution occurred over the subsequent days without additional complications. This case highlights a rare manifestation of heparin-induced ecchymosis in an elderly patient with multiple comorbidities and emphasizes the importance of recognizing uncommon cutaneous adverse reactions associated with anticoagulant therapy. Healthcare professionals should maintain a high index of suspicion for unusual skin manifestations following heparin administration. Early recognition and appropriate monitoring are essential to prevent misdiagnosis and to exclude serious complications such as heparin-induced thrombocytopenia.

Keywords: Adverse Drug Reaction, Anticoagulant Therapy, Cutaneous Reaction, Ecchymosis, Heparin.

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INTRODUCTION

Heparin is one of the oldest and most extensively used anticoagulant and antithrombotic agents in clinical practice. Since its discovery in 1916, it has remained indispensable in the prevention and treatment of thromboembolic disorders despite the development of several newer anticoagulants (Frizzell *et al.*, 2020). Heparin is commonly used in conditions such as ST-segment elevation myocardial infarction, deep vein thrombosis, pulmonary embolism, and atrial fibrillation.

Cutaneous Adverse Drug Reactions (CADRs), also known as toxidermia, are undesirable skin manifestations resulting from systemic drug administration (Jamula *et al.*, 2009). Their clinical presentation ranges from mild erythematous eruptions to severe life-threatening conditions such as toxic epidermal necrolysis. The diagnosis of CADRs may be challenging because many lesions lack specific clinical features that clearly establish drug causality (Nagasubbu *et al.*, 2023).

Ecchymosis is defined as the extravasation of blood into the subcutaneous tissue due to rupture of blood vessels, resulting in black, blue, red, or purple discoloration measuring more than 1 cm in diameter. Although thrombocytopenia, anemia, and bleeding complications are well-known adverse effects of heparin therapy, ecchymosis is an uncommon cutaneous manifestation (Nayak and Acharya, 2008).

We report a case of rapid-onset ecchymosis following intravenous unfractionated heparin administration in an elderly female patient with multiple comorbidities and no previous history of drug allergy or cutaneous adverse reactions.

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CASE DESCRIPTION

A 75-year-old female was admitted with complaints of breathlessness, palpitations, and generalized weakness. Her past medical history was significant for type 2 diabetes mellitus and systemic hypertension for 20 years, chronic kidney disease for one year, and Parkinson's disease for ten years.

On admission, the patient was conscious, oriented, and afebrile. Her blood pressure was 160/100 mmHg, and her pulse rate was 145 beats/minute. Electrocardiography revealed atrial fibrillation with frequent multifocal premature ventricular complexes and aberrant ventricular conduction. Laboratory investigations demonstrated elevated serum creatinine (3.7 mg/dL) and blood urea (100 mg/dL). Urinalysis revealed glucose (++), albumin (++), and blood (++).

Prior to admission, the patient was receiving glimepiride, dapagliflozin-sitagliptin, nifedipine, sodium bicarbonate, and levodopa-carbidopa.

Based on the clinical presentation and laboratory findings, she was diagnosed with accelerated hypertension, acute pulmonary edema, atrial fibrillation, and acute left ventricular failure.

Following admission, the patient received intravenous furosemide (10 mg), intravenous heparin (4000 IU), pantoprazole (40 mg), morphine (3 mg), cefoperazone-sulbactam (1.5 g), isosorbide dinitrate-hydralazine (20/37.5 mg), clonidine (0.1 mg), bisoprolol fumarate (5 mg), aspirin-clopidogrel-rosuvastatin (75/75/10 mg), amiodarone (100 mg), sodium bicarbonate (500 mg), acetylcysteine (600 mg), apixaban (2.5 mg), spironolactone (25 mg), eplerenone (25 mg), and ropinirole (0.25 mg).

Approximately five hours after administration of intravenous heparin, the patient developed a large blackish, non-blanching ecchymotic patch over the right forearm. The lesion was painless and measured more than 10 cm in diameter. There was no history of trauma, previous similar lesions, drug allergies, or cutaneous hypersensitivity reactions.

A detailed assessment suggested a probable association between heparin administration and the development of ecchymosis. The causality of the adverse reaction was evaluated using the Naranjo Adverse Drug Reaction Probability Scale, yielding a score of 8, which indicates a probable adverse drug reaction.

The patient was managed conservatively with close clinical observation. No further enlargement of the lesion was noted. During follow-up, the ecchymotic patch gradually resolved without the development of necrosis, hematoma, or additional cutaneous lesions. The patient remained clinically stable and recovered without long-term sequelae (Figure 1).

This case was managed at the Vivekanandha Medical Care Hospital, Department of Cardiology, Tiruchengode, Namakkal.

DISCUSSION

Cutaneous adverse drug reactions occur in approximately 1-3% of hospitalized patients and represent an important cause of drug-related morbidity (Schindewolf *et al.*, 2009). Heparin-induced skin reactions are uncommon and include a broad spectrum of manifestations such as erythematous plaques, delayed hypersensitivity reactions, skin necrosis, bullous hemorrhagic dermatosis, and ecchymosis (Sharma and Bagrodia, 2024).

In the present case, the patient developed a large, painless, non-blanching ecchymotic lesion within five hours of receiving intravenous unfractionated heparin. The close temporal relationship between drug exposure and lesion onset, combined with the absence of a prior history of similar reactions, supports a probable causal association.

Several mechanisms have been proposed to explain heparin-induced skin lesions. These include delayed-type hypersensitivity reactions, immune-mediated thrombocytopenia, and direct anticoagulant-induced bleeding into the skin. Female sex, obesity, prolonged heparin therapy, and thrombocytopenia

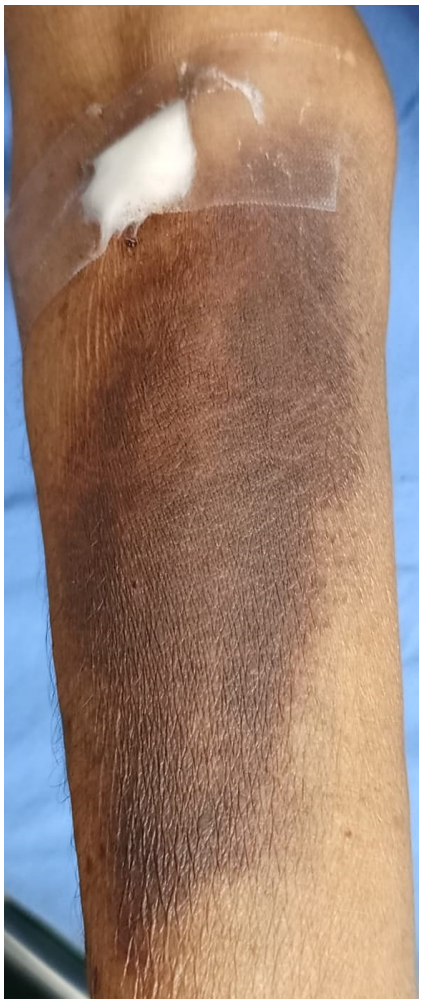

Figure 1: Ecchymotic Patches.

have been identified as potential risk factors for the development of cutaneous adverse reactions (Simeon and Thenmozhi, 2021).

Heparin-induced ecchymosis typically presents as painless, non-blanching lesions and may occasionally progress to more severe manifestations such as hematomas or bullous hemorrhagic dermatosis (Qiu *et al.*, 2021). Although most cases are self-limiting and resolve spontaneously or after discontinuation of therapy, clinicians should be aware that cutaneous lesions may occasionally represent an early manifestation of heparin-induced thrombocytopenia, a potentially serious immune-mediated complication associated with thrombotic events (Varghese *et al.*, 2015).

In the present case, the lesion remained localized and resolved gradually with conservative management. The Naranjo score of 8 further strengthened the likelihood of a drug-related adverse event. Early identification and monitoring prevented unnecessary diagnostic interventions and facilitated appropriate patient management.

CONCLUSION

This case highlights a rare occurrence of heparin-induced ecchymosis in an elderly female patient with multiple comorbid conditions. The rapid onset of a painless, non-blanching ecchymotic lesion shortly after intravenous heparin administration and a Naranjo score of 8 support a probable causal association. Although such reactions are generally self-limiting, prompt recognition and careful monitoring are essential to differentiate benign cutaneous manifestations from potentially serious complications such as heparin-induced thrombocytopenia. Increased awareness among healthcare professionals can contribute to early diagnosis, appropriate management, and improved patient safety during anticoagulant therapy.

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ABBREVIATIONS

CADR: Cutaneous Adverse Drug Reaction; **IU:** International Unit.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

SUMMARY

Heparin is a widely used anticoagulant that is generally safe but may rarely cause cutaneous adverse drug reactions such as ecchymosis. This case report describes a 75-year-old female with a history of type 2 diabetes mellitus, hypertension, chronic kidney disease, and Parkinson's disease who was admitted with accelerated hypertension, acute pulmonary edema, atrial fibrillation, and acute left ventricular failure. Following intravenous administration of heparin (4000 IU), she developed a large, painless, non-blanching ecchymotic patch on her right forearm within 5 hours.

The temporal association between heparin administration and the onset of the skin lesion suggested heparin-induced ecchymosis. Although uncommon, such reactions may occur due to anticoagulant effects, immune-mediated mechanisms, or hypersensitivity reactions. Most cases are self-limiting; however, early recognition and monitoring are essential to differentiate them from more serious complications such as heparin-induced thrombocytopenia.

This case highlights the importance of awareness of rare heparin-associated cutaneous reactions and emphasizes careful clinical monitoring to ensure timely diagnosis and appropriate management.

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