



A case report on contact dermatitis and acute renal failure following topical administration of heparin gel

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ABSTRACT

Heparin is an anticoagulant, used in the management of superficial thrombophlebitis. Adverse drug reactions to heparin have been rarely reported. There are only a few reports of Allergic contact dermatitis associated with topical heparin use. Here we report a case of 40 year old female, diagnosed with carcinoma rectum who developed contact dermatitis followed by acute renal failure after application of Heparin gel (prescribed for the thrombophlebitis occurring at the sites of intravenous cannula). Heparin was immediately withdrawn, but the skin lesions progressed. Her condition was further complicated by the development of anuria. Antihistaminics could only contain the pruritus associated with dermatitis. She was finally managed by Hemodialysis.

INTRODUCTION

Contact dermatitis is an inflammatory skin condition induced by exposure to an environmental agent. Eczema and dermatitis are used synonymously to denote a polymorphous pattern of skin inflammation characterized (at least in its acute phase) by erythema, vesiculation and pruritus. Substances responsible for contact dermatitis after single or multiple exposures are non protein chemicals, i.e. haptens, that induce skin inflammation through activation of innate skin immunity (irritant contact dermatitis) or both innate and acquired specific immunity (allergic contact dermatitis). Allergic contact dermatitis (ACD), a delayed-type hypersensitivity reaction, is mediated by hapten-specific T cells. Recent advances in the pathophysiology of ACD have shown that the occurrence of ACD, as well as its magnitude and duration, is controlled by the opposite functions of CD8 effector T cells and CD4 regulatory T cells. From these studies ACD can be considered as a breakdown of cutaneous immune tolerance to haptens.[1] Heparin is a powerful anticoagulant. The common side effects associated with oral heparin are bleeding, thrombocytopenia, osteoporosis, hypersensitivity. Abnormal laboratory test results, adrenal problems, angioedema, asthma, bleeding, chills, cyanosis, eyesight problems, urticaria have been reported rarely. Topical heparin is considered to be very safe. There are very few reports of allergic contact dermatitis

associated with topical heparin use.[2]

We report a case of a 40 year old woman who developed clinical manifestations of Allergic Contact Dermatitis (ACD) and Acute Renal Failure (ARF) after applying Topical Heparin locally, with convincing evidence for its causality due to the drug.

CASE REPORT

A 40 year old, woman was admitted to the surgery ward of Gauhati Medical College and Hospital, Guwahati with history of alternating diarrhea & constipation, sense of incomplete evacuation of the bowel & blood in stool (either bright red or very dark) for a period of 3 months. Extensive haematological, biochemical & radiological investigations were done and a diagnosis of Carcinoma rectum, stage IIA was made. She underwent Lower Anterior Resection for her ailment. She was cannulated (routine procedure) on both the upper limbs for administration of intravenous fluids and parenteral drugs. 3 days after surgery, thrombophlebitis developed in the veins of the upper limb. She was then cannulated in the veins of her lower limbs, which also started showing signs of thrombophlebitis. Topical Heparin gel (Thrombophobe) was prescribed for the thrombophlebitis on the 4th postoperative day. 6 hrs after the application of the Heparin gel she developed redness over the Heparin gel application sites and within 24 hrs she complained of intense itching. Non blanching, non palpable, erythematous rash

had developed over the application sites (both upper and lower limbs). On general examination, patient was feverish (temperature of 100°F), conscious and well oriented. Vitals: heart rate, BP, respiration were within normal limits. Clinical examination of the respiratory system and cardio vascular system was normal. Heparin gel was withdrawn and injection pheniramine maleate was administered. She was relieved of the intense pruritus. From the 5th postoperative day, the cutaneous lesions begun to expand, overlying skin begun to peel off leading to superficial ulcers and fluid filled blisters started to appear all over the body. Dermatology consultation was taken, diagnosis of contact dermatitis was made and Dexamethasone was added. On the 7th postoperative day, the patient showed concerning signs. Urine output in the last 24hrs was only 100ml and her blood

pressure was falling (mean systolic pressure : 80mm Hg; mean diastolic pressure : 50mm Hg). Nephrology consultation was taken and all the necessary investigations done. RBS(126mg/dl), Haemoglobin (10gm/dl), Na⁺ (136meq/l), K⁺ (4.3meq/l), Mg²⁺ (2.3meq/l), were normal. TLC (14,000 cells per microlitre), BUN (234 mg/dl), serum creatinine (3.6mg/dl) were raised. A diagnosis of Acute Renal Failure was made.

She was put on Noradrenaline and Meropenam and underwent Haemodialysis. Patient showed signs of improvement after 4 cycles of hemodialysis. Urine volume increased to 1.8 Litres in 24 hours. Superficial skin ulcers were managed with silver sulfadiazine ointment.

Subsequently patient became stable and her parameters improved and was discharged after seven days of observation.



Figure 1: Erythematous skin lesions along with fluid filled blisters in the lower limb after application of Heparin gel.



Figure 2: Erythematous lesions in the right upper limb following Heparin gel administration at the site of i.v. cannula. Superficial ulcers can also be seen. The lesions have extended from the site of application of Heparin gel.

DISCUSSION

Heparin is a sulfated glycosaminoglycan with anticoagulant properties. It is usually injected intravenously or subcutaneously and is also available for topical application.[2] It is reported to be very safe, with no risks of adverse effects when used topically.[3] But cutaneous allergic reactions due to subcutaneously injected heparin, though rare have been reported.[4,5,6] A very rare case of patch-test-negative allergic contact dermatitis, later diagnosed by scratch patch testing, from heparin gel has also been reported.[7] Allergic contact dermatitis that develop subsides after 4-5 days of oral corticosteroid treatment and are hence not life threatening. Adverse Drug Reaction (ADR) is defined by World Health Organization as “A response to a drug, which is noxious and unintended and which occurs at doses normally used for prophylaxis, diagnosis or therapy of disease, or for the modification of physiologic function.” [8] With the introduction of vast amount of new drug entry in the market everyday and ever changing prescription patterns, this risk is always increasing.

Here we present the case of Contact Dermatitis & Renal failure associated with heparin use. This is a serious life threatening adverse event. Significant temporal association of Heparin with Contact Dermatitis & Renal failure was found in this woman who was treated with heparin for thrombophlebitis. The reaction appeared after the drug was introduced. There was no previous history of similar drug use, and the patient was not taking any medications (herbal preparations included) in the past. However, no clinical improvement was noted after the drug was discontinued. On the contrary, the skin lesions kept progressing even after discontinuation. The type of the adverse cutaneous drug reaction was life- threatening, hence rechallenge with heparin couldn't be done. With thorough history taking, clinical examination and available laboratory investigations we could not find any other etiology for this constellation of symptoms. Due to lack of logistic support, detection of the drug concentration in the body fluid could not be carried out. The Adverse Drug Reaction is considered as “Probable” for Heparin gel based on the WHO assessment scale for causality. [9] On Naranjo causality analysis, a score of 5 was obtained which indicates 'probable' ADR..[10] The progression of the skin condition even on discontinuation of the offending agent points towards a delayed type hypersensitivity reaction as the etiology. The case is reported for its rarity in occurrence and associated significant morbidity & mortality if not diagnosed and treated immediately.

CONCLUSION

Heparin gel (Thrombophobe) is a commonly used drug for several conditions including thrombophlebitis. It is frequently used in indoor settings for treating thrombophlebitis in cannulated site and sometimes also prescribed to continue its use following discharge. The treating physician should always keep in mind the possible risk of this dangerous condition while prescribing this drug, because at times seemingly innocuous drugs can be the culprit. To conclude, early diagnosis of adverse drug reactions and immediate withdrawal of the offending drug is essential to avoid extra complications and facilitate early recovery.

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