Case Report

Nephrogenic systemic fibrosis following hair-dye ingestion induced acute renal failure

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ABSTRACT

We report a patient who developed acute renal failure following the ingestion of a hair-dye with a suicidal intent. He was managed by hemodialysis and other symptomatic measures. He developed generalized seizures and underwent MRI scan of the brain using gadolinium containing contrast material followed by development of bilateral and symmetrical thickening and induration of the skin over the extremities and verrucous papules and plaques over the lower back. Skin biopsy and immunohistochemistry showed typical features of nephrogenic fibrosing dermopathy as well as deposits of calcium. Successful management of renal failure resulted in clearing of all skin lesions except a small bony hard plate like area overt the left leg, the biopsy of which showed features of osseous metaplasia.

Key words: Hair-dye poisoning, nephrogenic systemic fibrosis, renal failure

INTRODUCTION

Nephrogenic systemic fibrosis is a recently described, acquired, idiopathic fibrosing disorder exclusively seen in patients with renal dysfunction. Cowper *et al.* in 2000, described this condition as "scleroderma-like cutaneous disease" in patients who were on hemodialysis or after renal transplant.[1] The same author later published the unique histopathologic features and coined the term "nephrogenic fibrosing dermopathy."[2] Systemic nature of the disease was subsequently reported with involvement of diaphragm, lungs, liver, muscle, heart and it was re-designated as "nephrogenic systemic fibrosis."[3] (NSF). We report a case of NSF in a patient with acute renal failure caused by hair-dye poisoning.

CASE REPORT

A 22-year old male, weighing 52 kilograms alleged to have consumed about 200 ml of supervasmol, a hair-dye, in an attempt to commit suicide. This was soon followed by pain in the oral cavity and throat, swelling of the tongue and shortness of breath. By the end of the third day the patient had complete renal shut down and was started on hemodialysis. During the hospital stay patient developed generalized edema, more pronounced over the extremities, pleural effusion and about three weeks later suffered two episodes of generalized seizures. Investigations revealed low hemoglobin (7.2 g/dl), raised leucocyte count (18,400/cumm), erythrocyte sedimentation rate (71 mm/hr), C-reactive protein (292 mg/L), elevated blood urea (128 mg/dl), serum creatinine (7.7 mg/dl) and decreased serum albumin (1.6 grams/dl). Serum calcium and phosphorous levels were within normal limits, chest x-ray revealed right-sided pleural effusion. Magnetic resonance imaging (MRI) of brain with gadolinium-based contrast (omniscan) was done two days after seizure. 3.8 grams gadodiamide (gd) was administered. MRI findings were suggestive of posterior reversible leucoencephalopathy syndrome (PRES). Patient was managed by hemodialysis, antibiotics, antiepileptics and other supportive therapy. Renal and other biochemical parameters gradually started improving and the patient was discharged about six weeks after admission.

During the first follow-up (one month after discharge), patient was referred to dermatology consultation for asymptomatic, firm, verrucous papules and plaques over the lower back, back of forearms and elbows [Figure 1]. The upper and lower extremities showed diffuse, hyperpigmented, indurated, sclerodermoid plaques [Figure 2]. Histopathology of sclerodermoid

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plaques and verrucous papules showed prominent and thickened collagen bundles, significant collection of CD34 positive spindle shaped fibroblast like cells throughout the dermis [Figures 3 and 4]. Alcian blue

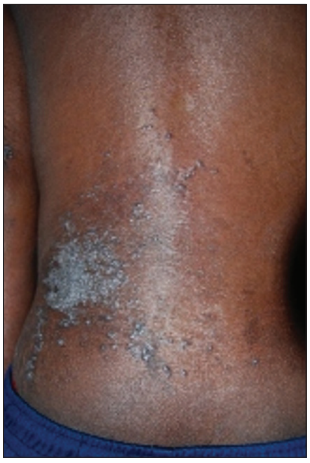

Figure 1: Lower back and back of the left arm showing verrucous papules and plaques

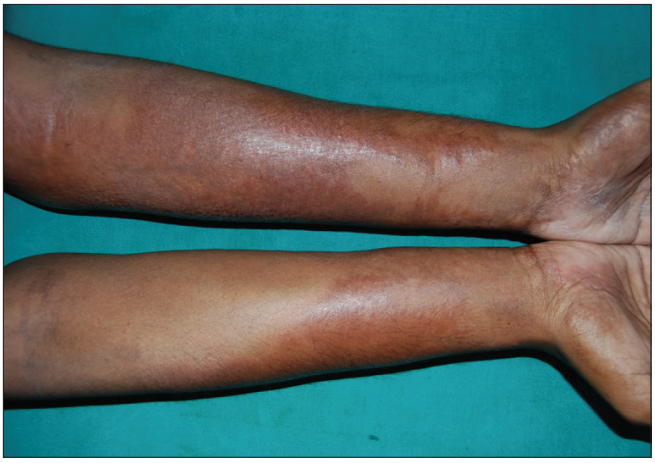

Figure 2: Forearms showing sclerodermoid changes

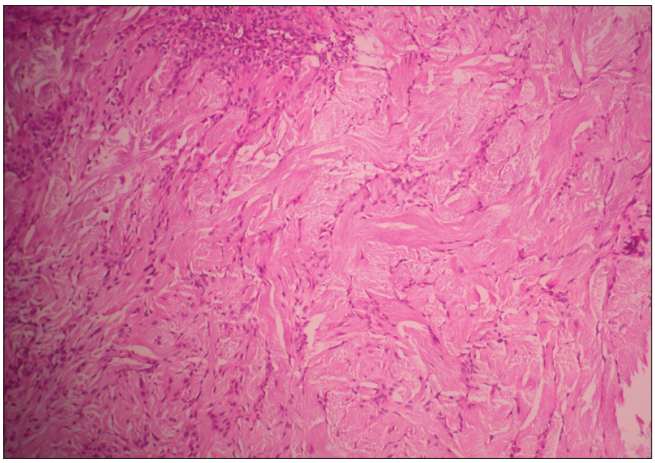

Figure 3: Deeper dermis with thickened collagen bundles and dense collection of plump. spindle shaped cells (H&E, ×400)

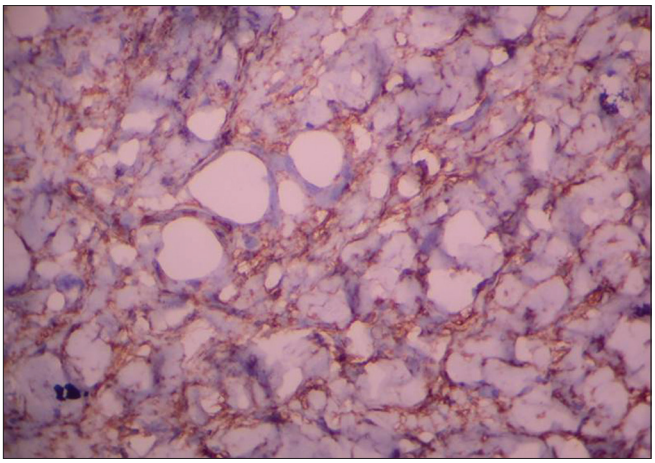

Figure 4: CD 34 immune stain showing positivity in the spindle cells (×400)

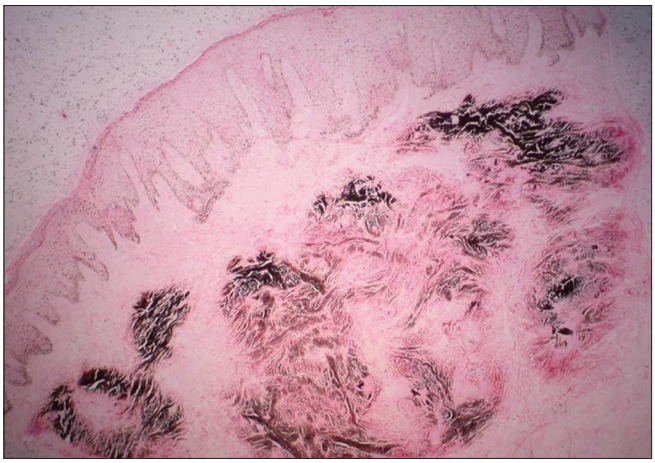

Figure 5: Von Kossa stain showing deposits of calcium in the dermis (×100)

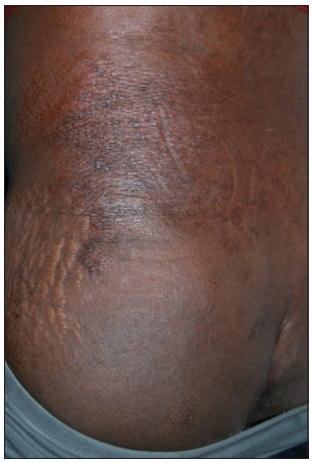

Figure 6: Complete resolution of papules and plaques over the back

stain showed foci of mucin deposits between collagen bundles. Fine basophilic granular stippling of the reticular dermis was observed in H and E sections, which was confirmed as calcium on von Kossa stain [Figure 5]. Correlating the back ground events (acute renal failure, hemodialysis and administration of gd based contrast), clinical presentation and histopathology, the diagnosis of NSF was made. Patient was treated with topical steroids and emollients. Subsequent follow-ups showed normal laboratory parameters including blood urea, creatinine and skin lesions started resolving. At the end of one year verrucous papules and plaques over the elbows and back resolved completely leaving behind redundant folds of skin resembling cutis laxa and prominent follicular ostia [Figure 6]. The indurated plaques over the extremities resolved completely except a small area over the back of left leg which showed a bony hard plaque, the biopsy of which showed features of osseous metaplasia.

DISCUSSION

NSF is a fibrosing skin disorder which occurs exclusively in patients with renal disease. It presents as indurated papules, nodules and firm, bound down plaques involving the extremities and trunk. The fibrotic changes involve not only the skin but also the deep fascia, muscles, myocardium, diaphragm, renal tubules and rete testes. The histopathologic findings include increased collagen, markedly increased dermal cellularity with CD34 positive spindle-shaped fibrocytes and increased dermal mucin. Though NSF has typical clinical and histopathological features, the exact etiology and pathogenesis are not known.[4] Renal insufficiency of varying severity is a common factor, with most but not all having undergone hemodialysis or peritoneal dialysis. Endothelial damage, triggered by events such as a major surgery (renal transplant), placement of dialysis fistulas, central venous lines, hypercoagulable states and thrombotic events may play a role in the pathogenesis.[5] The antihypertensive drugs, especially angiotensin-converting enzyme inhibitors which is extensively used in these patients is considered as one of the factors.[6] Erythropoietin used in patients with end-stage renal disease is known to have profibrogenic and proinflammatory properties.[7] Grobner was the first to recognize the relation between the onset of NSF and exposure to gadolinium (gd) used as a contrast agent with MRI.[8] Subsequently, multiple studies confirmed the gadolinium as the main implicating factor.[9,10] The half-life of gd in patients with normal renal function is 90 minutes, but in patients with impaired renal function, elimination half-life can be prolonged to more than 30 hours. Copper, zinc, iron and calcium ions can substitute for gadolinium ions, leading to the release of free gadolinium by transmetallation.[11] The gd and other metals have been identified in the skin by scanning electron microscopy and energy dispersive spectroscopy.[12] The markedly increased CD34 positive spindle cells in the dermis are believed to be circulating fibrocytes of hematopoietic origin.[13] Ortonne *et al.* observed that a recently introduced material possibly a contrast agent, a medication,or other allergen might be deposited in the tissues and act as a target for circulating fibrocyte to induce fibrosis.[14] It has been suggested that fibrosis and rarely observed calcium deposits in the affected tissue is mediated by transforming growth factor-beta (TGF-beta), a cytokine elaborated by CD34 positive fibrocyte.[15]

Hair dye ingestion for suicidal purpose though rare in west, is not uncommon in certain parts of the world such as East Africa, middle-east and Indian subcontinent. The main manifestations of hair dye poisoning are angioneurotic edema, rhabdomyolysis and acute renal failure.[16] Hair dye induced acute renal failure, hemodialysis and administration of gd containing contrast were probably the likely events which precipitated NSF in our patient.

This case is presented for the following reasons:

- To the best of our knowledge, hair dye ingestion induced acute renal failure resulting in NSF has not been reported.
- NSF is commonly associated with chronic kidney disease and very few cases have been reported following acute renal failure.
- Development of dermal calcification and osseous metaplasia in the lesions of NSF have been rarely reported in the literature.[17]

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