Refractory Cutaneous Vasculitis in a Young Child with Granulomatous Polyangiitis Successfully Treated with Rituximab: A Case Report

Dear Editor,

Granulomatous polyangiitis (GPA) is a rare vasculitis affecting the small vessels predominantly, associated with necrotizing granulomatous inflammation and pauci-immune vasculitis.[1] Overall, pediatric GPA has an incidence of 1.8 cases per million population reported by the US administrative database study.[2] GPA is an anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) with IgG antibodies directed against proteinase-3.

Cutaneous manifestations in pediatric GPA are rare. As per a study by Wright *et al*.,[3] cutaneous manifestations at the onset were noted in only 7.7% of patients. Due to its rarity, there are no established guidelines for the management of isolated cutaneous involvement, more so, in children. We describe a case of an 11-year-old girl who presented with refractory papular blisters that eventually responded to rituximab.

An 11-year-old girl, firstborn of a non-consanguineously married Indian parentage, presented with pain in multiple joints for three months. Subsequently, she developed papular blisters for a week, involving both legs and soles. The lesions were painful, lasting 8-10 days, and healed with pinpoint hyperpigmented spots [Figure 1a]. At 11.6 years, she developed bilateral scleritis and marginal keratitis that responded to treatment with topical steroids, and at age 12, she had bilateral nasal stuffiness and epiphora.

On examination, her weight was 33 kg, height was 154 cm, and body mass index was 13.9 (5-10th centile). She had erythematous, purplish blisters over the posterior aspect of elbows, palms, and soles. She also had arthritis involving her left elbow, bilateral wrists, and right fifth proximal interphalangeal joint. Her systemic examination was unremarkable.

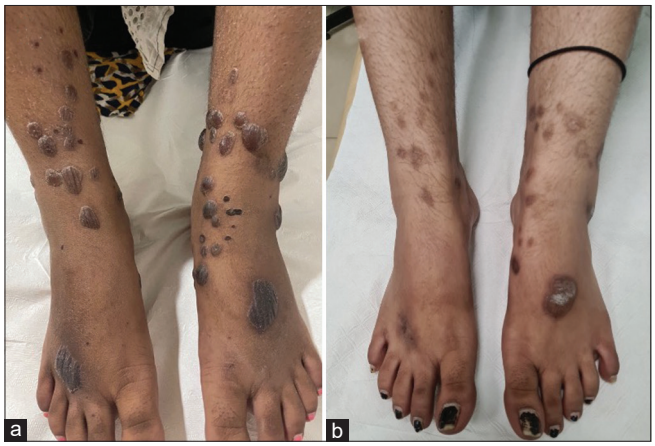

Figure 1: (a) Papular erythematous blisters involving both ankles. (b) Healed residual hyperpigmentation at the site of blisters on follow-up after rituximab infusion

Her baseline hemogram showed thrombocytosis (Hemoglobin 11.5 g/dl, total leukocyte count 8.8 × 10^9/L, neutrophils 55%, lymphocytes 40%, platelet count 450 × 10^9/L). Erythrocyte sedimentation rate (ESR = 90 mm/hr) and C-reactive protein (CRP = 24 mg/l) were raised. Antinuclear antibody by immunofluorescence (IF) was negative, and IgM Rheumatoid factor (RF) was 157 U/mL (Normal <18). C-ANCA by was positive (2+) on IF. A skin biopsy from the lesions was performed, which showed dermal nuclear debris, interstitial infiltrate of neutrophils, eosinophils, and extravasated red cells suggestive of small vessel vasculitis. The direct IF showed capillary IgM and C3c deposits. Diagnostic endoscopy showed bilateral nasal polyposis. Renal function test, urinalysis, and high-resolution computed tomography scan of the lungs were normal.

Considering the clinical profile of upper respiratory involvement, small vessel vasculitis, and C-ANCA positivity, she was diagnosed with GPA. She was treated with oral steroids, subcutaneous methotrexate (15 mg/m^2/week), and cotrimoxazole initially for four months. Arthritis responded well to methotrexate; however, the rashes worsened. She was later treated with azathioprine (2 mg/kg/day) for three months followed by three doses of intravenous cyclophosphamide (500 mg/m^2) monthly. Despite treatment, she developed worsening cutaneous lesions and a recurrence of upper respiratory symptoms. Injection rituximab (375 mg/m^2) was administered two weeks apart, following which the blisters healed over 10 days with residual hyperpigmentation [Figure 1b]. She is currently doing well on azathioprine, cotrimoxazole, and tapering doses of steroids.

GPA is a multi-systemic disease with a predilection to affect the respiratory and renal systems. Cutaneous manifestations have been well described in adults; however, there is a dearth of literature in the pediatric population. The most common cutaneous manifestation is purpura or petechiae, followed by painful skin lesions and maculopapular rashes.[1] Other manifestations include mucocutaneous aphthosis, pyoderma gangrenosum-like ulcers, subcutaneous nodules, vesicles, digital necrosis, livedo reticularis, and papulo-necrotic lesions.[1,4,5] Lower limbs are predominantly involved, followed by the olecranon region.[6] Studies have shown a potential association of cutaneous lesions especially palpable

purpura with renal disease.[7] RF positivity is reported in 34.5 to 50% of cases of GPA.[8]

In the cohort of 39 patients reported by Montero-Vilchez *et al*.,[7] various medications, including cyclophosphamide, methotrexate, azathioprine, mycophenolate, and rituximab, were used for the treatment of cutaneous vasculitis in GPA. Some patients (n = 4) needed more than two immunosuppressive agents to control the disease. At the end of the follow-up period (median 6 years), 20 out of 39 patients were reported to be in remission, four patients had uncontrolled disease, and three died despite treatment, highlighting that severe cutaneous involvement may be a harbinger of serious disease and may carry poor prognosis.

Rituximab was first used in refractory GPA in 2001 and is an established drug for refractory life-threatening AAV. It has been sparingly used in the management of isolated cutaneous vasculitis. Ragab *et al*.[1] reported a 24-year-old man with blisters similar to the index case, who was treated with rituximab. In the index case, rituximab was administered as she failed to respond to methotrexate, azathioprine, and cyclophosphamide.

In conclusion, GPA can present with severe cutaneous vasculitis in the absence of systemic involvement. Refractory cutaneous lesions must be treated aggressively, and rituximab is a potential option in this setting.

Ethics approval

Institutional Ethics Committee (IEC), Aster CMI Hospital, has provided ethical approval for the study.

Declaration of patient consent

Written informed consent obtained from the patient.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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