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Case Report

Urticarial vasculitis – A curious case with overlapping presentation

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ABSTRACT

Urticarial vasculitis is a clinicopathologic entity characterized by recurring wheals along with histopathologic evidence of leukocytoclastic vasculitis. If associated with systemic involvement, it can lead to substantial morbidity. Associated hypocomplementemia and systemic symptoms need thorough evaluation to rule out possibility of connective tissue disorders and autoinflammatory syndromes. We, hereby, present a case of a 19-year-old male who presented to us with recurrent urticarial wheals along with disabling myalgia and joint pain.

Keywords: Hypocomplementemic urticarial vasculitis syndrome, Autoinflammatory syndrome, Schnitzler syndrome

INTRODUCTION

Urticarial vasculitis (UV) is characterized clinically by the presence of urticarial wheals lasting more than 24 h and histopathologically by vessel wall inflammation, perivascular hemorrhage, fibrinoid necrosis, and leukocytoclasis. About 5–10% of patients with chronic urticaria emerge to have UV.[1] Schnitzler syndrome, a type of autoinflammatory syndrome, is characterized clinically by chronic appearance of wheals and associated monoclonal gammopathy along with increased markers of systemic inflammation.[2] We report a case of a 19-year-old male who presented to us with overlapping features of both hypocomplementemic UV syndrome (HUVS) and Schnitzler's syndrome.

CASE REPORT

A 19-year-old male presented with the complaints of repeated attacks of reddish raised skin lesions associated with burning sensation over both flanks, chest, and upper back. Lesions over palms were associated with myalgia and lesions over soles were painful causing difficulty in walking and carrying out routine activities along with joint pain for the past 7 months. The occurrence of such lesions was occasional but progressively became more frequent over the past 15 days. There is no history of oral erosions, photosensitivity, and headache. There was no history of recent travel, animal exposure, raw milk, or drug ingestion.

On examination, multiple, discrete wheals, and a few non-blanchable macules were present on bilateral flanks and palms [Figure 1]. Individual episodes last for more than 24 h and leave behind post-inflammatory hyperpigmentation. Lymph node examination was non-contributory and there was no hepatosplenomegaly. Provisional diagnosis of UV was made and the patient was worked up to find secondary causes and to rule out common association of UV.

Serum complement C3 – 140 mg/dl (normal range: 79–152 mg/dl) and serum complement C4 – 34 mg/dl (normal range: 16–38 mg/dl) levels were within normal limits but serum C1 esterase inhibitor level was decreased (115 mg/L). Normal range is 195–345 done by protein quantitation based on radial immunodiffusion method. C-reactive protein and erythrocyte sedimentation rate were increased. [Table 1] shows investigations done for this patient. On histopathology, mild perivascular and sparse interstitial inflammatory infiltrate of predominantly lymphocytes and eosinophils were seen along with few neutrophils and karyorrhectic debris. Fibrinoid necrosis or significant extravasated erythrocytes were not seen. Papillary dermal edema was seen.

The patient was started on antihistaminics (Tab. loratadine 10 mg bd). On no response, it was up dosed to 20 mg bd. Still new lesions kept occurring so he was given short course of systemic corticosteroids (0.5 mg/kg body weight) along with tab. colchicine 0.5 mg bd. There was no improvement in frequency of attacks and systemic symptoms. Hence, in consultation with rheumatologist, methotrexate was added, and currently, the patient is stable on tab. methotrexate 15 mg/week after 6 months of starting this treatment.

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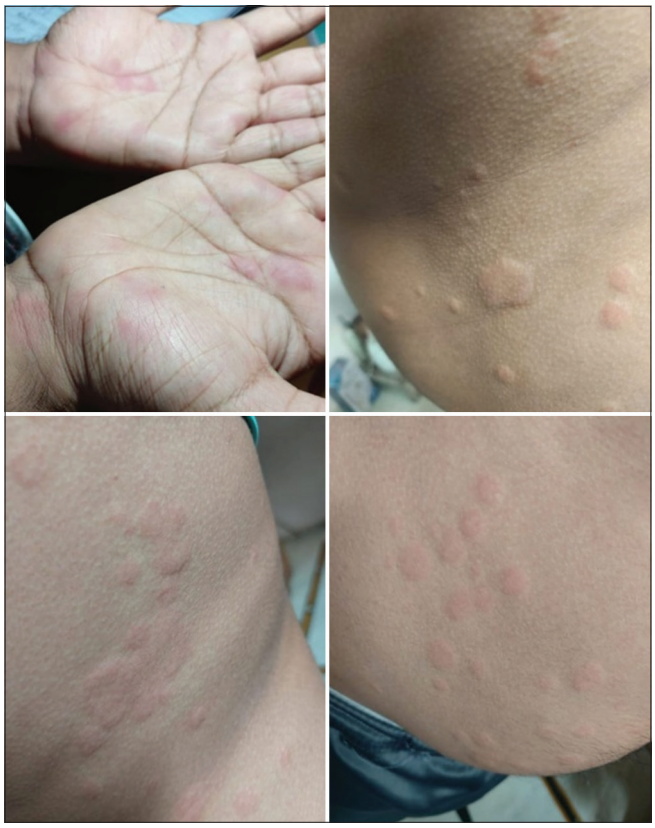

Figure 1: Presence of Erythematous to skin colored wheals and raised plaques on both palms, flanks and anterior abdomen.

Table 1: Laboratory investigations.

Investigation	Value
Total leukocyte count	↑ (12,100/mm^3)
Neutrophils	↑ (73%)
ESR	↑ (20 mm)
CRP	↑ (16.2 mg/dl)
Serum IgG	↑ (19.20 g/L)
Kappa light chains	↑ (5.55 g/L)
Free kappa light chains	↑ (34.20 mg/L)
Protein electrophoresis	
Albumin-to-globulin ratio	↓ (1.1)
Beta-2 globulin	↑ (1.02 g/dl)
Gamma globulin	↑ (1.45 g/dl)
C1 esterase inhibitor	↓ (115 mg/L)

ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein

There was a history of repeatedly falling down and instability of gait before 4 years. Magnetic resonance imaging of the brain showed ganglionopathy in the form of demyelination patches at bilateral periventricular, gangliocapsular, midbrain, and pons region. The patient responded to systemic corticosteroids for the above brain involvement and there has been no similar episode of dysequilibrium in the past 4 years.

DISCUSSION

By definition, HUVS is "a rare immune complex-mediated small-vessel vasculitis characterized by urticaria and hypocomplementemia (low C3, C4, and/or C1q), and usually associated with circulating anti-C1q autoantibodies. Arthritis, pulmonary disease, and ocular inflammation are common systemic manifestation." Criteria for diagnosis are having urticaria persistent for 6 months and hypocomplementemia plus two or more minor criteria: (1) Vasculitis on skin biopsy; (2) arthralgia or arthritis; (3) uveitis or episcleritis; (4) glomerulonephritis; (5) recurrent abdominal pain; or (6) positive C1q precipitin test with a low C1q level.[3] Patients with hypocomplementemia who do not meet the criteria for HUVS are considered to have hypocomplementemic UV (but not HUVS). Arthralgias of the hands, elbows, knees, ankles, and feet occur in half of all patients with UV, but up to 50% of patients with HUVS have frank arthritis.[4]

The relationship of HUV to systemic lupus erythematosus (SLE) is complex with many overlapping features (manifestations of HUV are present in 10% of SLE patients and 50% of patients with HUV will later be diagnosed as having SLE). Other syndromes such as mixed cryoglobulinemia and Schnitzler syndrome should be excluded from the study. The differential diagnosis also includes disorders that clinicopathologically present with urticarial lesions and an interstitial neutrophilic infiltrate as seen in various autoinflammatory syndromes such as Schnitzler syndrome, adult-onset Still disease, and cryopyrin-associated periodic syndromes.[5]

Pertaining to this, one very close differential in our case is Schnitzler syndrome, a type of autoinflammatory syndrome. It is a rare and underdiagnosed entity with a specific criteria which include (1) chronic urticarial rash and monoclonal IgM or IgG as obligate criteria and (2) recurrent fever, (3) objective findings of abnormal bone remodeling with or without bone pain, (4) a neutrophilic dermal infiltrate on skin biopsy, and (5) leukocytosis and/or elevated CRP as minor criteria. Definite diagnosis requires two obligate criteria and at least two minor criteria if IgM, and three minor criteria if IgG and probable diagnosis requires two obligate criteria and at least one minor criterion if IgM, and two minor criteria if IgG.[6]

The monoclonal IgM component associated to a kappa light chain in almost 90% of patients is an important feature of the syndrome. There are some reports of Schnitzler syndromes (<10% of reported cases) being associated with a IgG monoclonal component.[7,8] In around 25% of the patients, lowered levels of IgG or IgA may occur.[7] Complement levels are normal or increased in patients with this syndrome. To support the clinical diagnosis, histopathology showing neutrophilic infiltrate along the collagen bundles in dermis is typical without any other signs of vasculitis.[9] [Table 2] shows specific points in favor of HUVS and Schnitzler syndrome along with overlapping features in our case.

Table 2: Points in favor of HUVS and Schnitzler syndrome with the overlapping features in our case.

Specific points in favor of HUVS	Specific points in favor of Schnitzler syndrome	Overlapping features
• Decreased C1 esterase inhibitor	• Increased serum IgG, beta-2 globulin, and gamma globulin • Increased kappa light chain	• Persistent urticarial lesions with myalgia and joint pain
• Histopathological findings showing perivascular and sparse interstitial inflammatory infiltrate of predominantly lymphocytes and eosinophils with few neutrophils and karyorrhectic debris along with papillary dermal edema.	• Leukocytosis with increased neutrophil count	• Raised ESR and CRP

HUVS: Hypocomplementemic urticarial vasculitis syndrome, ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein

CONCLUSION

Non-availability of specific tests to measure C1q levels and anti-C1q precipitin levels to confirm the diagnosis of HUVS and similarly no single blood or laboratory test to confirm the diagnosis of Schnitzler syndrome is a hindrance in labeling our case into a specific diagnosis.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

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