***no patient handout*

Urticarial vasculitis

Synopsis

Urticarial vasculitis is a subtype of small vessel (leukocytoclastic) **vasculitis**. It is characterized by cutaneous findings of urticarial plaques with a predilection for the trunk and proximal extremities, with or without angioedema, and with histological findings of leukocytoclastic vasculitis on skin biopsy.

The lesions of urticarial vasculitis must be distinguished from those seen in acute and chronic **urticaria**. In contrast to the itch that predominates in acute and chronic urticaria, the plaques of urticarial vasculitis are often described as having a burning or painful sensation with mild itch. Additionally, each plaque in urticarial vasculitis persists for more than 24 hours and leaves behind residual hyperpigmented discoloration as it resolves. In contrast, each wheal of acute and chronic urticaria generally resolves within 24 hours and without residual discoloration.

Urticarial vasculitis is thought to represent a type III immune reaction with deposition of circulating immune complexes. It may be idiopathic in origin or may be precipitated by infections, medications, or neoplasms, and may be associated with connective tissue disease or paraproteinemia.

Complement levels in urticarial vasculitis may either be normal (normocomplementemic form) or low (hypocomplementemic form). While both forms can be associated with systemic symptoms including arthralgia (most common), the hypocomplementemic form is most commonly associated with more pronounced systemic involvement including pulmonary, ocular, gastrointestinal (GI), renal, and cardiac findings. Progressive **chronic obstructive pulmonary disorder** has been noted in hypocomplementemic urticarial vasculitis, particularly in smokers. There are also reports of bibasilar panacinar **emphysema** in these patients. Controversy exists as to the relationship between hypocomplementemic urticarial vasculitis and **systemic lupus erythematosus** (SLE), with some authors arguing that they are related disorders, or even potentially along one spectrum of disease.

Urticarial vasculitis can occur at any age, although it is most frequently noted in women in the fifth decade. It is rare in children; however, cases of both normocomplementemic and hypocomplementemic urticarial vasculitis have been reported. When hypocomplementemic urticarial vasculitis is seen in children, it is often associated with renal involvement.

Prognosis for urticarial vasculitis is generally noted to be positive, although outcomes largely depend on the presence of any associated or underlying disease. Rarely, marked renal involvement has been seen with hypocomplementemic urticarial vasculitis, more frequently in children than in adults. Additionally, there is one case report describing pulmonary hemorrhage in a child with urticarial vasculitis.

Codes

ICD10CM:
L95.9 – Vasculitis limited to the skin, unspecified

SNOMEDCT:
402656007 – Urticarial vasculitis

Look For

- Fixed urticarial plaque that lasts for >24 hours (although, importantly, resolution of lesion within 24 hours cannot completely exclude urticarial vasculitis).
- Plaques are described by the patient to be burning or painful, rather than itchy, and they leave behind hyperpigmentation as they resolve.
- Sites of predilection include the trunk and proximal extremities.
- Angioedema

Evaluate patient for potential associated systemic symptoms and signs (more common with hypocomplementemic urticarial vasculitis than normocomplementemic urticarial vasculitis):

- Musculoskeletal: arthralgia, arthritis
- Pulmonary: dyspnea
- GI: abdominal pain, nausea, vomiting, diarrhea
- Ocular: episcleritis, uveitis, conjunctivitis
- Lymphadenopathy
- Splenomegaly

Diagnostic Pearls

Unlike acute or chronic urticaria, the lesions of urticarial vasculitis can persist for >24 hours, may be painful or have a burning sensation, and leave behind residual hyperpigmentation as they resolve.

Diascopy reveals pinpoint petechiae within urticarial plaques.

If Jaccoud arthropathy (arthritis with deformity of hands and toes) is seen in patients with hypocomplementemic urticarial vasculitis, an echocardiogram can be considered as these patients have an increased risk of aortic and mitral valve pathology.

Differential Diagnosis & Pitfalls

- **Urticaria** (acute versus chronic) – Transient urticarial lesions that last <24 hours and resolve without residual pigmentary changes. Lesions are characterized as acute urticaria when they occur for <6 weeks and chronic when they are of ≥6 weeks duration.
- Neutrophilic urticaria – Variant of urticaria that shows a neutrophilic infiltration on biopsy but no vasculitis.
- **Serum sickness**
- **Systemic lupus erythematosus**
- **Cryopyrin-associated periodic syndromes** (CAPS) – Familial cold autoinflammatory syndrome (FCAS), Muckle-Wells syndrome (MWS), and neonatal onset multisystem inflammatory disease (NOMID, also known as chronic infantile neurologic cutaneous and articular syndrome [CINCA])
- **Schnitzler syndrome**
- **Cogan syndrome**
- **Mixed cryoglobulinemia**
- **Henoch-Schönlein purpura**

Best Tests

Skin biopsy shows neutrophilic infiltration, leukocytoclasia, and fibrinoid necrosis into the vessel wall of arterioles, capillaries, and post-capillary venules.

Associated work-up:

- C3, C4, C1q: low in hypocomplementemic form, normal in normocomplementemic form
- Cryoglobulins: low positive titers may be seen
- Rheumatoid factor: can be elevated in hypocomplementemic form due to consumption of complement
- Antinuclear antibodies (ANA): low titer can be positive in urticarial vasculitis; if positive, investigate further for SLE
- Erythrocyte sedimentation rate (ESR): often elevated

- IgG antibodies to the collagen-like domain of C1q: seen in ~55% of patients with hypocomplementemic form but is not specific to urticarial vasculitis and has been described in SLE as well
- Serum creatinine, urinalysis: renal involvement seen in hypocomplementemic form
- Pulmonary function tests, chest x-ray, or chest CT scan: to look for chronic obstructive pulmonary disease
- Anti-RNP, anti-ds DNA, ant-Ro, anti-La: has been associated with connective tissue disease

Management Pearls

Hypocomplementemic urticarial vasculitis may be associated with multiorgan involvement. Consult dermatology and rheumatology to assist with management. Consider consulting additional specialists such as ophthalmology, pulmonology, nephrology, and gastroenterology, depending on the clinical picture.

Therapy

Currently, there are no established guidelines for treatment of urticarial vasculitis.

Antihistamines have been used but are thought to be primarily helpful in addressing any pruritic component of the presentation.

Oral corticosteroids are often efficacious in urticarial vasculitis, but high doses may be required and flares frequently arise with medication taper. Some data suggests that hydroxychloroquine and colchicine may be just as effective as corticosteroids in hypocomplementemic vasculitis. Dapsone has also been used. For refractory cases, immunosuppression with mycophenolate mofetil, cyclophosphamide, and azathioprine has been suggested. Case reports describing the use of IVIG, rituximab, and plasmapheresis have also been reported. Finally, recent reports suggest success with the human monoclonal antibody (anti-IgE) omalizumab, the IL-1 receptor antagonist anakinra, and the anti-IL-1 antibody canakinumab.

Drug Reaction Data

Below is a list of drugs with literature evidence indicating an adverse association with this diagnosis. The list is continually updated through ongoing research and new medication approvals. Click on Citations to sort by number of citations or click on Medication to sort the medications alphabetically.

Medication	Citations
ACE inhibitor	1

Medication	Citations
Angiotensin II receptor blocker	1
Antiarrhythmic	1
Anticonvulsant	1
Antimetabolite	1
Calcium channel blocker	1
cimetidine	2
cocaine	1
diltiazem	1
enalapril	1
fluoxetine	3
glatiramer acetate	1
Histamine H2 antagonist	2
infliximab	1

Medication	Citations
levetiracetam	1
NSAID	1
paroxetine	1
pemetrexed	1
potassium iodide	2
procainamide	1
Selective serotonin reuptake inhibitor	3
simvastatin	1
statin	1
telmisartan	1