169 Other Forms of Vasculitis

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Hypocomplementemic Urticarial Vasculitis Syndrome

Definition

Hypocomplementemic urticarial vasculitis syndrome (HUVS) is a rare vasculitic disorder characterized by recurrent attacks of erythematous, urticarial, and hemorrhagic skin lesions associated with arthritis and sometimes abdominal distress. HUVS can also be distinguished by the presence of angioedema, urticaria, uveitis, and chronic obstructive pulmonary disease.

Etiology and Pathogenesis

Exact etiology of the diseases is unknown. HUVS is an immune complex disease characterized by the presence of anti-C1q antibodies at a high titer in all patients. Anti-C1q is thought to contribute to the formation of circulating or locally formed immune complexes. Furthermore anti-C1q may be pathogenic by disturbing the clearance of apoptotic cells, resulting in induction of autoimmunity or aggravating the autoimmune inflammatory state.

Clinical Manifestations, Laboratory Findings, and Pathology

Although rare, HUVS must be considered in the differential diagnosis for all patients with urticarial rash (*Fig. 169.1*). Renal disease affects up to 50% of patients and usually occurs within 4 years of onset of the rash. The laboratory hallmark of HUVS is hypocomplementemia involving the early components of the classical complement pathway. Urinalysis may be normal or can demonstrate hematuria and/or proteinuria.

The skin biopsy shows leukocytoclastic vasculitis whereas the kidney involvement may vary from crescentic glomerulonephritis to membranoproliferative or membranous lesions.

Differential Diagnosis

Systemic lupus erythematosus (SLE), cryopyrin associated periodic fever syndromes and other hypocomplementemic diseases should be considered in the differential diagnosis. A certain portion of the patients may progress to SLE as well.

Treatment and Prognosis

No specific therapy is currently available for HUVS. Skin lesions appear to be poorly responsive to antihistamines. Prednisone, hydroxychloroquine, or dapsone has been used successfully in anectodal reports. Pulmonary disease associated with HUVS can be life threatening, and no therapies have been shown to be consistently effective. Some patients with progressive renal deterioration have responded to high-dose prednisone, with or without cyclophosphamide. Prognosis depends on the extent of systemic involvement.

Cogan Syndrome

Definition

Cogan syndrome (CS) is a systemic vasculitis characterized by sensory neural hearing loss and nonsyphilitic interstitial keratitis.

Etiology and Pathogenesis

Etiology and pathogenesis remain unknown although association with some particular infections has been suggested. Organ-specific autoimmune processes have been implicated.

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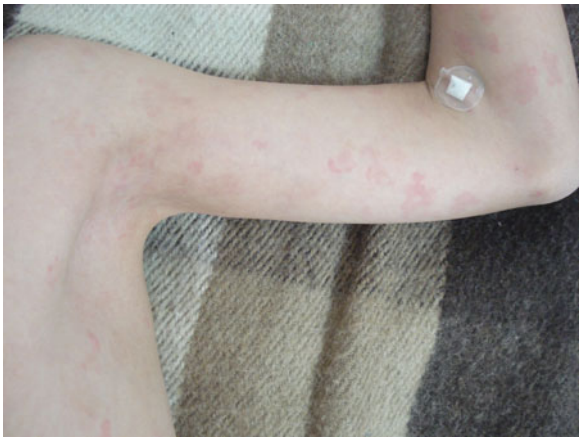

Figure 169.1
Typical urticarial lesions in hypocomplementic urticarial vasculitis in a girl

Clinical Manifestations and Laboratory Findings

Clinical manifestations include inflammatory eye disease (i.e., interstitial keratitis, conjunctivitis, scleritis, retinitis, retinal vasculitis) and vestibuloauditory dysfunction. Systemic vasculitis affecting aorta or small-/medium-sized arteries and aortic valve insufficiency and constitutional symptoms may be observed. Acute phase reactants are elevated and antinuclear antibody may be positive.

Differential Diagnosis

In differential diagnosis, one should consider Takayasu arteritis, Wegener's granulomatosis, and polyarteritis nodosa.

Treatment and Prognosis

Early diagnosis and treatment are mandatory to avoid ophthalmologic and otologic sequelae. A combination of corticosteroids and corticosteroid-sparing immunosuppressive drugs such as cyclophosphamide and methotrexate have been advocated. Disease course may be characterized by flares and remissions over years. A significant proportion of the patients become deaf.

Central Nervous System Vasculitis

Definition

Primary vasculitis (or angiitis) of the central nervous system (CNS) is inflammatory vasculitis affecting the CNS vessels alone. Diagnostic criteria have been suggested for adults including (1) a newly acquired neurologic deficit, (2) angiographic and or histologic features of CNS vasculitis, and (3) no evidence of systemic condition. CNS vasculitis can also be secondary to a number of infectious diseases or systemic lupus erythematosis.

Etiology and specific pathogenesis of the primary CNS vasculitis are unclear.

Clinical Manifestation, Laboratory Findings, and Pathology

Headache, transient ischemic attacks, paresis and plegia, seizures, encephalopathy, and neurocognitive impairment may all occur. The diagnosis may be considered in any child with sudden onset neurologic deficit.

Acute phase reactants and cerebrospinal fluid examination may be completely normal. There may be an increased protein and mild pleocytosis in the cerebrospinal fluid. An angiography is indicated for the assessment of CNS vasculitis. In large/medium vessel vasculitis, a magnetic resonance (MR) angiography may suffice. However, for small-vessel involvement a conventional angiogram has higher sensitivity and should be considered in the presence of typical MR changes. Angiography may be negative in small-vessel CNS vasculitis where only a brain biopsy will provide the definite diagnosis.

The histopathology reveals infiltration of mainly mononuclear cells around the vessel and sometimes granuloma formation.

Differential Diagnosis

Differential diagnosis includes systemic rheumatological diseases with CNS involvement including: SLE, Behcet's disease, polyarteritis nodosa, Kawasaki disease, Henoch–Schonlein purpura, and ANCA-associated vasculitides. Bacterial infections due to streptococcus, mycobacteria; viral infecations such as *Varicella zoster*, *Ebstein-Barr virus*; spirochetal infections such as *Borelia burgdorferi* and fungal infections such as aspergillus should also be considered. Finally, the differential diagnosis also includes neoplasms of the brain.

Treatment and Prognosis

There are no established treatment protocols but it is suggested to treat children with CNS vasculitis with corticosteroids and cyclophosphamide. Long-term follow-up is necessary to define the neurological, cognitive, and behavioral outcome. Distal artery involvement is associated with poorer outcome. Permanent neurologic deficit may occur.

Hypersensitivity Vasculitis

Definition, Etiology, and Pathogenesis

Hypersensitivity vasculitis (HV) is an inflammatory vascular disease characterized by prominent skin involvement with the existence of a trigger (usually a drug or vaccine). ACR defines HV as palpable purpura, precipitated by a medication or other agent with characteristic biopsy. It has been described after treatment with heterologous antiserum.

Pathology

Pathology is characterized by the perivascular or extravascular infiltration of the small vessels with polymorphonuclear leukocytes and the presence of leukocytoclasia.

Clinical Manifestations and Laboratory Findings

Skin lesions (i.e., purpura, urticaria, and palpable nodules) are predominantly located on the legs, although the upper limbs and trunk may also be affected. Generally the disease lasts few weeks with a self-limiting course. Relapsing and chronic course has been defined.

Leukocytosis usually occurs and is sometimes accompanied by eosinophilia and circulating immune complexes. The erythrocyte sedimentation rate is often normal.

Differential Diagnosis

Other causes of leukocytoclastic vasculitis should be considered in the differential diagnosis.

Treatment

Management is usually symptomatic consisting of antihistamines and NSAIDs. If systemic symptoms are present, corticosteroid therapy is indicated.

References

Agnello V, Koffler D, Eisenberg JW et al (1971) C1q precipitins in the sera of patients with systemic lupus erythematosus and other hypocomplementemic states: characterization of high and low molecular weight types. J Exp Med 134:228s–241s

Calabrese LH, Michel BA, Bloch DA et al (1990) The ACR 1990 criteria for the classification of hypersensitivity vasculitis. Arthritis Rheum 33:1108–1113

Calabrese LH, Furlan AJ, Gragg LA, Ropos TJ (1992) Primary angiitis of the central nervous system: diagnostic criteria and clinical approach. Cleve Clin J Med 59:293–306

Cassidy J, Petty RE (2001) Vasculitis. In: Cassidy JT, Petty RE (eds) Textbook of pediatric rheumatology, 4th edn. WB Saunders, Philadelphia

Elbers J, Benseler S (2008) CNS vasculitis in children. Curr Opin Rheumatol 20:47–54

Enriquez R et al (2005) Crescentic MPGN and hypocomplementemic urticarial vasculitis. J Nephrol 18:318–322

Kallenberg CGM (2008) Anti-C1q Autoantibodies. Autoimmun Rev 7:612–615

Schwartz HR, McDuffie FC, Black LF, Schroeter AL, Conn DL (1982) Hypocomplementemic urticarial vasculitis: association with chronic obstructive pulmonary disease. Mayo Clin Proc 57:231–238

St Clair EW, McCallum RM (1999) Cogan's syndrome. Curr Opin Rheumatol 11:47–52

Wisnieski JJ, Jones SM (1992) Comparison of autoantibodies to the collagen-like region of C1q in hypocomplementemic urticarial vasculitis syndrome and systemic lupus erythematosus. J Immunol 148:1396–1403