Pediatric Vasculitis

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KEYWORDS

• Vasculitis • Pediatrics • Review

Childhood vasculitis is a challenging and complex group of conditions that are multisystem in nature and often require integrated care from multiple subspecialties, including rheumatology, dermatology, cardiology, nephrology, neurology, and gastroenterology. Vasculitis is defined as the presence of inflammation in the blood vessel wall. The site of vessel involvement, size of the affected vessels, extent of vascular injury, and underlying pathology determine the disease phenotype and severity. Vasculitis can be secondary to infection, malignancy, drug exposure, and other rheumatic conditions, such as systemic lupus erythematosus and juvenile dermatomyositis. This article explores the classification and general features of vasculitis, as well as the clinical presentation, diagnostic evaluation, and therapeutic options for the most common primary systemic vasculitides.

DIAGNOSIS

Making the diagnosis of vasculitis is often challenging, as presenting symptoms may be subacute, nonspecific, and nondiagnostic. Fever, malaise, diffuse pain, and laboratory evidence of elevated acute-phase reactants may be the only early symptoms to suggest systemic inflammation. As vessel damage evolves, more specific clinical features, such as a purpuric rash, evidence of organ involvement, such as glomerulonephritis, or detection of certain antibodies, such as antineutrophil cytoplasmic antibodies (ANCA), may heighten the suspicion of vasculitis. The presenting symptoms can vary widely depending on the size and location of involved vasculature.

If vasculitis is suspected, then a thorough history and physical examination are paramount. The history should include recent infections, drug exposure, and a detailed family history. The physical examination should include a 4-extremity blood pressure evaluation. Takayasu arteritis (TA) may present with a blood pressure difference of greater than 10 mm Hg between arms, and hypertension is common with many of the vasculitides. In addition, careful auscultation for bruits (carotid, axillary, aortic,

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renal, and iliac vessels) and palpation of peripheral pulses is essential. Absent peripheral pulses may help identify areas of vessel involvement. A thorough skin examination is also important; the presence of painful nodules, purpura, ulcerations, microinfarctions, or livedo reticularis is common. A neurologic examination should evaluate for peripheral neuropathy; polyarteritis nodosa (PAN) is associated with mononeuritis multiplex. A fundoscopic examination and nailfold capillaroscopy are also helpful to visualize small vessel abnormalities.

The laboratory evaluation for vasculitis should include a complete blood count and acute phase reactants, such as the erythrocyte sedimentation rate and C-reactive protein, which can be markedly elevated. Liver enzymes, blood urea nitrogen and creatinine, and urinalysis will evaluate for hepatic and renal involvement. Specific antibody testing, such as antinuclear antibodies and ANCA, and complements should be sent depending on the vasculitis being considered. When clinical suspicion is high, imaging, such as computed tomography (CT) angiography, magnetic resonance (MR) angiography, or conventional angiography may help detect blood vessel abnormalities. Imaging may demonstrate prototypical patterns of vessel involvement, such as beading and aneurysms in PAN and TA, respectively. Typically, imaging is most useful when there is suspicion for medium-vessel or large-vessel disease. The diagnostic gold standard for diagnosis, however, is tissue biopsy.

CLASSIFICATION

Primary vasculitis can be classified according to clinical manifestations, size of the affected vessels, or histopathology, including the presence or absence of granuloma. In 2005, the European League Against Rheumatism (EULAR) and the Pediatric Rheumatology European Society (PReS) developed the first pediatric-specific classification of vasculitis (**Box 1**).[1] This classification system is primarily based on size of affected vessels and the presence or absence of granuloma.

EPIDEMIOLOGY AND PATHOGENESIS

The annual incidence of primary vasculitis in children and adolescents younger than 17 years is approximately 23 per 100,000.[2] Primary vasculitis accounts for approximately 2% to 10% of all pediatric conditions evaluated in pediatric rheumatology clinics.[3–6] Of the primary vasculitides, Henoch Schönlein purpura (HSP) and Kawasaki disease (KD) are the most common, accounting for 49% and 23% of all childhood vasculitis, respectively.[6] The prevalence of diseases may be different based on the population studied. For example, the incidence of KD and Behçet's disease is higher in Asian and Turkish children, respectively, than in other ethnicities.

These ethnic differences in prevalence suggest that genetics and environment may play an important role in disease susceptibility and pathogenesis. Other theories of pathogenesis include humoral factors, as manifest by ANCA-associated vasculitides. Abnormal regulation of immune complex formation may be contributory, as in HSP. Impaired lymphocyte regulation, specifically T-regulatory cell dysfunction, may also be involved. Antecedent infections, particularly streptococcal infections, have been implicated in many of the vasculitides including HSP, granulomatosis with polyangiitis (GPA), and PAN.

Henoch Schönlein Purpura

Etiology and epidemiology

HSP is a leukocytoclastic vasculitis that predominantly affects the small blood vessels. It is also known as anaphylactoid purpura or purpura rheumatica. The EULAR/PReS