HEMORRHAGIC VASCULITIS IN CHILDREN

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ANNOTATION

Vasculitis means inflammation of the blood vessel wall. Any type of blood vessel in any organ could be affected. This vasculitis is characterized by fibrinoid necrosis, thrombosis and sometimes granulomatous reaction.

Key words. Vasculit, blood wessel, Henoch Schönlein purpura (HSP), Kawasaki disease (KD), Behcet's disease (BD)

INTRODUCTION

The term vasculitis covers heterogeneous disorders that share the presence of inflammation of blood vessel walls. Immune cell infiltrates can vary significantly and involve granulocytes or mononuclear cells. Vasculitis can be a symptom of other underlying disorders or the underlying cause of organ specific or systemic disease.

Vascular damage may occur venules, capillaries, and arterioles causing local and systemic clinical manifestations, depending on the organ involvement. Systemic manifestations results from release of chemical mediators from inflamed blood vessels. They include fever, night sweats, malaise, weight loss, arthralgia, myalgia and laboratory features such as normocytic normochromic anaemia, leucocytosis, thrombocytosis and raised erythrocyte sedimentation rate (ESR) and C reactive protein (CRP). Treatment of some form of vasculitis secondary to infection or drugs is different from that of primary vasculitis. It is important to exclude such conditions that are likely to cause secondary vasculitis.

Classification of childhood vasculitis is based on clinic, the size of predominantly affected vessels, and the histopathology of inflammatory infiltrates. Timely and accurate diagnosis and (where necessary) treatment initiation determine disease progression and outcomes. In light of new developments and the identification of autoinflammatory conditions with vasculitis, new classification tools may be discussed.

Classification of Primary Vasculitis on the Basis of Size of Affected Blood Vessel

Large vessel vasculitis

I. Giant cell arteritis
II. Takayasu arteritis

Medium vessel vasculitis

I. Polyarteritis nodosa
II. Kawasaki disease

Small vessel vasculitis

I. Wegener's granulomatosis
II. Churg-Strouss syndrome
III. Microscopic polyangitis
IV. Henoch-Schonlein purpura

V. Cutaneous leucocytoclastic angitis

The annual incidence of primary vasculitis in children and adolescents younger than 17 years old is approximately 23 per 100,000. Primary vasculitis accounts for approximately 2–10% of all pediatric conditions evaluated in pediatric rheumatology clinics.

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. The prevalence of diseases may be different based on the population studied. For example, the incidence of KD and Behçet's disease are higher in Asian and Turkish children, respectively, than in other ethnicities.

METHODS

If vasculitis is suspected then a thorough history and physical exam are paramount. The history should include recent infections, drug exposure, and a detailed family history. The physical examination should include a four-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. Additionally, careful auscultation for bruits (carotid, axillary, aortic, 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 neurological exam should evaluate for peripheral neuropathy; polyarteritis nodosa (PAN) isassociated 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 (ESR) and c-reactive protein (CRP), 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 (ANA) and ANCA, and complements should be sent depending on the vasculitis being considered. When clinical suspicion is high, imaging such as CT angiography, 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 or large vessel disease. The diagnostic gold standard for diagnosis, however, is tissue biopsy.

RESULTS

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 infections, particularly streptococcal infections, have been implicated in many of the vasculitides including HSP, granulomatosis with polyangiitis (GPA), and PAN. Several forms of vasculitis can affect vessels of variable types and diameters.

Behcet's disease (BD) is characterized by inflammatory lesions in vessel walls of all sizes, which may lead to endothelial damage, thrombosis, and aneurysms. Chronic recurrent oral and/or genital ulcers occur can be accompanied by additional

cutaneous (erythema nodosum, cutaneous pustular vasculitis, etc.), ocular (posterior uveitis, retinal vasculitis), articular (nonerosive poly- or oligo-arthritis), gastrointestinal (abdominal pain, nausea, diarrhea, etc.), and/or central nervous symptoms (aseptic meningitis, vascular thrombosis). Cases of BD can be seen across the globe and in all ethnicities. However, prevalence is highest in countries along the Silk Road, where it ranges between 77 and 100/100,000 individuals (0.1–15.9/100,000 in Western Europe). While most patients develop symptoms in young adulthood, 5–10% exhibit childhood-onset BD. The pathophysiology of BD is incompletely understood, but genetic associations are likely involved and may be influenced by environmental factors. HLA-B51/B5 allele carriers have considerably high risk for BD indicating a possible genedose effect.

Cogan syndrome (CS) is characterized by predominantly large vessel vasculitis, but can affect any vessel size. CS is an extraordinarily rare multisystem inflammatory condition that can involve eyes (keratitis, uveitis, episcleritis) and inner ears (sensorineural deafness, vestibular dysfunction). Unspecific systemic symptoms occur in 50% of all patients, including arthralgia and manifestations of mediumsize and small vessel vasculitis. To date, only few pediatric patients have been reported. Based on the rarity and lack of pathophysiological understanding of the disorder, data on effective treatments are lacking. Available reports favor DMARDs (AZA, MTX) in combination with TNF inhibitors

CONCLUSIONS

Vasculitis are rare conditions in children and young people that can be subdivided and classified based on clinical phenotypes (e.g., organ-specific vs. systemic) underlying causes (primary vs. secondary disease), histological patterns (granulomatous, non-granulomatous, necrotizing, etc.), and primarily affected vessel sizes (Chapel Hill and EULAR/PRES classifications: small/medium/large). Timely and accurate diagnosis and (where necessary) treatment initiation are essential, provided the variable severity and outcomes of individual forms of vasculitis. Pediatricians should consider vasculitis as part of the differential diagnosis in children with evidence of systemic inflammation and multisystem disease that cannot be otherwise explained.

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