Vasculitis in children: Classification and clinical presentation

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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 a blood vessel that may occur as a primary process or secondary to an underlying disease. In children, vasculitis is rare, with reported annual incidences that range from 12 to 53 per 100,000 children under 17 years of age. Annual incidences of primary vasculitis accounting 2-10% of all pediatric rheumatology clinics.

Vasculitis can be secondary to infection, malignancy, drug exposure, and other rheumatic conditions such as systemic lupus erythematosus and juvenile dermatomyositis.

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.

This classification system is primarily based upon size of affected vessels and the presence or absence of granuloma.

EULAR/PReS classification of pediatric vasculitis

Predominately large vessel
- Giant cell (temporal) arteritis
- Takayasu arteritis

Predominately medium vessel
- Childhood polyarteritis nodosa
- Cutaneous polyarteritis
- Kawasaki disease
Predominately small vessel
Granulomatous
Wegener's granulomatosis
Churg-Strauss syndrome

Non-granulomatous
microscopic polyangiitis
Henoch-Schönlein purpura
isolated cutaneous leukocytoclastic vasculitis,
hypocomplementemic urticarial vasculitis

other
Behcet's disease
vasculitis secondary to infection, malignancy, drugs
vasculitis associated with connective tissue diseases
isolated vasculitis of the CNS
Cogan syndrome
Unclassified

incidence of primary pediatric vasculitis
Henoch-Schönlein purpura (IgA vasculitis) is the most common vasculitis accounts almost half (49%)
followed by Kawasaki disease (KD) the second common (24%) and polyarteritis nodosa (PAN) accounting almost 3%
of primary pediatric vasculitis.

Takayasu arteritis which occurs more frequently in children from the Far East and Africa and ANCA-positive vasculitides affect one child in a million each year. Since these conditions are so rare in the pediatric age group diagnosis may be significantly delayed leading to more disease-related damage at the time therapy is initiated.

Eosinophilic granulomatosis with polyangiitis, formerly Churg-Strauss syndrome, is extremely rare in children
temporal arteritis is not seen in pediatric patients.

What is the Initial Clinical Approach to a Child with Vasculitis?
The initial evaluation of any child suspected of having vasculitis includes a detailed history, comprehensive physical examination, and basic laboratory testing. The goal is to both support a diagnosis of vasculitis and to exclude other more common conditions that may present similarly. In most cases, the diagnosis of a primary vasculitis is made based upon clinical findings and pattern recognition of the characteristic findings associated with the specific disease.

Some forms of childhood vasculitis are essentially clinical diagnoses. Entities such as KD and HSP, acute hemorrhagic edema of infancy (considered widely as an infantile form of HSP) are examples. In other situations if a detailed history and clinical examination suggests vasculitis, the next step is to categorize the dominant vessel size involved. This helps to prioritize the investigative process.

CLINICAL PRESENTATION
Constitutional symptoms, such as malaise, fatigue, and fever are frequently present. These early findings are neither specific nor sensitive for vasculitis and may be found in other conditions including common infections. In patients with such nonspecific systemic symptoms, vasculitis should be strongly considered if symptoms do not resolve as would be expected in a "self-limited" infectious illness. In addition to systemic symptoms, the presence of multiorgan involvement should heighten one's suspicion of vasculitis. In some cases, certain combinations of clinical features or patterns of organ involvement are suggestive of, and sometimes sufficient for the diagnosis of, a specific vasculitis (pattern or syndrome recognition).

As an example, the combination of lower extremity purpura, abdominal pain, joint pain, and glomerulonephritis would suggest the diagnosis of Henoch-Schönlein purpura (IgA vasculitis), whereas the syndrome of persistent fever, conjunctivitis, rash, mucocutaneous changes, and swelling of the hands and feet would suggest the diagnosis of Kawasaki disease.

HSP is the most common form of small-vessel vasculitis in children. HSP occurs in 5–10% of patients with familial Mediterranean fever (Ozdogan et al. 1997). It has also been reported in some children with the hyper-IgD syndrome. Only 2% of children with HSP have bullous lesions.

Biopsy should be considered:
- if bullous lesions are present
- if there is evidence of tissue necrosis
- since this complication is extremely uncommon in children with HSP, Kawasaki disease, and Henoch-Schönlein purpura (IgA vasculitis) are primary vasculitides of childhood that are relatively common compared with the other vasculitides and are usually acute and self-limited. Their clinical features have been well described in children. The other chronic idiopathic vasculitides (eg, granulomatosis with polyangiitis (Wegener's), polyarteritis nodosa, microscopic polyangiitis, Takayasu arteritis) are relatively rare in childhood. Although typical characteristics and clinical "syndromes" have been described for adults with these vasculitides, the presentation in children may not be so "typical," and the diagnostic process often requires consideration.

Always, it should be remembered in children there may be secondary vasculitis and also conditions that may mimic vasculitis.

A careful and detailed history should identify which organ systems are affected and the extent and severity of their involvement.

The history should include the following:
- Recent illness, particularly infections, either in the patient or in close contacts.
- Exposure to any medications or toxins that may cause secondary vasculitis.
- History of any predisposing condition for secondary vasculitis, such as hepatitis, systemic lupus erythematosus (SLE), juvenile dermatomyositis, or malignancy.

Physical examination
- Palpation of all pulses for volume and symmetry.
- Measurement of blood pressure (BP)
- BPs should be measured in all four limbs because a significant asymmetry between limbs would raise the suspicion of Takayasu arteritis. 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.
Auscultation of the neck, abdomen, and extremities to detect the presence of a bruit, which would suggest altered blood flow through an affected vessel.
Examination of the skin for lesions suggestive of vascular insufficiency or inflammation, such as palpable purpura, livedo reticularis, nodules, ulcers, and nonblanchable rashes.
A neurological exam should evaluate for peripheral neuropathy; polyarteritis nodosa (PAN) is associated with mononeuritis multiplex.
Examination of the ocular fundi and preungual capillary beds for evidence of vascular abnormalities.

OUTCOME
The majority of children with primary vasculitis have a good outcome because the two most common disorders, Kawasaki disease and Henoch-Schönlein purpura (IgA vasculitis), are usually self limited and only a small minority of children have long-term sequelae from either damage or ongoing disease activity

Chronic disorders
Unlike Henoch-Schönlein purpura (IgA vasculitis) and Kawasaki disease, other primary systemic vasculitides, such as Takayasu arteritis, granulomatosis with polyangiitis (Wegener's), polyarteritis nodosa, microscopic polyangiitis, and Churg-Strauss syndrome) are characterized by chronic, often relapsing, disease courses

References:
7. Patricia Woo, Ronald M. Laxer and David D. Sherry. Pediatric Rheumatology in Clinical Practice 2007