Usual and Unusual Manifestations of Systemic and Central Nervous System Vasculitis

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KEYWORDS

• Vasculitis • Pediatrics • Arteritis

KEY POINTS

- Diagnosis of vasculitis requires understanding and recognition of the clinical manifestations associated with each disease.
- The different vasculitides can be distinguished clinically, histologically, and with laboratory testing and imaging studies.
- Although there are common clinical patterns for each vasculitis, there are additional unusual clinical manifestations associated with these illnesses.
- Infectious, congenital, genetic, and metabolic diseases may mimic vasculitis.

INTRODUCTION

The idiopathic vasculitides are a complex group of immune-mediated illnesses that share blood vessel inflammation as the common primary feature.[1,2] These illnesses characteristically affect multiple organ systems, may present acutely or indolently, have overlapping clinical signs and symptoms, may mimic infectious illnesses and other systemic diseases, and respond variably to immunosuppressive and antiinflammatory treatment. Therefore, the vasculitides are frequently challenging to both diagnose and manage.[1] With the understanding that all of the forms of vasculitis in children are uncommon, this article discusses the primary pediatric vasculitides that pediatricians might encounter. Both characteristic and unusual manifestations are discussed.

DEFINITION AND CLASSIFICATION

There have been multiple attempts to define and classify the idiopathic vasculitides.[3–9] Vasculitis may be specified and organized based on the type of vessels affected, the

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size of vessels affected, the histopathology, or the presence of specific laboratory findings (eg, antineutrophil cytoplasmic antibodies [ANCA]). The American College of Rheumatology developed classification criteria for several types of vasculitis in adults in 1990.[4,5] Subsequently, consensus criteria for adult patients known as the Chapel Hill criteria were developed in 1994,[10] adopting a classification scheme primarily based on vessel size, which were revised most recently in 2012[3] (**Box 1**). In 2005, the Pediatric Rheumatology European Society (PRES) developed a classification scheme and classification criteria specifically for pediatric vasculitis.[6] This group also adopted a classification based on vessel size (**Box 2**). In 2008, the criteria for some of the most common pediatric vasculitides (Henoch-Schönlein purpura [HSP], granulomatosis with polyangiitis [GPA], polyarteritis nodosa [PAN], and Takayasu arteritis) were subsequently revised and validated with support from the Pediatric Rheumatology International Trials Organization (PRINTO)[7,8] (**Box 3**). Each of these attempts to organize, define, and classify these illnesses will remain imperfect and a work in progress until the specific causes, and perhaps the potential genetic associations, of the different vasculitides are fully understood.

DIAGNOSIS

The most common pediatric vasculitides, such as Kawasaki disease and HSP, present acutely with characteristic clinical manifestations and are not associated with specific diagnostic laboratory tests. The diagnosis therefore is most often based on clinical features alone. For the other idiopathic vasculitides, in addition to recognizing a pattern of clinical and consistent laboratory findings, the diagnosis also requires the identification of characteristic imaging findings, histopathology, or both. The ANCA-associated vasculitides are an exception, because these diagnoses may be made with reasonable certainty in the presence of characteristic clinical findings and a positive test for ANCA. The classification criteria developed for adults[3] and children[8] may be helpful when considering a diagnosis of vasculitis by allowing clinicians to match the features of an individual patient to the usual manifestations of the disease. However, it is important to recognize that classification criteria are generally based on typical and common manifestations of diseases, and strictly adhering to such criteria may, at times, result in diagnostic error or delay when some manifestations do not seem to fit the typical pattern.

A thorough history and physical examination are of paramount importance in helping to guide diagnostic testing. It is most helpful to carefully define the timing of onset of symptoms, the specific body or organ systems affected, and the severity of the systems. Many of the systemic vasculitides are associated with nonspecific constitutional symptoms, such as fever, fatigue, malaise, poor appetite, and weight loss, which may dominate the patient's and family's concerns, resulting in decreased awareness of the significance of additional symptoms and signs. A comprehensive review of systems should be performed with attention to even the most seemingly innocuous complaint. A review of medications, past history, family, and social history may provide clues to a specific diagnosis and also help to differentiate the vasculitides from infections, drug reactions, and other mimics of vasculitis (**Boxes 4–6**).[11] A careful and thorough physical examination is also essential, because there may be subtle findings that the patient and family either have not noticed or have overlooked. Particular attention to vital signs (eg, tachycardia, tachypnea, hypertension), skin findings (eg, palpable purpura, petechiae), peripheral pulses, the joint examination, and neurologic abnormalities are most helpful. Vital sign changes may be the only clue to the presence of significant heart, lung, or renal disease associated with a vasculitis.