Imaging of Childhood Vasculitis

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KEYWORDS

• Children • Ultrasound • Computed tomography • MR imaging • Vasculitis

KEY POINTS

- Childhood vasculitis is a challenging and complex group of conditions that are multisystem in nature and often require an integrated multi-imaging approach.
- Diagnostic imaging has a pivotal role in the diagnosis of vasculitis. Selection of the most appropriate imaging modality to help proper diagnosis of pediatric vasculitis is of the upmost importance.
- In large and medium vasculitis, conventional DSA has been replaced in most cases by CT and MR angiography, whereas in small-vessel vasculitis cross-sectional imaging with ultrasound, CT, and MR imaging has a pivotal role in the evaluation of target organ damage.

INTRODUCTION

Primary childhood vasculitides are a complex group of rare multisystem diseases associated with significant morbidity and mortality with an estimated annual incidence of approximately 23 to 50 per 1 million.[1,2] These conditions account for approximately 2% to 10% of all disorders that are pertinent to pediatric rheumatology clinics.[3] Generally speaking, the term vasculitis refers to changes occurring in the vessel wall induced by inflammation. Initially, symptoms may be insidious and nonspecific, including fever, malaise, increased erythrocyte sedimentation rate and C-reactive protein, and diffuse regional pain. As damage progresses, aneurysmal dilatation, stenosis, and occlusion may occur and there may be onset of specific symptoms depending on the target organs, type and size of vasculature, and extent of vascular involvement. The pathogenesis of primary childhood vasculitis is not fully understood, although abnormal regulation of immunocomplex formation, impaired lymphocyte regulation, and antecedent infections have been variably implicated depending on the disease condition. Some ethnic difference in prevalence (eg, higher incidence in Asian and Turkish children) suggests that genetics and environment may play a pathogenetic role. In children, secondary vasculitis may be encountered following hepatitis B or C infection, drug therapies (eg, antithyroid agents, tumor necrosis factor-α inhibitors), other autoimmune diseases (eg, systemic lupus erythematosus, juvenile dermatomyositis, juvenile idiopathic arthritis), and malignancies.[3]

Nomenclature and Classification

Childhood vasculitis encompasses a wide range of subcategories that are mainly defined based on vessel size including predominantly large, medium, and small blood vessel vasculitis

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(granulomatous and nongranulomatous).[4] Clinical presentation and patient management significantly differ between adult and childhood vasculitis. Thus, in 2006, the vasculitis working group of the Pediatric Rheumatology European Society issued specific classification criteria for some of the most common childhood vasculitides, including IgA vasculitis (formerly Henoch-Schönlein purpura), childhood polyarteritis nodosa, childhood granulomatosis with polyangiitis (formerly Wegener granulomatosis), children Takayasu arteritis, and Kawasaki disease.[3] These criteria were modified and validated using a large international World Wide Web–based registry (PRINTO) and finally recognized and endorsed by the European Society of Pediatric Nephrology and the European League Against Rheumatism (http://ard.bmj.com/content/65/7/936.long).[5,6]

Diagnostic Work-up

The diagnostic work-up in childhood vasculitis requires thorough analysis of the patient's history and physical examination because presenting symptoms may be subacute, nonspecific, and can vary widely depending on the size and location of involved vasculature.[4] As damage progresses with more specific clinical features (eg, onset of purpuric rash; evidence of organ involvement, such as glomerulonephritis), careful auscultation for arterial bruits and palpation of four-extremity peripheral pulses is mandatory, as is extensive examination of the skin, fundoscopy, and nailfold capillaroscopy. Antinuclear antibodies and antineutrophil cytoplasmic antibodies (ANCA) and complement should also be assessed.[4]

Diagnostic imaging plays a critical role in securing the diagnosis of vasculitis affecting large- and medium-sized vessels, and in evaluating organ involvement in small vessel forms. In childhood vasculitides affecting predominantly large- and/or medium-sized blood vessels, ultrasound (US) complemented with Doppler techniques, MR angiography, and computed tomography angiography (CTA) are the imaging modalities of choice to provide an early detection of vessel changes.[7–9] All of these investigations are also used as outcome measures to monitor the efficacy of treatment and the evolution of damage in longitudinal studies.[4] In many instances, US is considered the first-line technique because of its excellent spatial resolution and ability to detect mural thickening and luminal changes without exposure to ionizing radiation. In the thorax, however, US has intrinsic limitations related to problems of access and when a vessel is deep-seated in the abdomen, its spatial resolution may be suboptimal to reveal initial wall abnormalities. CTA has excellent vascular resolution and three-dimensional rendering capabilities, but repeated studies using this modality should be avoided in children because of radiation exposure.[10,11] Although MR angiography has lower spatial resolution than CTA, its sensitivity is almost equal to conventional angiography in detection of luminal changes in large blood vessels.[12,13] In addition, by means of whole-body technique, MR imaging has proved to be a fast and accurate method for detecting, mapping, and monitoring vascular abnormalities throughout the body in systemic childhood vasculitides avoiding exposure to ionizing radiation.[14,15] As a rule, the use of intravenous administration of iodinated or gadolinium (Gd)-based contrast media has to be restricted to the real needs in these patients because renal function impairment may be an issue. Digital subtraction angiography (DSA) should be regarded as a challenging procedure in children in view of its invasive nature, radiation exposure, use of iodinated contrast material, and operator-dependence.[8] Although still considered as the gold standard for the diagnosis of pediatric vasculitides, it does not provide any direct information regarding the vessel wall. Its role is therefore limited as a guide for interventional procedures in cases of vasculitis-related complications and to map the extent of collateralization.[9] Fluorine-18-fluorodeoxyglucose positron emission tomography (PET) is able to detect increased metabolic activity in the wall of inflamed vessels.[8,16,17] Nevertheless, its ultimate role in childhood vasculitis has still to be defined. Aneurysms are typically encountered in vasculitis of medium-sized blood vessels. Most are localized in the coronary, mesenteric, and renal arteries. For evaluation of the coronary arteries and cardiac function, echocardiography plays a pivotal role.[18] In small-vessel disease, the role of diagnostic imaging to detect tissue damage related to microvasculature and perfusion abnormalities is limited because of insufficient resolution of imaging and restrictions for use of microbubble-based ultrasonic contrast agents in the pediatric age group.

LARGE-VESSEL VASCULITIS

Takayasu Arteritis

Takayasu arteritis is a granulomatous vasculitis of unknown cause that predominantly affects the aorta with its major branches (eg, the subclavian, and more rarely, the pulmonary, carotid, renal, and coronary arteries).[19,20] This condition has a definite female predominance (3:1) and is diagnosed during adolescence (peak age at onset,