

Childhood Polyarteritis Nodosa: A Clinical Diagnosis

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A six-year old boy presented with dry gangrene of toes and fingers with hypertension with no other systemic abnormalities. He had persistently high inflammatory parameters, was diagnosed as childhood classic polyarteritis nodosa and showed improvement with immunosuppressants along with antihypertensives. Toe gangrene required amputation in view of superadded infection.

Key words: *Childhood polyarteritis, Gangrene, Hypertension.*

Polyarteritis nodosa (PAN) is a rare systemic vasculitis characterized by necrotizing arteritis of predominantly medium sized vessels leading to micro-aneurysms, rupture and hemorrhages, and manifesting with multi-system involvement. Childhood presentation is rare and very few cases are reported from India(1-3).

Case Report

A 6-year-old boy presented to us with

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history of acute onset of blackish discoloration of bilateral toes and fingers associated with severe burning sensation and pain. There was no history of fever, abdominal pain, gastrointestinal bleeds, testicular pain, skin rash, photosensitivity, arthralgia, oliguria, hematuria, cough, dyspnea or hemoptysis. Examination revealed dry gangrene of right 3rd toe and impending gangrene of multiple toes, fingers and heel. Pulses were normal, there was no bruit and blood pressure (BP) in upper and lower limbs was normal (100/60; 110/60 respectively). Systemic examination was unremarkable. He had an episode of generalized seizures on 3rd day after admission when his BP was found to be 180/120 mm Hg. He required combination of three antihypertensive agents to control his BP and did not have recurrence of seizures subsequently. He remained conscious with no focal neurological deficits. Investigations revealed normocytic hypochromic anemia (Hb 10 g/dL polymorphonuclear leucocytosis (TLC 20,700 cells/cu mm, polymorphs 92%), normal platelet counts and raised erythrocyte sedimentation rate (120 mm 1st hour Westergren's). Urine, serum electrolytes, liver and renal functions were normal. Sickling test was negative. Antinuclear antibody (ANA), Antineutrophil cytoplasmic antibody (ANCA), anticardiolipin antibody (IgG, IgM), lupus anticoagulant and antistreptolysin O (ASLO) were negative. Hepatitis B surface antigen was negative. Chest X-ray, ultrasonography of abdomen and echocardiography were normal. Color doppler showed normal renal arteries. Histopathology and visceral angiography could not be done due to practical limitations. In view of gangrene with hypertension without any evidence of infection, the child was diagnosed as classic PAN and treated with oral steroids and oral cyclophosphamide in standard doses. There was no further progression of gangrene and line of

demarcation was formed in left toes. Right toes and hand gangrene completely improved. In view of extensive superadded infection in gangrenous left toes, the child required mid-foot amputation. He is presently under our follow up on maintenance with tapered dose of oral steroids for over one year now with no relapse. His antihypertensive dose has now come down to a single agent.

Discussion

Classic PAN is an uncommon disease characterized by predominantly medium-sized artery inflammation leading to involvement of skin, kidney, peripheral nerves, muscle and gastrointestinal tract. Involvement of other organs like lungs, brain and heart is rare. The involvement of kidney is classically limited up to the level of spiral arteries and glomerulonephritis is not seen. This is unlike Microscopic polyangiitis (MPA/microscopic PAN), where systemic vasculitis is associated with small vessel vasculitis causing glomerulonephritis and alveolitis.

Several diagnostic criteria intended to be fulfilled in epidemiological studies or drug trials have been recommended for clinicopathological diagnosis of PAN(4,5). The diagnostic criteria proposed by Ozen et al in 1992 for the diagnosis of childhood PAN(6) included 2 major and 10 minor clinical and laboratory features without the immediate need of angiography and biopsy. In this retrospective study of 31 patients, there was a good correlation of these criteria with histopathological diagnosis of PAN. The authors however, proposed to use these criteria for early diagnosis after a prospective study validation. This is a clinical criteria aiding in an early diagnosis while awaiting a definite diagnosis by angiography or biopsy. One major feature in this study included renal parenchymal involvement with proteinuria,

hematuria or rapidly progressive glomerulonephritis. As per the current understanding and the classifications proposed after the Ozen's criteria(7), the presence of proteinuria and or active urine sediments suggest the diagnosis of Wegener's granulomatosis and MPA, while classic PAN is associated with bland urine sediments. It may be likely that at least some patients from Ozen's study had either of these two conditions as also evidenced from pulmonary infiltrates or hemoptysis in some of these patients. MPA is a disease with autoantibody (p-ANCA) association in most, while classic PAN lacks the antibody in almost all, making further distinction between these two conditions(8). Our patient had a presentation where acute onset of gangrene was attributable to classic PAN in view of unexplained hypertension (suggestive of renal artery involvement) with no evidence of glomerulonephritis. Other features aiding in the diagnosis were polymorphonuclear leucocytosis, elevated ESR, negative autoantibodies (ANA, ANCA), neuropathic pain and no apparent infectious etiology. Although histopathology and or angiography is important for confirmation of PAN, practical limitations, as in our patient, may lead to situations where one may provisionally diagnose the disease as per Ozen's clinical criteria(6) without the aid from these specific tests. Despite lack of histopathology and angiography, our patient satisfied the required 3/10 of the ACR criteria for diagnosis of PAN but only 5 minor of the Ozen's criteria lacking major feature of renal parenchymal involvement, which we however contested above.

Other causes of gangrene in childhood like septicemia, bacterial endocarditis, left atrial myxoma, drugs, hypercoagulable states and frostbite should be excluded. Streptococcal and Clostridium infections in childhood are

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known to cause gangrene. Cutaneous PAN presenting with recurrent gangrene associated with Streptococcal infection has been described(9). Children with sickle cell disease have also been reported to develop infective gangrene(10). Other connective tissue diseases like childhood lupus and scleroderma may also cause gangrene and hypertension. We excluded all these causes in our patient. We did not entertain possibility of acquired deficiency of protein C, protein S or antithrombin III in our patient, which may lead to a prothrombotic state manifesting usually with venous thrombotic events.

Steroids, with or without cyclophosphamide is the recommended mode of therapy for PAN. Our patient showed significant improvement with early institution of this therapy. Despite being a rare disease, PAN should be included as a differential diagnosis in children with gangrene and or unexplained hypertension to enable early diagnosis and proper management which can lead to reduced morbidity and mortality.

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