CO-OCCURRENCE OF MEDIUM AND LARGE VESSEL VASCULITIS: DILEMMA IN CLASSIFICATION

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Abstract
Overlap among different autoimmune diseases is well known, but in vasculitis they are seen rarely. We report here two patients with vasculitis involving large and medium sized blood vessels thus defying any classification.

Introduction:
Many classification systems have been proposed for classifying patients with primary vasculitis. In most cases it is possible to categorize them in one or the other type but there are a few who either do not full criteria for diagnosis or have an overlap of two diseases the so called 'polyangitis syndrome'.

Case 1:
A 30 year old man presented with recurrent multiple, painful, subcutaneous nodules on both thighs and forearms since the age of 14 years. Each episode used to last for 7-10 days and lesions used to heal without scarring. Three years ago he had sudden onset of left temporal headache associated with diplopia in left eye. Contrast enhanced CT scan and cerebrospinal fluid examination was normal. Ten months ago, he had right sided headache followed by unsteady gait. Five months ago, he had epistaxis and was found to be hypertensive. He also had 3 episodes of testicular pain and swelling over last year lasting for a week each time. He had right vitreous hemorrhage leading to blindness. Since childhood he has been aware of absent pulses in left upper limb. He denied any history of claudication in any limb.

On examination, he had a pulse rate of 88/min with absent left brachial and radial pulses; blood pressure was 120/96 in right upper limb while it was not recordable in left upper limb. He had two tender subcutaneous nodule on left arm with overlying skin being normal.

His investigations were as follows: Hemoglobin 14.8 g/dl, total leukocyte count 12,400/cu mm with normal differential count. Erythrocyte sedimentation rate 5mm in first hour, C reactive protein 2.19 mg/dl. Serum creatinine 1.0 mg/dl, urine examination-normal; anti-nuclear antibody, anti-neutrophil cytoplasmic antibody, anti-cardiolipin antibody and HBsAg were all negative. Serum IgG, IgM, IgA, C3 and C4 were normal.

Digital subtraction angiography revealed 60% narrowing of proximal left subclavian and right common carotid artery. Both carotid arteries had segmental narrowing. Other branches of aorta were normal. Subcutaneous nodule biopsy revealed medium sized vessel involvement with degeneration of arterial wall, deposition of fibrinoid material, focal destruction of internal elastic lamina and fibrosis of vessel wall. Lumen was occluded with thrombus. There was perivascular inflammatory infiltrate composed of neutrophils, few eosinophils and lymphocytes.

Case 2:
A 31 year old man presented in July 1989 with abdominal angina, intermittent claudication of lower limbs with claudication distance of 50 meters, polyarthritis and low grade fever of 1 year duration. He had also noticed painless genital ulcers and small subcutaneous nodules over his arms for last 3 months. He had lost 25-Kg weight in the last 1 year. He denied any history of hypertension, neuropathy, oral ulcers, red eye, photosensitivity, jaundice or pedal edema.

On examination, he was emaciated and pale. The pulse rate was 100/min and blood pressure was 160/65 mmHg; femoral, popliteal and dorsalis pedis pulses on both sides were feeble. There were subcutaneous erythematous nodules, nearly 1 X 1 cm in size, over both the arms and an early diastolic murmur in the aortic area. Rest of the systemic examination was unremarkable.

Investigations revealed hemoglobin of 7g/dl, ESR 90mm fall in the first hour, serum bilirubin 0.7 mg/dl, ALT/AST 65/49 IU/L, serum creatinine 0.4 mg/dl, 24-hour urinary protein excretion 920 mg. Chest X-ray: aneurysmal dilatation of the ascending and descending aorta. Echocardiography confirmed aortic regurgitation due to aortic root dilatation and aneurysmal dilatation of ascending and descending aorta. Antinuclear antibody and rheumatoid factor were negative and HBsAg was positive. Immunoglobulin and complement levels were normal. Subcutaneous nodule...
biopsy revealed perivascular inflammatory infiltrate with fibrinoid necrosis of the vessel wall. Liver biopsy showed evidence of chronic persistent hepatitis. Digital subtraction angiography revealed bilateral renal artery stenosis, partial blockage of superior mesenteric artery and evidence of aneurysms in its branches. HLA typing for B locus revealed presence of B5 and B7 antigens.

He was treated with monthly bolus cyclophosphamide (1000 mg) and 0.5 mg/kg/day of prednisolone for 6 months which was followed by oral cyclophosphamide 100 mg/day and prednisolone 0.5 mg/kg every alternate day. He also underwent balloon angioplasty of right femoral artery to alleviate intermittent claudication. He remained asymptomatic for the next one year. He was lost to follow up for the next 3 years.

He came back in July 1993 with complaints of increasing intermittent claudication in lower limbs for one year. The claudication distance was only 200 meters. He denied any history of fever, weight loss, anorexia, neuropathy, jaundice, oro-genital ulcers. During the last 3 years, he had been taking 10-30 mg/day of prednisolone intermittently. On examination, the pulse rate was 84/min; the right carotid pulse and all pulses in both the lower limbs were feeble. Blood pressure in the upper limbs was 180/80 mmHg while in the lower limbs it was not recordable. Systemic examination was normal except presence of aortic regurgitation.

His investigations revealed: hemoglobin 11.6 g/dL, total leukocyte count 6.2 X10^9/L, erythrocyte sedimentation rate 47 mm fall in the first hour, normal urine examination, rheumatoid factor and anti-neutrophil cytoplasmic antibody - negative, HBsAg positive, CRP 5.6 mg/dL, serum proteins 8.0 g/dL, serum albumin 4.5 g/dL and ALT/AST 56/64 IU. A limited magnetic resonance angiography revealed bilateral renal artery stenosis and narrowing of the left femoral artery with good collateral blood flow.

Discussion:

Vasculitis is an inflammatory disorder of blood vessels leading to a compromise of lumen, which ultimately leads to ischemia of the region involved. Many classification systems have been proposed, depending on size of the vessel involved, type of inflammatory response, or clinical syndrome. Recently, American college of Rheumatology has proposed a preliminary criteria for diagnosis of various vasculitides but there are still a few patients who defy all classification systems.

These cases illustrate the problem of classification of patients with vasculitis. Our patients had evidence of medium and large vessel disease. In patient one he had overlap of Takayasu’s arteritis and cutaneous polyarteritis nodosa. Whereas in case presence of marked constitutional symptoms, subcutaneous nodules, HBsAg and aneurysms in the branches of superior mesenteric artery at the start of illness suggested polyarteritis nodosa but the subsequent course was dominated by large vessel involvement as occurs in Takayasu’s arteritis. Fauci et al have used a term ‘polyangitis overlap’ such patients. Overlap between TA and PAN has been described earlier. The commonest overlap reported has been between PAN and Churg-Strauss syndrome.

Presence of HBsAg and chronic persistent hepatitis is another interesting aspect of case 2. HBsAg is present in 30-40% of patients with PAN but its occurrence in polyangitis overlap syndrome has not been reported. HBsAg antigenemia is associated with immune complex mediated cutaneous vasculitis, PAN, cryoglobulinemic vasculitis and arthritis but large vessel involvement has not been reported. Thus it is difficult to attribute large vessel vasculitis in case 2 to hepatitis B virus infection. Prognosis in polyangitis overlap is good if treatment is started early with corticosteroids and immu-
nosuppressive drugs. Case 2 also had a good outcome at 5 years with normal renal functions and minimal morbidity. Thus, the present cases highlight a rare overlap vasculitic syndrome with involvement of medium and large vessels, which defy any classification and at best can be classified as polyangitis overlap.

References: