A Case of Classic PAN Presenting as Bilateral Foot Drop

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ABSTRACT

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Classic Poly Arteritis Nodosa (PAN or c-PAN) is a systemic vasculitis characterized by necrotizing inflammatory lesions that affect medium-sized and small muscular arteries and most commonly affects skin, joints, peripheral nerves, the gut, and the kidney. Peripheral neuropathy develops in as many as 60% of patients. Vasculitic neuropathy is often asymmetrical and presents as (1) mononeuritis multiplex, (2) distal polyneuropathy, or (3) cutaneous neuropathy. It can take the form of a pure motor, pure sensory or mixed sensorimotor polyneuropathy.

Here we present a case of a 58 year old male manual labourer who presented with progressively worsening difficulty in walking. He was evaluated in detail. Several rare manifestations were noted. A final diagnosis of Poly arteritis Nodosa was made which presented with Mononeuritis Multiplex (with the involvement of Right Median nerve and Bilateral Lateral popliteal nerve) and Sero negative Vasculitis. He was initiated on Corticosteroids and IV Cyclophosphamide.

The case is presented for its rare manifestations.

Keywords: Bilateral foot drop, Poly arteritis Nodosa, Mononeuritis Multiplex, Sero negative Vasculitis

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INTRODUCTION

Classic Poly Arteritis Nodosa (PAN or c-PAN) is a systemic vasculitis characterized by necrotizing inflammatory lesions that affect medium-sized and small muscular arteries. PAN, like other vasculitides, affects multiple systems, although it most commonly affects skin, joints, peripheral nerves, the gut, and the kidney. Peripheral neuropathy develops in as many as 60% of patients. Vasculitic neuropathy is often asymmetrical and presents as (1) mononeuritis multiplex, (2) distal polyneuropathy, or (3) cutaneous neuropathy. It can take the form of a pure motor, pure sensory or mixed sensorimotor polyneuropathy.

CASE REPORT

58 years old male, manual labourer who presented with difficulty in walking for 2 ½ months, insidious in onset & progressive over 2 months was examined. He had weakness of small muscles of right hand. There was H/o bilateral ankle joint pain & edema for 2 weeks. No significant past history. He was a chronic smoker for 30 years. On examination, Vitals were stable. Left radial pulsation was feeble. Gangrene present on the tip of left middle finger which was tender on palpation. Bilateral pitting pedal edema present. Purpuric lesions present over B/L elbow joint, B/L lateral malleoli and the lateral aspect of little toes. No Livedo reticularis. Punched out ulcers were present on the buccal mucosa, borders of tongue & over the gluteal region. Nervous system examination showed higher functions and cranial nerves normal. Evidence of right median nerve involvement was in the form of weakness of thenar muscles and long flexors on the right side. Pointing index sign and Oschners clasp test positive on right side. Sensory dulling on right median nerve distribution was present. Lower limb examination: Evidence of bilateral lateral popliteal nerve involvement with sensory motor deficit more on right side – B/L foot drop. No other focal neurological deficits. Other system examinations within normal limits. Investigations: Hb – 11.4 gm/dl, HCT – 33.6%, TC – 15430cells/cumm, N87 L10 E1 M2, Platelet – 486000 cells/cumm, ESR – 108 mm/hr, Creatinine –1.6 mg/dl, S. protein – 6.8, Albumin – 2.5, Globulin – 4.30, SGOT – 37, SGPT – 76, ALP – 295, Bil (T) – 1.4, Bil (D) – 0.45, Sodium – 137, Potassium – 4, Cortisol – normal CRP – 18.3 mg/dl, RA factor normal, ACCP – negative, ASO <200, ANA – negative, P and C ANCA – negative, VDRL, HIV, HCB, HBsAg : non reactive

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PBS – mild hypochromic microcytic anaemia, mild neutrophilia & thrombocytosis

USG abdomen & Doppler – renal cortical echo texture increased, No features suggestive of renal artery stenosis/ aneurysm.

Doppler of left upper limb – narrowing and Monophasic flow noted in radial artery.

CT angiogram of coeliac axis and renal arteries – normal, no aneurysms

Nerve biopsy – blood vessel showed fibrinoid necrosis and neutrophilic infiltrate, no granuloma. S/O of PAN

DIAGNOSIS AND TREATMENT

A final diagnosis of Poly arteritis Nodosa was made which presented with Mononeuritis Multiplex (with the involvement of Right Median nerve and Bilateral Lateral popliteal nerve) and Sero negative Vasculitis. He was initiated on Corticosteroids and IV Cyclophosphamide.

DISCUSSION

The first case of vasculitis was described by Kussmaul who was a German physician and Maier who was a pathologist in the year 1886.[1] In 2012, International Chapel Hill Consensus Conference (CHCC2012) was convened which consisted of a group of experts in vasculitis.[2] According to it PAN is defined as necrotizing arteritis of medium or small arteries without Glomerulonephritis or vasculitis in arterioles, capillaries or venules and not associated with antineutrophilic cytoplasmic antibodies (ANCAs)[3]

It spares aorta and its major branches. The inflammatory process involves all layers of vessel wall. Transmural necrosis of vessel wall gives a homogenous and eosinophilic appearance called fibrinoid necrosis. Segmental involvement followed by healing leads to aneurysm formation and ectasia. Endothelial proliferation leads on to stenosis of the artery, with resultant ischemia of the involved organ.

PAN is known to occur as a manifestation of HBV infection. It appears to be an immune mediated disease. Pathological specimens have shown deposits of HBV surface antigen, immune complexes & complements in the involved vessel. It is more severe when compared to idiopathic PAN

American College of Rheumatology Criteria for Classification of Polyarteritis Nodosa

- Weight loss ≥ 4kg
- Livedo reticularis
- Testicular pain or tenderness
- Myalgias, weakness or leg tenderness
- Mononeuropathy or polyneuropathy
- Diastolic blood pressure > 90mmHg
- Elevated blood urea nitrogen or creatinine
- Hepatitis B virus
- Arteriographic abnormality
- Biopsy of small or medium sized artery containing polymorphonuclear neutrophils

The onset of PAN is often sub-acute. Men and women are equally affected. Constitutional symptoms like fever, myalgia, malaise, and fatigue and weight loss occur in more than 90%. Patients often present with PUO. Arthralgia of large joints is common. First clue to diagnosis is combination of constitutional symptoms and ischemic symptoms in one or more organ systems.

Cutaneous manifestations include nodules, purpura and livedo reticularis and are seen in 49% of patients.

Mononeuritis multiplex occurs in about 70% of patients, caused by inflammation of the vasa nervosum. Clinically manifests as wrist drop or foot drop. Also may present with glove stocking type of peripheral neuropathy which is of asymmetrical onset.

GI manifestations occur in 37% to 50%. Range from GI bleeding, mesenteric ischemia, perforation, appendicitis and pancreatitis. Sometimes deaths are caused due to mesenteric infarction and aneurysmal rupture.

In the kidney there is inflammation of renal arteries, interlobar arteries and arcuate arteries. This process leads to renal infarction, hypertension and proteinuria. The small arteries which enter glomerulus are characteristically spared; therefore glomerulonephritis is not a feature.

Cardiovascular manifestations occur in up to 22% of patients. Range from vasculitis related cardiomyopathy to pericarditis.[5] Vascular manifestations are ischemia of digits, which can progress to digital necrosis with loss of digits.

Laboratory findings: ESR and CRP are not specifically elevated. ANCA is usually negative. Serum creatinine is not very significantly elevated.

Imaging: CT or MR angiography of coeliac axis and renal arteries are very useful in diagnosis. Most common angiographic findings are microscopic aneurysms of superior and inferior mesenteric arteries, renal arteries.

TREATMENT

Cornerstone of treatment is combination therapy with corticosteroids and cyclophosphamide (CYC). Oral prednisolone is started at dose of 1mg/kg for 3-4 weeks. Tapered by 5-10mg every 4 weeks, till the minimum effective to achieve and maintain remission.[4] Intravenous CYC 600mg/m^2 every 2 weeks for 4 weeks, then every month for 6 pulses is effective to induce remission. HBV related PAN should be treated with plasmapheresis 3 exchanges per week for 6 weeks.[6] Oral prednisolone is also started at 1mg/kg with rapid tapering for a period of 2 weeks. Antivirals (Lamivudine) should be started after prednisolone.

CONCLUSION

We report a case of classic PAN presented with medium vessel vasculitis, gangrene of left middle finger and Mono-neuritis Multiplex with involvement of B/L lateral popliteal nerve and right median nerve. Cutaneous manifestation as purpura and punched out lesions in skin of lower limb, gluteal region and buccal mucosa were observed. It is one of the rarest type of seronegative vasculitis.

END NOTE

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Editor's Remarks: Polyarteritis nodosa is a disease the detection of which needs a high index of suspicion. This article describes a rare presentation of this uncommon disease.

Conflict of Interest: None declared

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