Case Report

A Rare Clinical Presentation of Primary Anti-Phospholipid Antibody Syndrome

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Abstract:-
This case report is about mononeuritis multiplex with Central Retinal Artery Occlusion as rare manifestation of Primary Antiphospholipid Antibody Syndrome and management of the same. There has not been documented case report in Asia for primary APS. A 32 year old male patient presenting with Central Retinal Artery Occlusion and mononeuritis multiplex was admitted, following the patient subjected for investigation of vasculitis, laboratory results showed that presence of anti-beta 2 glycoprotein IgM, no other antibody were detected and there were no clinical manifestations of SLE or RA. Clinical and laboratory evidence supports modified SAPPORO’S criteria 2006, case was diagnosed as Primary Antiphospholipid Antibody Syndrome and patient was put on anticoagulants, antiplatelet and short course of steroids. The association of mononeuritis multiplex as a part of peripheral neuropathy, and retinal artery occlusion in combination with male patient is very rare manifestation of Primary Antiphospholipid Antibody Syndrome. In this case uniqueness is mononeuritis multiplex, a rarest manifestation of Primary Antiphospholipid Antibody Syndrome.

Introduction
Antiphospholipid antibody syndrome (APS) is an autoantibody mediated acquired thrombophilia characterized by recurrent arterial or venous thrombosis and/or pregnancy morbidity in the presence of autoantibodies against phospholipid(PL)-binding plasma proteins, mainly a plasma apolipoprotein known as beta 2glycoprotein I and prothrombin. It has mean age of 31years and common in
females. It may be primary, or in association with any other autoimmune diseases (secondary). Most common secondary APS is associated with systemic lupus erythematosus (SLE) (33%), and other autoimmune connective tissue disorders such as systemic sclerosis, Sjogren’s syndrome, dermatomyositis, rheumatoid arthritis and early undifferentiated connective tissue disease, ranges from 6-15%. It has a wide range of thrombotic events from mild to severe catastrophic APS.\(^1\) Most common manifestation is deep vein thrombosis 39%. It has wide range of neurological manifestations from stroke (highest 19.3%) to neuropsychiatric illnesses.\(^2\) Peripheral neuropathies are rarely seen with unknown incidence. Acute or sub-acute involvement of multiple individual nerves serially or almost simultaneously, which gives rise to distinctive clinical picture; that has been called mononeurits multiplex.\(^3\) Ocular syndromes vary from 15-88%, among them, retinal vein involvement more common than the retinal artery. Though it is rare; it is more aggressive and severe form. This case has unique correlation with rare manifestation of mononeurits multiplex with retinal arterial occlusion in Primary APS in a male patient. This association is rare and there has been very few cases reported.\(^4\) The aim of this overview is to review the clinical features of neurological manifestation associated with APS.

**Case Description**

31 year old male presented with progressive motor and sensory weakness in right hand and left foot since 4 months and sudden spontaneous painless loss of vision right eye, no history suggestive of any cranial or cerebellar involvement or seizures and loss of consciousness. No clinical features suggestive of Systemic Lupus Erythematosus (SLE) or Rheumatoid Arthritis (RA). On admission his blood pressure 120/80 mmHg, pulse 84 bpm, all peripheral pulses felt. On physical examination right partial claw hand was seen (fig 1). Fundoscopy revealed right side pale retina with cherry red spot with spared cilioretinal artery (fig 2). On systemic examination central nervous system: right eye hand movements, perception of light present, marcusgunn pupil present, direct and consensual light reflex is absent for right eye, left eye only consensual is lost. Motor system: right hand hypothenar, 3\(^{rd}\) and 4\(^{th}\) lumbrical muscles wasting and weakness noted, with absent supinator jerk, decreased sensations in right little and ring fingers in both flexor and dorsal aspect. The Left foot dorsi-flexor weakness present with decreased sensations over the dorsal aspect foot. All routine investigations are within normal limits, except erythrocyte sedimentation rate 52 at 1hr. Serum Homocystiene levels are marginally high. Fudus flourescent angiography (FFA) and electroretinogram (ERG) are suggestive of Central Retinal Artery Occlusion (CRAO) features. Electroneuromyography (ENMG) studies showed right ulnar motor/sensory, radial sensory axonal and left common peroneal motor/sensory neuropathy recorded. Nerve biopsy revealed focal neo-vascularization, sparse perivascular inflammation present, however frankvasculitis not seen. Extended antiphospholipid antibody syndrome profile: anti-beta 2 glycoprotienIgM is strongly positive (93), after 12 weeks it remains elevated (74). Antinuclear antibody profile was negative. Confirmatory diagnosis was CRAO with mononeuritis multiplex due to Primary Antiphospholipid Antibody Syndrome. Immediately patient was started on low molecular weight heparin (LMWH), along with short course of intravenous therapy of methylprednisolone (1 gm OD) for 5 days and tapered, then shifted to oral
combination of methylprednisolone, oral anti-coagulant (warfarin) and low dose of aspirin.

Discussion:
Neurological manifestations are diverse in Antiphospholipid Antibody syndrome. But peripheral neuropathies are not common \[^5\]. Mononeuritis are rarest of unknown incidence. Different manifestations are stroke (20%), transient ischemic attack (11%), Sneddon’s syndrome, convulsions / epilepsy (7%), dementia (2.5%), cognitive deficits, headaches / migraine (20.2%), chorea (1.3%), multiple sclerosis, transverse myelitis (<1%), ocular symptoms (15-88%) and Guillain–Barre syndrome. Pathogenesis of peripheral neuropathy involves immune and vascular mechanisms.\[^5\] Inflammation and lesions of the nerves might be caused by autoantibodies or immune complex deposits, or might be directly vasculitis/thrombosis of vasovasorum.\[^6\] One case reported by Jeruce et al, \[^7\] 49 yr old patient with no clinical or lab evidence of autoimmune disease/systemic vasculitis, who developed mononeuritis multiplex secondary to vasculitis with positive anticardiolipin antibodies. Diagnosis of antiphospholipid antibody syndrome is by modified SAPPORO’S criteria.\[^7\] (Table 1)

Primary antiphospholipid antibody syndrome is predominantly seen in young women with Male-Female ratio 3.5:1. CRAO is seen in only 7% of all thromboembolic in antiphospholipid antibody syndrome. Patient should be treated with warfarin after the first thrombotic event, to maintain international normalized ratio (INR) in the range of 2.5 to 3.5. Pregnancy morbidity can be prevented by heparin and aspirin 80 mg daily. Intra-venous immunoglobulin 400 mg/kg for 5 days may also be useful. Inpatient suffering from catastrophic antiphospholipid antibody syndrome along with immunoglobulin, anti-CD20 monoclonal antibody 375 mg/m\(^2\) per week for 4 weeks may benefit.\[^1\]

Conclusion:
We report a case of young man presenting with CRAO and Mononeuritis multiplex as a part of primary APS. Since this is a very rare and unique combination in primary APS. To our knowledge there are very few cases reported worldwide. Such cases should always be thought in the background of thrombophilia as a differential diagnosis to treat accordingly and appropriately, so that morbidity and mortality associated with APS can be tackled at the earliest. Currently APS is recognized as severe but potentially treatable cause of neurological disease.
References:

Figures

Fig 1: Right partial claw hand
Fig 2: Right fundus shows pale retina with cherry red spot with spared cilioretinal branch of retinal artery

Fig 3: Fundus fluorescent angiograph right sided shows delayed filling of contrast suggesting CRAO