Multiple Cerebral Venous Sinus Thrombosis as Fist Manifestation of Primary Anti-Phospholipid Antibody Syndrome

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Abstract
Antiphospholipid antibody syndrome (APS) is an autoimmune disorder, mainly found in young females, presenting with vascular thrombosis and/or obstetric complications. Thrombosis at anatomically significant sites may lead to considerable morbidity and/or mortality. We here present a case of primary APS presenting with sudden onset bilateral multiple cerebral venous sinus thrombosis. The patient, a 17 year old female with no prior rheumatological history, presented with sudden onset bilateral painful blindness and massive proptosis. MRI venography was instrumental in diagnosis. She also had significant thrombocytopenia. Except for the visual dimness, the other symptoms responded to therapy. Such massive cerebral venous thrombosis is extremely rare in primary APS.

Introduction
Antiphospholipid antibody syndrome (APS) is a thrombophilic disorder, mainly found in young women, characterized by the persistent presence of antibodies to certain phospholipid or their associated proteins in blood. This syndrome may remain asymptomatic or may present with arterial or venous thrombosis or obstetric complications. Sometimes catastrophic complications of the syndrome may occur, mainly due to blood vessel thrombosis at anatomically significant sites. We here report such a life threatening presentation of APS due to multiple cerebral venous sinus thrombosis.

Case Report
A 17 year old girl presented to the emergency with sudden onset severe headache and swelling of both eyes for one day. She had profound nausea but no history of seizures. She had no history of trauma to the head or any surgical intervention. There was no fever, arthritis or skin rash. She was not receiving any drugs. At presentation, the eyes were massively swollen (Figure 1) with complete ophthalmoplegia, chemosis and no light perception. Pupils were bilaterally dilated and non-reactive to light. Blood pressure was 150/97 mm of Hg. In view of this presentation, as a medical emergency, a provisional diagnosis of cavernous sinus thrombosis (CST) was made and she was started on intravenous vancomycin and meropenem. She was also started on intravenous heparin. An initial MRI scan of the brain was normal.

After three days, as the patient stabilized, an MRI venography of the brain was done which revealed (Figure 2) thrombosis of multiple venous sinuses including superior sagittal sinus, inferior sagittal sinus, cavernous sinus and bilateral transverse sinuses. In addition to the heparin and antibiotics, oral acenocoumarol was also started to attain an INR of 3. The imaging revealed diffuse cerebral edema. Hence, a CSF study was decided against.

Other laboratory tests revealed a hemoglobin of 6.6 gm/dl, total leukocyte count of 9790/cmm (Neutrophil 81%; lymphocyte 16%) and platelet count of 60000/cmm. ESR was 90 mm in the 1st hour and C reactive protein was 15 mg/l (N<6). Peripheral blood smear did not reveal any abnormality. Direct Coomb’s test was negative. Urea/creatinine were 23 and 0.7 mg/dl respectively and liver function test was normal. Routine urine examination was normal. Blood and urine culture were negative. Urine pregnancy test was negative. D-dimer level was 862.1 ng/ml (N<400). INR was 2.6 and aPTT was 47 seconds (control: 28), even after stopping heparin 8 hours before the test. Anti-nuclear factor was negative.

Fig. 1: Marked proptosis at presentation

Fig. 2: MRI venography of the patient showing thrombosis and obliteration of superior sagittal sinus (A), inferior sagittal sinus (B), transverse sinuses (C) straight sinus (D) and sigmoid sinus (E)
for adequate period), which was normal. Lipid profile was also normal. There were no new venous or arterial thrombosis. However, visual acuity was still decreased and bilateral ocular movement was partially restricted. Also, she required anti-hypertensives persistently.

**Discussion**

APS is characterized by thrombosis in both arteries and veins, although veins are more commonly affected. It can be in the form of involvement of large veins like deep vein thrombosis in legs or involvement of small veins in the skin leading to livedo reticularis. Paradoxically, the platelet count is often low although bleeding is rare. Our patient also had thrombocytopenia at presentation.

Cerebral venous thrombosis (CVT) can occur due to a variety of etiologies like infection, post-neurosurgery, cerebral hypotension or hereditary thrombophilic states. Anti-phospholipid antibodies as a cause of CVT has been infrequently reported. Usually, previous published case reports have shown thrombosis of unilateral single cerebral venous sinus in APS. But in our case, as the imaging shows, multiple venous sinuses were involved bilaterally. In single sinus involvement, the presenting symptoms may be subtle like prolonged headache or intermittent visual problems. But in a case like ours with multiple sinus involvement, the presentation is acute with dramatic symptoms. In one of the reported cases, chronic hepatitis was associated with APS. But in our case, no other system was involved. Some authors have reported associated other extra-cerebral sites of venous thrombosis in patients of CVT in APS. However, in our case, no other site of venous thrombosis was evident.

However, the mere presence of anti-phospholipid antibody in a case of CVT does not indicate a cause-effect relationship. As a recent study shows, even in patients who were APLA+, other etiologies like sickle cell trait or pregnancy also contributed to the CVT. Hence, even if APS is diagnosed, other common etiologies like use of oral contraceptives, infection or hereditary thrombophilias should still be searched.

**APS may have other central nervous system (CNS) manifestations.** Headache, epilepsy and chorea can occur in APS without any venous thrombosis. Cerebrovascular accident, that is arterial thrombosis, may also occur. However, most CNS manifestations are found in secondary APS associated with SLE. Primary APS presenting with CVT is extremely rare.

Multiple cerebral venous sinus thrombosis is very rare. In a recent study from India, out of a series of CVT cases, only 20% were multiple. The mortality in this group of patients was extremely high. Our patient survived the episode but had long term visual sequelae, as stated above.

We report this case to highlight this rare complication of APS. Such a manifestation of primary APS has not yet been reported from the subcontinent.

**References**