Middle cerebral artery infarct in transient antiphospholipid antibody syndrome

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Abstract

The antiphospholipid antibody syndrome (APS) is an acquired prothrombotic state where thrombosis is related to the presence of antiphospholipid antibodies. It can occur in the absence of associated disease when it is termed primary antiphospholipid syndrome, or it can be secondary to an underlying autoimmune disease, most commonly systemic lupus erythematosus. We report a case of a male child with no underlying infectious or autoimmune disease who presented to us with a large middle cerebral artery (MCA) infarct secondary to transient APS. Although lupus anticoagulant antibodies can be detected in plasma in early-stage, their persistence should be confirmed by repeating the test again after 12 weeks as transient APS is well known in the pediatric population. The exact prevalence of pediatric APS and its manifestation in Asian and particularly Indian children are unknown and further epidemiological studies are warranted.

Keywords: Antiphospholipid antibody syndrome, infarct, middle cerebral artery, stroke

INTRODUCTION

Antiphospholipid antibody syndrome (APS) is an acquired prothrombotic state where thrombosis is related to the presence of antiphospholipid antibodies. The simultaneous presence of antiphospholipid antibody (APL) in the serum and thrombotic events defines the APS. The most common antibodies include lupus anticoagulant (LAC), anticardiolipin antibodies, and anti-β2-glycoprotein I (GPI) antibodies. It can occur in the absence of associated disease when it is termed primary APS, or it can be secondary to an underlying autoimmune disease, most commonly systemic lupus erythematosus. Antiphospholipid antibody elevation is often transient in the pediatric population secondary to frequent infections. APL antibody positivity should be confirmed twice in children since the postinfectious elevation of APL levels may only be transient.

Herein, we report a case of a male child with no underlying infectious or autoimmune disease who presented to us with large right middle cerebral artery (MCA) infarct secondary to transient APS. He also had thrombosis of the left posterior tibial artery where the arterial line was inserted.

CASE REPORT

A 20-month-old male toddler, the second born of nonconsanguineous marriage, developmentally normal, with no significant history, was brought with complaints of unprovoked generalized tonic–clonic seizure which lasted...
for about 10 min. He also had fallen from bed (2 feet high) during seizure. He was unconscious and in the postictal state when he was brought to the hospital.

At arrival in the hospital, his heart rate was 156/min, blood pressure was 109/78 mmHg, respiratory rate was 28/min, Glasgow Coma Scale was 9/15, with normal breathing pattern. Pupils were bilaterally equal and reacting to light. He had decreased movement of the left side of the body (upper and lower limb-hemiparesis). He had another episode of convulsion in pediatric intensive care unit. As he had poor sensorium and was not maintaining airway, he was intubated.

There was no history of fever, cough, cold, loose stools, vomiting, trauma, drug intoxication, or significant family history of hematological disorders.

Noncontrast computed tomography was done immediately which reported an acute extra-axial hematoma with maximum thickness of 8 mm in the right frontoparietal area with 2 mm midline shift.

During hospitalization, he had multiple episodes of generalized tonic-clonic convulsions, which were refractory to injection levetiracetam, injection fosphenytoin, injection phenobarbitone, injection valproate, injection midazolam infusion; hence, thiopental infusion was commenced after which his seizures got controlled.

After stabilization, magnetic resonance imaging brain with angiography was done which was suggestive of restricted diffusion, involving right parieto-occipital lobe and right capsular region and mild cerebral edema with midline shift of 2 mm and angiogram showing absent signal in cavernous part of the right internal carotid artery along with reduced flow signals involving right MCA [Figure 1]. Hence, he was started on low-molecular-weight heparin (LMWH) and oral aspirin.

Initial blood investigations done including complete blood count with peripheral smear, liver function test, renal function test, serum electrolytes along with coagulation profiles (bleeding time, prothrombin time, international normalized ratio, and activated partial thromboplastin time) were within normal range. Blood culture was sterile.

Further investigations revealed prolonged dilute Russell viper venom time and a positive LAC antibody detected by clot-based assay. Protein C and Protein S levels were on lower side. Vitamin B12, homocysteine level, blood ammonia level, sickling test, and cholesterol levels were within normal limit. Antinuclear autoantibody, anti-B2 glycoprotein, and anti-cardiolipin antibodies were negative [Table 1].

Serial neuroimaging showed increasing cerebral edema with increase in midline shift. Despite all neuroprotective measures, he had unequal pupils on day 6 of admission. CT brain done on the same day was suggestive of increase in cerebral edema with increase in midline shift of 5–6 mm for which he underwent right fronto-temporoparietal decompressive craniotomy with subdural hemorrhage evacuation. Postcraniotomy, his sensorium improved and signs of raised intracranial pressure subsided. He was subsequently extubated within the next 48 h. Gradually, anticonvulsants were reduced over 2 weeks’ period.

During hospitalization, he also had thrombosis of the left posterior tibial artery where arterial line was inserted. He had gangrene of tip of the left great toe. Arterial line was promptly removed, and anticoagulation therapy was continued. During follow-up, it was found to fell off.

After 25 days of hospital stay, he was discharged, on nasogastric feeding. On follow-up after 6 months, his hypertonia on the left side was improving, and he was
able to sit with support, had palmar grasp, was recognizing parents, was using monosyllables, and was able to take food orally.

Repeat test for LAC after 12 weeks was negative after which LMWH was stopped and oral aspirin was continued.

**DISCUSSION**

APS is considered as the most common acquired hypercoagulation state of autoimmune origin in children.\(^5\) The true prevalence of pediatric APS is not known.\(^3\) Well-designed multicenter studies on APS in pediatric populations are scarce; consequently, there is only a little accurate information on the pediatric aspects of APS.

The thrombotic process can virtually involve any organ, and a wide spectrum of manifestations may be seen within any organ system.\(^5\) The prevalence of APL positivity in children having presented events of ischemic nature in the central nervous system, mostly in the area supplied by the MCA, is high, oscillating from 16% to 76%.\(^6\)

Although LAC antibodies are detected their presence should be confirmed by repeating test 12 weeks after as transient APS is well known in pediatric population.\(^7,8\) β2GP-1 antibodies are only found in case of autoimmune diseases, whereas antibodies against cardiolipin can be detected in APS and certain infections (syphilis, Borreliosis, AIDS, hepatitis, tuberculosis). The detection of these antibodies provides a serological aid for the differentiation of autoimmune diseases from infections.\(^8\)

A large cohort of pediatric patients with APS (n = 121) published by Avcin et al. revealed venous thrombosis occurred in 60% and arterial thrombosis in 32% of patients. Among patients with arterial thrombosis ischemic stroke was the most common presentation (26 out of 32 patients with arterial thrombosis had ischemic stroke and two patients had peripheral arterial thrombosis). Further, comparisons between different subgroups revealed that patients with primary APS were younger and had a higher frequency of arterial thrombotic events, whereas patients with APS associated with underlying autoimmune disease were older and had a higher frequency of venous thrombotic events associated with hematologic and skin manifestations.\(^9\)

Our patient was young, had MCA ischemic stroke and did not had any evidence of any autoimmune disorder which is very similar to the study described above. He also had the left posterior tibial arterial thrombosis where arterial

Table 1: Coagulation profile of patient at admission and after 12 weeks

|          | Plasma protein C | Plasma protein S | APTT | DRVV screen time | DRV confirm | DRVV confim ratio | APTT confirm ratio |
|----------|------------------|------------------|------|------------------|-------------|------------------|-------------------|
| At admission | Low 54%          | Low 51%          | High 61.5 second | High 121 second | High 56.1 second | Normal 3.28      | Normal 1.69       |
| After 12 week | High 37.4 second | Normal 41.3 second | Normal 37.4 second | Normal 41.3 second | Normal 110 second | Normal 1.16      | Normal 1.16       |
line was inserted. Further, the simultaneous involvement of two different arteries (one cerebral and other peripheral) is extremely rare. Repeat testing done 12 weeks apart was negative for LAC antibody which confirmed the transient nature of disorder. The absence of β2GP-1 antibodies further supported it. We gave LMWH and antiplatelet dose of aspirin. After 12 weeks, LMWH was stopped, and aspirin was continued.

**CONCLUSION**

The exact prevalence of pediatric APS and its manifestation in Asian and particularly, Indian children are unknown. Therefore, large epidemiological studies are warranted, and setting up pediatric APS registry will help to understand and manage this rare disease entity.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**

There are no conflicts of interest.

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