

## Case Report

# Antiphospholipid Syndrome in an Infant Presenting with Stroke

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**ABSTRACT**

We report an infant who presented with stroke as a manifestation of antiphospholipid syndrome. To our knowledge, this report is the first case report of

primary antiphospholipid syndrome in an infant from the Gulf region

KEYWORDS: anticardiolipin antibodies, antiphospholipid antibodies, stroke

**INTRODUCTION**

The reported incidence rate of cerebrovascular disorders in children is 2.5 cases per 100,000 population per year<sup>[1,2]</sup>. Stroke in children is more commonly caused by or related to congenital heart disease, infection, metabolic disorders, haematologic diatheses, and vasculitic disorders. Antiphospholipid syndrome (APS), although very rare in children, is increasingly being recognized. Thrombosis is the most striking clinical manifestation of APS<sup>[1]</sup>. It can occur anywhere in the venous or arterial circulation and involves vessels of all sizes<sup>[1,3]</sup>. The most common manifestations are stroke and deep vein thrombosis of the leg<sup>[3]</sup>. Serum antiphospholipid antibodies (APLa) constitute a heterogeneous group of antibodies including most commonly a lupus anticoagulant (LAC), anticardiolipin antibodies (aCL) and a biologic false-positive serologic test for syphilis<sup>[3,4,5]</sup>. We describe here an infant who developed a stroke with right-sided hemiparesis and both LAC and aCL were present in the blood. Our case suggests that APS should be considered in the differential diagnosis of stroke in children.

**CASE REPORT**

An 11-months old Arab infant presented to Al-Amiri hospital with two days history of repeated vomiting, decreased feeding and drowsiness. After admission he developed brief right-sided tonic-clonic convulsions which were aborted by rectal diazepam. At the age of nine months he was admitted with a similar picture of vomiting, drowsiness and decreased activity. CNS infection was suspected but parents refused spinal tap. A cranial CT scan at that time was normal (Fig. 1) and

acute phase reactants were normal. He was discharged after receiving a seven days' course of intravenous cefotaxime. He is a product of a full term breech delivery after an uneventful pregnancy. His birth weight was 3.6 kg. There were no perinatal problems. He received all basic immunization appropriate for his age. His growth and development before his recent illness were completely normal. He is the third child born to healthy non-consanguineous parents. His mother had two abortions in her previous two pregnancies and recently she aborted at 12 weeks of gestation. Physical examination on admission: he was normotensive and afebrile, his weight and length were on the 50<sup>th</sup> percentile for his age. There were no dysmorphic features. His consciousness was impaired but he responded to painful stimuli by flexion withdrawal. He was hypotonic with increased deep tendon reflexes. The heart sounds were normal, there was no murmur and the peripheral pulses were equal and normal. Examination of other systems was unremarkable. Over the next few days he improved slowly and regained consciousness and started to feed. He was noted to have weakness of the right upper and lower limbs with increasing tone. He also developed clear left-hand preference although he was able to move his right upper and lower limbs against resistance but with some weakness. Cranial nerves were intact and fundi were normal. There was no cranial bruit.

Pertinent laboratory investigations were as follows: a complete hemogram showed white cell count  $20.2 \times 10^9/l$ , hemoglobin concentration 11.8 g/dl, platelet count  $559 \times 10^9/l$ , erythrocyte sedimentation rate 6 mm in the first hour, C reactive

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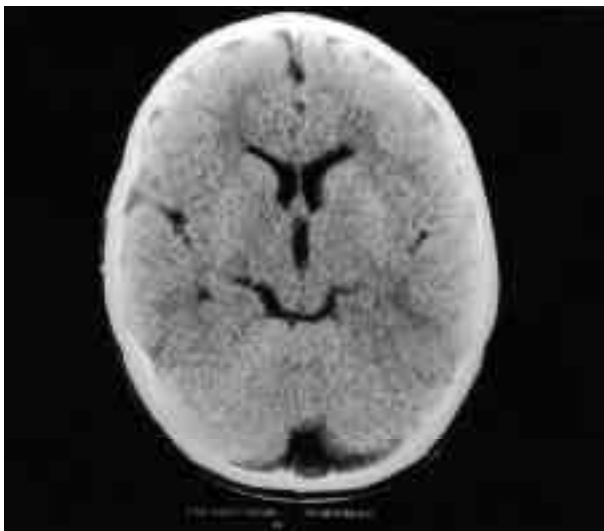


Fig. 1: A normal cranial CT scan at the age of 9 months.

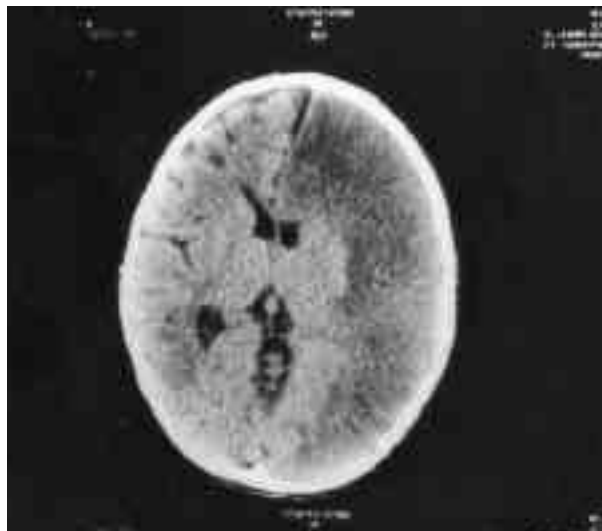


Fig. 2: Cranial CT scan at the age of 11 months showing a massive infarction involving the left frontal, temporal, parietal, and occipital regions, sparing the left basal ganglia and thalamus.

protein < 0.06 mg/l, prothrombin time 16.7 seconds (control 13 seconds), partial thromboplastin time 66 seconds (control 32 seconds), protein C 42% (normal range 70-140 %), protein S 97% (normal range 60-140 %), Anti-Thrombin III 93% (normal range 84%-124%), anti-nuclear antibodies and anti-double strand DNA were negative. Serum triglyceride, VLDL (calculated from triglyceride) and total cholesterol levels were normal. Cerebrospinal fluid examination was normal, and PCR for herpes virus was negative. Urine chromatography for amino acids was normal. The LAC test was positive. The aCL of the IgG isotype was 6.5 MPL U/ml (normal < 13.3) and the IgM isotype 25 MPL U/ml (normal < 9.8). VDRL test was negative. Plain axial CT scan of the head showed a massive infarction involving the left frontal, temporal, parietal and occipital regions, sparing the left basal ganglia and thalamus (Fig. 2). Echocardiography did not reveal signs of cardiac disease. Doppler study for the carotid arteries was normal. He initially received a full course of intravenous cefotaxime (100 mg/kg) and acyclovir (30 mg/kg) for 10 days and his seizures were controlled first with phenytoin (5 mg/kg) then phenobarbitone (5 mg/kg). He was treated with aspirin (5 mg/kg) to prevent further thrombotic episodes. We investigated the mother because of recurrent abortions; LAC was absent, aCL IgG isotype was 3.4 MPL U/ml (normal < 13.3) and IgM isotype 13 MPL U/ml (normal < 9.8), VDRL test was negative, anti-nuclear antibodies and anti-double strand DNA were negative. The patient serum APLa was repeated after three months. LAC was positive, aCL IgM 13.7 MPL U/ml (normal < 9.8), aCL IgG 29 GPL U/ml (normal < 13.3), protein C 49% (reached normal level later). He is still on prophylactic aspirin with no recurrence of thrombotic events for the last

two years. He has residual mild right-sided hemiparesis.

## DISCUSSION

Stroke is very rare in children and the etiology escapes detection in approximately 30% of the pediatric patients in whom stroke occurs<sup>[2]</sup>. Rivkin M and Volpe J have detailed the causes of strokes in their review of strokes in children<sup>[2]</sup>. APS has been mainly described in children with systemic lupus erythematosus<sup>[5]</sup>. Cerebral ischemia is the most common neurologic symptom associated with APS. Patients with APS are defined as having at least one clinical and one serological feature at some time in their disease course. The clinical features are venous thrombosis, arterial thrombosis, recurrent fetal loss and thrombocytopenia, while the serological features are either positive LAC test or positive IgG and/or IgM aCL at moderate to high level ( > 15 AU) in two determinations performed more than eight weeks apart. The term "primary" APS has been introduced by Asherson to define those patients who have circulating APLa and one or more clinical manifestation of APS (generally thrombosis) but do not show any of the major clinical or serological features of systemic lupus erythematosus, nor any other underlying or predisposing conditions such as malignancy or infection<sup>[3]</sup>. Our patient satisfied the criteria for the diagnosis of APS<sup>[1,4]</sup>.

To our knowledge this report is the first case report of primary APS in an infant from the Gulf Region. Wang HC had reported the first case of childhood ischaemic stroke secondary to primary antiphospholipid syndrome in Taiwan in a 13-years old girl<sup>[6]</sup>. The presentation at the age of 9 months possibly was an episode of a transient ischemic

attack (TIA). The onset is abrupt and the episode lasts less than 24 hours, and recovery is complete. A TIA frequently portends the subsequent occurrence of a stroke and its resultant fixed deficit<sup>[2]</sup>. The neurological conditions associated with APLa may be grouped, according to the literature with firstly, cerebrovascular diseases and secondly, neurological diseases other than stroke.

The neurological disorders include chorea, migraine, partial epilepsy, transverse myelitis, benign intracranial hypertension and Guillain-Barre' syndrome<sup>[5]</sup>. A spinal cord infarction associated with primary APS in a child has been reported<sup>[7]</sup>. Infants of APLa positive mothers may have vascular thrombosis due to transplacental transfer of APLa and should be carefully monitored for signs of thrombo-embolism<sup>[3,8]</sup>. This could not be the cause in our patient because the maternal aCL is an IgM molecule that cannot cross the placenta. Recurrent fetal loss is another major feature of the syndrome. Most women with APLa appear to have high-risk pregnancies. Raised serum APLa was found in 13% of women with unexplained recurrent fetal loss<sup>[3]</sup>. The mother of our patients had three abortions, the aCL was positive but of low level and so does not fulfill the criteria of APS. Moya moya syndrome was one of the differential diagnoses in our patient but the presence of APLa has suggested the diagnosis of APS, so MRI angio was not justified. Protein C deficiency is a rare cause of thrombo-embolism in infancy and childhood. Temporary protein C deficiency in children with cerebral arterial thrombosis has been described<sup>[9]</sup>. Our patient had low protein C level at presentation which had normalized after 6 months.

Children with APS appear to have a long-term risk of pulmonary embolism and recurrent thrombosis. Because of the rarity of such cases the proper treatment and prevention of long term recurrence is a controversial issue. Some patients were managed with long-term anticoagulation<sup>[1,2,3,9,10]</sup>. Warfarin is effective in patients who have had venous thrombosis<sup>[3]</sup>. However, there is a risk of major bleeding in long-term administration, even more so in children with histories of stroke who are more prone to trauma<sup>[9]</sup>. Other patients were treated with low dose aspirin<sup>[1,3,9]</sup>. The use of antiplatelet aggregation agents such as aspirin or dipyridamole may be the best form of treatment for preventing

arterial thrombosis<sup>[3]</sup>. There is at present no general agreement on the optimum treatment of APS-related thrombosis. It has been recommended that therapy should continue for as long as APLa are present<sup>[3]</sup>.

## CONCLUSION

APS is a very rare cause of stroke in children; but it should be considered in infants who are diagnosed with idiopathic infantile hemiplegia. The determination of serum APLa should be included in the work up of these children.

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