

## Stroke in an Infant; Its Association with Antiphospholipid Antibody and Acquired Protein C and S Deficiencies

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### ABSTRACT

We present the first reported case of antiphospholipid syndrome with stroke in an Iranian boy (7-month-old) who had two ischemic strokes within a period of 2 months. Serum anticardiolipin antibody was positive and the patient had low levels of protein S and C. This case emphasizes the importance of antiphospholipid antibody in children with unexplained ischemic stroke.

**Keywords:** Antiphospholipid Antibody, Deficiency, Infant, Protein C, Protein S, Stroke

### INTRODUCTION

Childhood stroke are uncommon but it is an important cause of mortality and morbidity in children. Some studies have suggested an incidence of 2-2.5/100000 in children younger than 15 years of age per year. Approximately 50% of childhood strokes are ischemic in nature, of which half of them are idiopathic.<sup>1,2</sup> Therefore, at least one-quarter of childhood strokes are unexplained ischemic events.

Antiphospholipid syndrome is a thrombotic disorder characterized by the association of arterial and venous thrombosis with antibodies directed against phospholipids.<sup>3</sup> This syndrome is the most common cause of acquired thrombophilia, associated with either venous or arterial thrombosis or both.<sup>4</sup> Clinical features include stroke, livedo reticularis, thrombocytopenia, recurrent fetal loss, chorea, hemidystonia, guillain bare syndrome, benign intracranial hypertension, dementia with repeated infarction, optic neuropathy, branch retinal artery occlusion, transverse myelitis, myocardial infarction and renal artery thrombosis.<sup>5-8</sup>

The syndrome was initially recognized in patients with systemic lupus erythematosus who had a hemorrhagic disorder and a circulating anticoagulant.<sup>9</sup>

Subsequently, a paradoxical relationship between "lupus anticoagulant" and thrombosis was recognized.<sup>10</sup> Secondary antiphospholipid syndrome described this phenomenon in patients with known underlying rheumatological process. Antiphospholipid syndrome may also occur as a primary syndrome in the absence of such diseases. The criteria for diagnosing primary antiphospholipid syndrome are high titers of antiphospholipid antibody and one or more clinical manifestations of antiphospholipid syndrome in an individual without any underlying rheumatic disease.<sup>11</sup> We present one of the youngest cases with primary antiphospholipid syndrome and most probably the first child with the stroke due to antiphospholipids in Iran.

### CASE REPORT

A 7-month old boy was referred to us due to irritability and right hemiparesis affecting the face, upper and lower extremities. There was no history of infection, trauma, toxic ingestion or prodromal illness. The patient had a history of left sided hemiparesis one month earlier with normal brain CT scan. The patient recovered from the first episode without any treatment. Prenatal and natal histories were not significant. The patient had normal development before the problem started. Family history for collagen diseases, stroke and repeated abortion was negative. In physical examination, the patient had

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## Association of Recurrent Stroke and Antiphospholipid Antibody

right facial palsy and hemiparesis of upper and lower extremities, on the same side.

Paraclinical investigations revealed old ischemic changes in right basal ganglia and fine ischemic changes in left periventricular white matter in his cranial magnetic resonance imaging (MRI). Complete blood count, ESR, blood glucose, electrolyte, cerebrospinal fluid analysis, Hb electrophoresis, triglyceride, cholesterol, antinuclear antibody, C3, C4, factor V layden, echocardiography and brain magnetic resonance angiography (MRA) were all normal. Anticardiolipin antibody was 20.8 u/ml (>11 positive). Protein C was 67% (70-130), protein S was 45% (65-140) and APPT of the patient was 40.7%.

After 2 months without any treatment the tests were repeated and anticardiolipin antibody was found to have decreased to 12.5 u/ml. Protein C and S had risen to 73% and 69%, respectively. Low dose aspirin (5mg/kg) was initiated for the patient and after 3 months the patient showed a relative improvement in his paresis, and his anticardiolipin antibody had decreased to normal (8.5 u/ml).

After eight months the patient had no new stroke attacks, his facial palsy improved completely. However, mild spastic hemiparesis, on the right side, remained.

### DISCUSSION

The clinical features of primary antiphospholipid syndrome in children are similar to that of adults. The most common presentation in the pediatric population is stroke. The age onset of primary antiphospholipid syndrome ranges between 8 months to 16 years, with the mean of 10.2 years. To confirm the diagnosis, it is crucial that any patient who presents with an acute thrombosis be tested for the presence of lupus, anticoagulant, anticardiolipin antibody and other antiphospholipid antibodies and recent infections must be ruled out. It should be noted that in many cases, antiphospholipid antibodies can transiently rise following a viral infections.<sup>1,2,6</sup>

Our case had 2 episodes of ischemic stroke which are suggestive of a small vessel occlusion. These findings differ from those of adults in whom large vessels are usually occluded. In contrast, in children ischemic stroke secondary to antiphospholipid antibody involves the small vessels.<sup>2</sup> Our case had two interesting and rare features. First, stroke had

occurred at a very early age (7 months). The youngest age reported previously was 8 months.<sup>6</sup>

The second important aspect of our case was low protein C and S levels. Our patient may have had the recently diagnosed syndrome in which lupus anticoagulant is associated with acquired protein S and C deficiencies. Antibodies to these proteins result in a transient free protein deficiency, probably secondary to increased clearance of proteins from the circulation.<sup>7,9</sup> The association of antiphospholipid antibody with stroke has not yet been reported, in the Iranian children population. Unfortunately no data are available regarding established therapy for children with cerebral thrombosis when associated with antiphospholipid syndrome. In adults, recurrent thrombosis may require treatment with high dose of oral anticoagulants. However, the risk of recurrence in children with idiopathic ischemic strokes, which presumably includes some patients with antiphospholipid antibody syndrome, is negligible.

Some reports suggest therapy with low dose aspirin because of its perceived safety.<sup>6</sup> Moreover analysis suggest that some children who present with features of primary antiphospholipid syndrome may progress to develop systemic lupus erythematosus or lupus like syndrome; therefore more follow up is needed.<sup>12</sup>

We recommend that all children with idiopathic ischemic stroke should be completely investigated and evaluated for antiphospholipid antibody.

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