Case Report

Fatal catastrophic antiphospholipid syndrome at presentation of juvenile lupus

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ABSTRACT

Catastrophic antiphospholipid syndrome (CAPS) is a severe and rare form of antiphospholipid syndrome, extremely uncommon in the pediatric age group, characterized by multiple site thrombosis involving small, medium, and large blood vessels occurring over a short period of time (usually 1 week) causing multiorgan failure. We report the case of an 8-year-old girl presenting with fever, lymphadenopathy, and pain abdomen with refractory mitral regurgitation diagnosed as systemic lupus erythematosus with CAPS. All three antiphospholipid antibodies positivity in high titers further confirmed the diagnosis. In spite of the early initiation of adequate triple therapy (anticoagulation, steroids, and cyclophosphamide), our patient succumbed. The report aims to incorporate a greater awareness among clinicians for timely diagnosis and treatment of this condition and throws light on the varying ways in which lupus can present in children.

Key words: Anti-cardiolipin antibody, Antiphospholipid syndrome, Catastrophic antiphospholipid antibody, Juvenile lupus, Lupus anticoagulant

Antiphospholipid antibody syndrome (APS) is a heterogeneous multisystem autoimmune disorder of hypercoagulation and thromboembolic events in the presence of elevated antiphospholipid antibodies (aPL) [1]. The predominant antibodies associated are lupus anticoagulant, anti-cardiolipin, and beta2 glycoprotein 1. In primary APS, it may occur as an isolated entity and secondary APS; it is associated with other diseases such as systemic lupus erythematosus (SLE). Although there is no reliable data on the incidence of APS in children, reportedly <3% of all APS occurs in childhood [2]. Since it is associated with high morbidity and mortality, the best approach seems to be early diagnosis and an aggressive treatment regimen.

Here, we present a case of probable catastrophic antiphospholipid syndrome (CAPS) with skin involvement and rapidly progressing encephalopathy, renal failure, and refractory cardiac failure.

CASE REPORT

An 8-year-old girl presented with complaints of high-grade intermittent fever for the past 1 month. There were associated pain abdomen, weight loss of 1.5 kg, and neck nodes for the same duration. On examination, the child looked pale was tachycardic (heart rate 160/min), hypotensive (90/64 mmHg) with a systolic murmur, and saturation in room air of 98%. There were tender hepatomegaly and generalized lymphadenopathy.

Laboratory investigations showed anemia with a hemoglobin of 6.2 g/dl, positive direct Coombs' test, neutrophilic leukocytosis (total leukocyte count 16200/cumm, neutrophil 82%), with hypoalbuminemia (2.8 gm/dl), C-reactive protein 3.2 mg/L, and erythrocyte sedimentation rate of 68 mm in the 1st h. Blood and urine cultures as well as screening for tuberculosis were negative. Lymph node biopsy revealed reactive follicular hyperplasia.

Within 5 days of admission, she started worsening; pain abdomen increased, with S3 gallop, and signs of cardiac failure. Simultaneously, there was the development of acute renal failure (urea 234 mg/dl, creatinine 2.8 mg/dl, with fractional excretion of sodium >1) along with hypoalbuminemia (2.3 g/dl), bicytopenia (platelet count 20,000/cumm and hemoglobin of 5.9 g/dl), and deranged coagulation profiles (International Normalized Ratio 2.32). Echocardiography showed mitral leaflet prolapse with chordae tendineae tear, severe mitral regurgitation, and flow reversal in pulmonary veins. Antinuclear antibody was positive in 1:1000 titer (homogeneous), C3 66 mg/dl, C4 <6 mg/dl, anti-ds DNA, and anti-Sm were negative.

She was diagnosed as SLE with CAPS and started on pulse methylprednisolone (30 mg/kg/day), hydroxychloroquine with cardiotropic (milrinone), and inotropic support. B-type natriuretic peptide was 24,000 pg/ml, immunoglobulin (Ig)M anti-beta2 glycoprotein1 (>200 RU/ml), IgM anti-cardiolipin antibody (118.19 MPL/ml), and lupus anticoagulant were all positive in high titers. She started having mucosal bleeds, erythroderma-like rashes with

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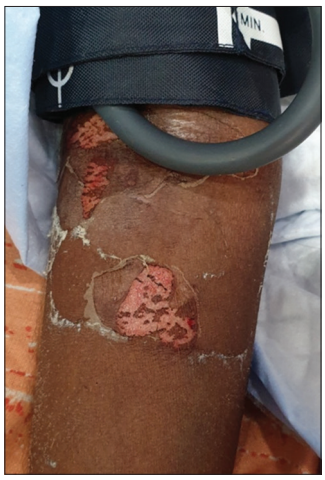

Figure 1: Necrosis of skin associated with microvascular thrombosis of dermal vessels

rapidly progressing epidermal necrosis, and peeling (Fig. 1). Because of the mucosal bleeds, unfractionated heparin was avoided and low molecular weight heparin (LMWH) was started but sensorium worsened with the development of severe encephalopathy. Following three methylprednisolone pulses, she was given one dose of intravenous (IV) cyclophosphamide 500 mg/m^2, methylprednisolone pulses were continued for 2 more days. Cardiac failure continued to worsen and she was put on mechanical ventilation. However, the child suffered a cardiac arrest after 5 days and succumbed.

DISCUSSION

CAPS was first described by Asherson *et al*. in 1992, as a fatal variant of APS occurring in 1% of APS patients [3], pediatric cases being rarer. The international pediatric APS registry revealed a mean age of onset of 10.7 years with a slight female preponderance [4]. Many children who are diagnosed to have primary APS on follow-up develop either SLE or an SLE-like illness.

As per the CAPS registry, the major organs involved during catastrophic episodes were renal (71%), lungs (64%), brain (62%), heart (51%), and skin (50%), with variable affection of liver and gastrointestinal tract [5].CAPS associated with lupus is seen more in the younger population, shows more cerebral and cardiac involvement, and usually has a grave prognosis.

The diagnosis and treatment are challenging for physicians [6]. Due to its rapid and fatal course, management needs to be prompt. In 220 patients reported from the CAPS registry, more than half had an infection as a precipitating factor and 4% had lupus flares [7]. Anti-cardiolipin antibodies are detected in 84% of the patients, the lupus anticoagulant in 76%, the antinuclear antibodies in 62%, anti-double-stranded DNA in 36%, and anti-Ribonucleoprotein in 8% of CAPS patients [8]. Thrombocytopenia is found in 63–68% of the patients and hemolytic anemia in 26–32%. Cardiac symptoms include valve abnormalities (thickening and vegetations), coronary artery disease, myocardial dysfunction, pulmonary hypertension, and intracardiac thrombi. In a meta-analysis of aPL-associated heart valvular diseases (HVD) in SLE patients, nearly 90% had positive aPL compared to 44% without HVD [9].

All these findings correlated with our case as well. Although microthrombosis is one of the typical histological markers of a CAPS event, it may be difficult to confirm and the diagnosis in our patient could only be labeled as "probable" CAPS. The extensive skin necrosis (Fig. 1) that was clinically evident possibly resulted from cutaneous microvascular thrombosis, but considering the moribund condition of the child a skin biopsy was not done.

A combination of steroids, anticoagulants, and drugs reducing aPL titers such as IVIg or plasmapheresis form the backbone of the treatment protocol. The addition of cyclophosphamide decreases mortality in SLE-CAPS as per the international registry [10,11]. Our patient was initiated on methylprednisolone pulses and LMWH for the CAPS. However, she developed multiorgan failure within 48 h, and administration of cyclophosphamide too was unable to halt the progression and allow administration of other therapies such as rituximab or plasmapheresis.

CONCLUSION

An extremely rare occurrence in children, the case is a prototype of CAPS that can be rapidly fatal even with early institution of therapy.

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