Case Report

All that seems sepsis is not sepsis

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Abstract

Catastrophic antiphospholipid antibody syndrome (CAPS) resembles severe sepsis in its acute presentation, with features of systemic inflammatory response syndrome (SIRS) leading to multiple organ dysfunction. Infections are the best known triggers of CAPS. This emphasizes the need for early diagnosis and aggressive treatment as the mortality is as high as 50%. We present a 42-year-old woman who developed SIRS postoperatively and was eventually diagnosed as CAPS.

Keywords: Catastrophic antiphospholipid syndrome, sepsis, systemic lupus erythematosus

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Introduction

The antiphospholipid antibody syndrome (APS) is defined by:

1. Presence of at least one type of autoantibody known as an antiphospholipid antibody (aPL)
2. The occurrence of venous or arterial thrombosis and/or pregnancy morbidity.

aPL are directed against serum proteins bound to anionic phospholipids and may be detected as: Lupus anticoagulants, anticardiolipin antibodies, antibodies to β2-glycoprotein I (β2GPI). A small subset of patients with APS has widespread thrombotic disease with multiorgan failure, which is called "catastrophic APS" (CAPS). Less than 1% of patients of APS develop CAPS. Among 1,000 patients with the APS followed for a mean of 7 years, only eight (0.8%) developed CAPS.[1] A total of 60% of patients having CAPS have a triggering factor. Infections are the commonest triggers accounting for 25% of cases.[2] Since CAPS and sepsis both produce systemic inflammatory response syndrome (SIRS), it is difficult to differentiate between the two.

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Case Report

A 42-year-old P3L2 became symptomatic with pain on the right side of abdomen and recurrent vomiting, ultrasound revealed thick edematous gall bladder wall with multiple calculi. She was diagnosed with chronic cholecystitis and open cholecystectomy was done. Her symptoms improved, however on fourth postoperative day she developed high grade fever. She had tachycardia, hypertension (BP 186/100 mmHg), chest was clear and normal S1 and S2. She had neutrophilic leucocytosis (29,500/mm^3 with 91% polymorphs), decreased platelets (66,000/mm^3), and peripheral blood smear (PBS) showing shift to left, toxic vacuoles, metamyelocytes of 10%. She had direct hyperbilirubinemia (total bilirubin 2.7 mg/dl, direct 1.7 mg/dl) with transaminitis (AST 254 IU/dl, ALT 466 IU/dl, AlkPhos 354 IU/dl); and urea 56 mg/dl, creatinine 2.6 mg/dl, and procalcitonin 30.50 ng/ml (>2 high risk of sepsis). She was started on broad spectrum antibiotics (meropenum), however she continued to deteriorate.

On fifth postoperative day, she developed orthopnea with coarse crackles in lungs and X-ray suggestive of pulmonary edema [Figure 1]. Electrocardiogram (ECG) showed sinus tachycardia with T-wave inversion in V1-V4. Troponin T was negative. B-type natriuretic peptide (BNP) was 1,120 pg/dl. 2D-ECHO showed dilated left ventricle with ejection fraction of 40%. There

was no regional wall motion abnormality. Her counts increased to 34,000/mm^3 and platelets dropped further to 30,000/mm^3.

Patient was referred to our centre with a diagnosis of postoperative sepsis with disseminated intravascular coagulation (DIC). On examination; she had pallor, malar rash, bilateral pedal edema, oral ulcers, and multiple palpable purpura in both legs. Pulse 102/min regular BP 124/70 mmHg. Chest had bibasilar crackles and left ventricular third heart sound was audible. Patient had prolonged APTT (activated partial thromboplastin time) which was not corrected by mixing studies [Table 1]. Her aPL were positive: IgG 34.21 GPL U/ml (Normal 0.50-10.00) and positive direct Coombs test, corrected reticulocyte count of 2.8%, and microcytic hypochromic cells with MCV 75 fL. Antinuclear antibody (ANA) was positive by indirect fluorescent antibody (IFA) with titres of 1:40, dsDNA positive 131.8 IU/ml by ELISA, ESR 56 mm, and low C3 58 ng/dl (Normal 90-100) and normal C4 levels.

Skin biopsy (No. B/2570/201) [Figures 2 and 3] of palpable purpura showed subcorneal blisters with inflammatory cell infiltrate, dermis showed perivascular lymphomonouclear and neutrophilic inflammatory infiltrate. There was no evidence of fibrinoid necrosis. Direct immunofluoresence showed IgG, IgM, and C3 granular fine basement membrane positive. Patient was fulfilling the criteria of CAPS

She was diagnosed as a case of systemic lupus erythematosus (SLE) in flare with myocarditis and left ventricular failure, secondary antiphospholipid syndrome, and CAPS (triggered by recent surgery). She was started on broad spectrum antibiotics, diuretics, heparin, corticosteroids, and intravenous immunoglobulins (120 gm over 5 days). She responded to the treatment and her clinical and biochemical parameters normalized, except prolongation of APTT. She was discharged on oral warfarin 5 mg once a day and tab. prednisolone 40 mg once a day.

Table 1: Coagulation profile of the patient

	Patient	Control
PT	15.7	13.5
APTT	101	32
INR	1.21	1
Mixing studies		
PT	13.5	13.5
APTT	90	32
INR	1.0	1

PT: Prothrombin time; APTT: Activated partial thromboplastin time; INR: International normalized ratio

Discussion

APS can be primary or secondary. Secondary APS is associated with SLE, lymphomas, malignancies. Among

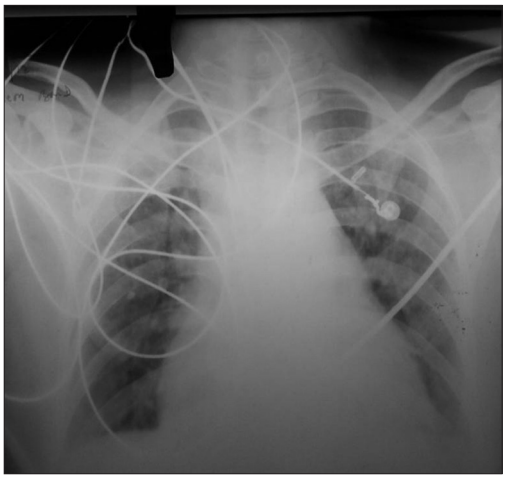

Figure 1: X-ray showing pulmonary edema

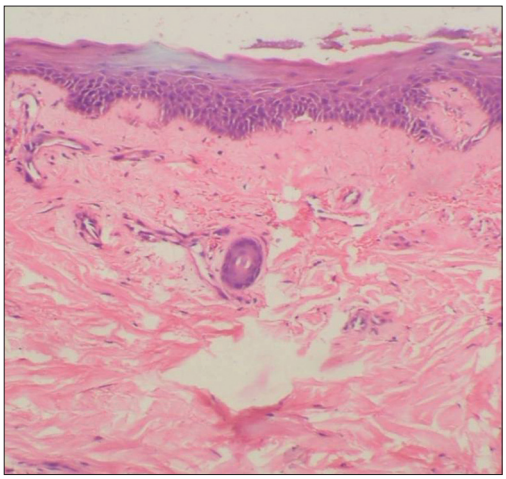

Figure 2: Skin biopsy (No. B/2570/201) of palpable purpura showing subcorneal blister with inflammatory cell infiltrate

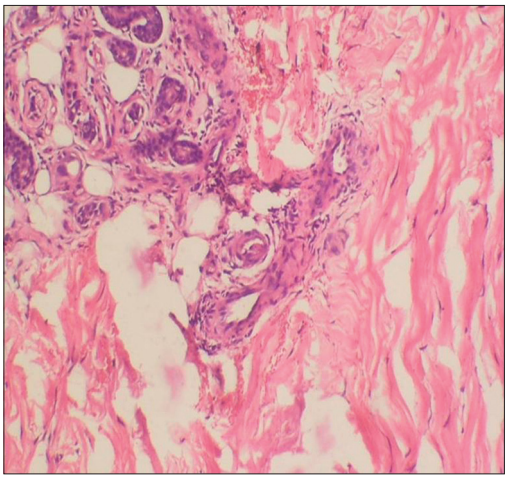

Figure 3: Skin biopsy (No. B/2570/201) of palpable purpura showing perivascular lymphomonouclear and occasional neutropillic inflammatory infiltrate in dermis

patients of SLE prevalence of aPL is 12-30% and 15-34% for lupus anticoagulant.[3]

Proposed mechanisms for aPL-mediated thrombosis include,[3] endothelial cell and monocyte activation resulting in the expression of adhesion molecules, platelet activation, and inhibition of protein C activation.

Patients with high-titer aPL antibodies can present with fulminant disease with multiorgan system involvement and thrombosis which is known as CAPS (thrombotic storm).[4] CAPS can be precipitated by infection and surgery. These subsets of patients require aggressive management as mortality is as high as 50%.[3] Fortunately, CAPS is an unusual form of presentation that represents less than 1% of the APS cases.[3]

International classification criteria for CAPS are:[5]

i. Evidence of involvement of three or more organs/systems
ii. Development of manifestations in less than 1 week
iii. Significant evidence of thrombosis, although vasculitis may coexist occasionally
iv. Laboratory confirmation of the presence of aPL antibodies, detected on two or more occasions at least 12 weeks apart.

Definite CAPS: When all the above four criteria are fulfilled.

Probable CAPS: All four criteria, except for involvement of only two organs, systems, OR all four criteria, except for the absence of laboratory confirmation at least 12 weeks.

Our patient had evidence of cardiovascular, hepatic, and renal involvement. She had developed these manifestations within a week after surgery and had aPL antibodies. Though we could not demonstrate vessel thrombosis, there was evidence of vasculitis. She fulfilled all the four criteria of CAPS.

Both sepsis and CAPS have SIRS in common. The cause of SIRS in CAPS was explained by "molecular mimicry" by Asherson and Shoenfeld.[6] Anti-β2-glycoprotein can activate endothelial cells simulating lipopolysaccharides in sepsis.[7,8] The prevalence of thrombocytopenia is 60% in CAPS and 20% in APS; thrombocytopenia in aPL-positive patients does not protect against thrombosis, on the contrary can be associated with more severe disease.[9] Proposed mechanism of thrombocytopenia is immune-mediated antibodies against glycoprotein IIb/IIIa complex.[9]

CAPS requires aggressive management as mortality is as high as 50%.[3] Anticoagulants, corticosteroids, plasma exchange, intravenous gammaglobulins, and cyclophosphamide; are the most commonly used treatments for CAPS patients. Use of drugs like fibrinolytics, prostacyclin, danazol, cyclosporine, azathioprine, hemodialysis, and splenectomy[10,11] have also been reported.

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