Catastrophic Primary Antiphospholipid Syndrome

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Catastrophic antiphospholipid syndrome (CAPLS) was diagnosed in a 64-year-old male who was admitted to our hospital with dyspnea. The clinical and radiological examinations showed pulmonary thromboembolism, and so thromboembolectomy was performed. Abdominal distention rapidly developed several days later, and the abdominal computed tomography (CT) abdominal scan revealed thrombus within the superior mesenteric artery with small bowel and gall bladder distension. Cholecystectomy and jejunoileostomy were performed, and gall bladder necrosis and small bowel infarction were confirmed. The anticardiolipin antibody was positive. Anticoagulant agents and steroids were administered, but the patient expired 4 weeks after surgery due to acute respiratory distress syndrome (ARDS). We report here on a case of catastrophic APLS with manifestations of pulmonary thromboembolism, rapidly progressing GB necrosis and bowel infarction.

Index words: Antiphospholipid syndrome
Pulmonary arteries, thrombosis
Intestines, infarction

Some patients suffering from antiphospholipid syndrome (APLS) may present with a catastrophic condition characterized by multiple vascular occlusions that often result in death if appropriate treatment is not quickly applied. In the great majority of cases, patients with catastrophic APLS show a spontaneous tendency to develop microvascular thrombosis that affects multiple organs. However, arterial reactivity leading to acute thrombosis after operation or a procedure has rarely been reported on [1, 2]. We report here on a case characterized by a succession of thrombotic accidents that occurred during or immediately after arterial angiographies or arterial surgery, and catastrophic arterial reactivity was strongly suspected.

Case Report

A 64-year-old man was admitted with a 10-day history of dyspnea. On admission, he presented with exertional dyspnea (class IV according to the functional classification of the New York Heart Association). A physical examination revealed a blood pressure of 150/80 mmHg, a pulse of 102 beats/minutes, respiration of 28 breaths/minutes and a body temperature of 36.0°C. Coarse breathing sounds were evident in both lung fields, but the cardiac sounds were normal.

The laboratory findings were as follows: white blood
cell count = 11,900/mm³, hemoglobin = 10.2 g/L, platelet count = 359,000/mm³, BUN/creatinine = 33.9/1.8 mg/dL, aPTT = 45.4 sec, PT = 12.4/93.3/1.09 sec/%/INR, CRP = 3.9 gm/dL, fibrinogen = 367 mg/dL, FDP = 12.5 ug/mL and D-dimer = 0.85 mg/dL. Blood coagulation testing proved positive for lupus anticoagulant, but a search for anticardiolipin antibodies proved negative [IgG: 9.7 GPL, n < 20, IgM: 16 MPL, n < 20]. Other laboratory data revealed no abnormalities. Chest radiographs at admission revealed the presence of cardiomegaly without mediastinal widening, and his electrocardiogram disclosed tachycardia of 100 beats/minutes with no ST-T wave changes. Echocardiography revealed tricuspid regurgitation and pulmonary hypertension, and a CT chest scan showed extensive pulmonary thromboemboli (Fig. 1A). The patient underwent open-thromboembolectomy (Fig. 1B). After several days, his abdomen rapidly distended and a CT abdominal scan revealed thrombi in the upper abdominal aorta, celiac trunk, superior mesenteric artery (SMA), and superior mesenteric vein (SMV), and there was small bowel and gall bladder distension with wall thickening (Fig. 1C). SMA arteriography showed occlusion of the SMA (Fig. 1D). Thrombolysis was undertaken with using urokinase (400,000 IU) and then follow-up angiography showed good patency of the SMA lumen. However, several abdominal pain and signs of bowel infarction developed a few days later. A follow up abdominal CT scan revealed multivessel thrombi and the progression of small bowel infarction (Fig. 1E). Exploratory laparotomy was performed, and the resected small bowel and gall bladder showed ischemic necrosis. Microscopic findings of the specimens disclosed ischemic necrosis with epithelial sloughing, mucosal destruction, submucosal edema, congestion and extensive neutrophil infiltration.

His postoperative course was dismal: ARDS and multisystemic failure developed, and he died 4 weeks after admission.

Discussion

Antiphospholipid syndrome (APLS) is diagnosed by arterial or venous thrombosis, or recurrent fetal losses, and positive antiphospholipid antibody tests for antcardiolipin antibodies and lupus anticoagulant. Thrombotic disease, fetal losses and transient positive antiphospholipid antibodies (aPL) are common events for APLS patients. When these events occur, APLS should be considered as primary if these events are unassociated with any other underlying disease, or the APLS is secondary when it appears in association with other autoimmune disorders, mainly systemic lupus erythematosus (SLE). Also, this syndrome can be associated with other conditions such as vasculitic syndromes, carcinoma, drug administration and etc. An international workshop recently issued a consensus statement on the classification criteria of APLS. Pulmonary manifestations, including pulmonary embolism and infarction, pulmonary hypertension, adult respiratory distress syndrome (ARDS), intra-alveolar hemorrhage and primary thrombosis of lung vessels (both large and small), as well as pulmonary capillaritis, may be associated with this syndrome in both its primary and secondary forms (3).

All the vasculopathies of APLS may be inherent to the syndrome itself, and APLS can present with protean vascular abnormalities without any associated vasculitis. The vascular pathophysiology remains unclear. Numerous mechanisms have also been implicated in the thrombosis, including the binding of antiphospholipid antibodies to platelets and endothelial cells and this leads to the induction of procoagulant proteins or adhesion molecules by these cells (4). Moreover, endothelial cell disruption, which occurs in vasculitis, may produce immunologically hidden antigens and so stimulate antiendothelial antibodies, which may be part of the spectrum of APLS antibodies (5).

Single thrombotic events occur in the vast majority of APLS patients, and when recurrent events do occur, they may do so many months or even years after the initial vascular occlusion. However, some reports published over the past years have shown that some patients, albeit a small minority, may present with or develop an acutely catastrophic or devastating syndrome characterized by multiple vascular occlusions that often results in death [1, 6–9]. Catastrophic antiphospholipid syndrome (CAPLS) is a rare and severe variant of APLS that is characterized by multiple widespread microvascular occlusions (7, 8). CAPLS presents as multiorgan failure within a short time sequence with various other manifestations, including disseminated intravascular coagulation (DIC), thrombocytopenia and hemolytic anemia. 60% of these patients appear to have developed CAPLS following trigger factors, for example, infections, trauma, anticoagulation problems, neoplasia, obstetric, lupus and others (7). Twenty-five of the 50 patients reviewed by Asherson et al [9] died despite intensive treatment, and this treatment included corticosteroids,
plasmapheresis and cyclophosphamide.

Certain differences have emerged from a review of 10 patients [6], and these differences appear to distinguish this minority group of patients who suffer from CAPLS from the overwhelming majority of APLS patients. The major differences appeared to be large vessel, peripheral venous and arterial involvement, and these things were relatively uncommon in the patients suffering with

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**Fig. 1.** A 64-year-old man with catastrophic antiphospholipid syndrome (CAPLS).

A. The initial chest CT scan reveals pulmonary thromboemboli in the pulmonary arteries (arrows).

B. The gross specimen shows thromboemboli extracted by thrombectomy.

C. The immediate postoperative CT scans show a filling defect [meaning thromboemboli] within the proximal superior mesenteric artery (SMA, arrow).

D. SMA arteriography shows occlusion of the SMA (arrow) and thrombolysis was undertaken with using urokinase.

E. The follow up abdominal CT scan reveals thrombus progression within the SMA, and the scan was taken at the same level as Figure 1D (arrow).
CAPLS, who seemed to demonstrate small vessel (microvascular thrombosis) involvement that affected various combinations of multiple organs such as the lungs, heart, brain, kidney, liver, adrenal glands or gastrointestinal tract.

Many patients with APLS remain stable for long periods, but an acute episode may unpredictably proceed to a catastrophic state. Aggressive multi-therapy with anticoagulation, steroids, plasmapheresis or intravenous gammaglobulin leads to a survival rate of about 70% [9]. However, the treatment of CAPLS is not currently standardized, and a review of 10 cases [6] and a more recent analysis of 31 cases [5] have suggested that the use of plasmapheresis is associated with an improved outcome. We also believe that this combination should probably be used in patients with catastrophic APLS; however, our case did not demonstrate any benefit from the combined treatment.

The prognosis may be poor when the CAPLS is associated with arteriopathies, as described in our case. We conclude that CAPLS is an uncommon, but potentially life-threatening condition that requires a high level of clinical awareness.

References