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Case Report

Multi-organ Involvement in Catastrophic Antiphospholipid Syndrome: A Challenging Case with a Fatal Outcome

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Abstract

Catastrophic antiphospholipid syndrome (CAPS) is a rare, life-threatening variant of antiphospholipid syndrome (APS) characterized by extensive thrombosis, multi-organ involvement, and high mortality. Despite advances in the understanding and management of APS, CAPS remains a challenge because of its rapidly progressive and potentially lethal course. We report the case of a 33-year-old man with a history of chronic venous insufficiency and recent surgery for chronic thromboembolic pulmonary hypertension (CTEPH) who presented with abdominal pain, exertional dyspnoea, and rapidly worsening clinical status leading to multi-organ dysfunction. Despite aggressive treatment, including anticoagulation, corticosteroids, intravenous immunoglobulin, and immunosuppression, the patient succumbed, highlighting the aggressive nature of CAPS. Initial treatment consisted of anticoagulation with low-molecular-weight heparin and warfarin, supplemented by immunosuppressive therapy including hydroxychloroquine, corticosteroids, and cyclophosphamide. The complexity of management escalated with the development of diffuse alveolar hemorrhage, which required broad-spectrum antibiotics and hemodiafiltration for acute renal failure. Despite multidisciplinary efforts and adherence to recommended CAPS protocols, the patient's condition progressively deteriorated, culminating in fatal multiorgan failure. The unpredictable and aggressive nature of CAPS and the limitations of current management strategies are highlighted in this case. This case highlights the need for increased awareness and early aggressive treatment of CAPS patients. It also highlights the importance of ongoing research into more effective treatment modalities and the potential benefits of a multidisciplinary approach in the management of such complex cases. Early recognition and intervention remain critical to the improvement of the prognosis and outcome of patients with CAPS.

Keywords: Catastrophic antiphospholipid syndrome, multi-organ failure, aggressive treatment, case report, mortality

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Introduction

Catastrophic antiphospholipid syndrome is the most severe form of antiphospholipid syndrome and accounts for approximately 1% of cases. CAPS is characterized by systemic thrombotic events, often leading to rapid multi-organ involvement and a high mortality rate, and is an autoimmune disease with increased thrombotic risk due to antiphospholipid antibodies.[1] The presence of antiphospholipid antibodies, particularly lupus anticoagulant, cardiolipin, and beta2-glycoprotein I antibodies, plays a central role in the pathogenesis of CAPS, although the pathophysiology is not fully understood. By damaging endothelial cells, plasma proteins, and platelets, these antibodies increase the propensity for thrombosis. Particularly at the microvascular level, this process can lead to multiple organ failure.[2]

The majority of cases of CAPS result in multiple organ dysfunction. The most commonly affected organs are the kidneys, the lungs, the nervous system, and the skin. CAPS is diagnosed based on clinical findings and laboratory evidence of antiphospholipid antibodies.[3] Diagnostic criteria include the involvement of three or more organs, systems, or tissues within a given time period, laboratory evidence of antiphospholipid antibodies, and the development of these findings within one week. The treatment of CAPS can be challenging and often involves a combination of therapeutic approaches. The main aim of treatment is to prevent thrombosis and treat thrombotic events, which is usually achieved by using anticoagulants, corticosteroids, plasmapheresis, and immunosuppressive therapies such as intravenous immunoglobulin (IVIG). In refractory cases, biologics such as rituximab may be considered.[4]

CAPS has a much better prognosis with early diagnosis and treatment. In spite of treatment, there have been reports of a high mortality rate. The prognosis depends on several factors. These include the number and functional status of the organs affected and the timing of treatment. Although CAPS is rare, it is an important condition in the context of the understanding and management of APS. Early recognition and aggressive treatment of this syndrome can help to reduce the high levels of mortality and morbidity associated with the disease. Patients suspected of having CAPS should therefore be given a rapid, comprehensive assessment and managed using a multidisciplinary approach. This case report highlights the multi-organ involvement of catastrophic antiphospholipid syndrome[3] and the failure to prevent mortality despite effective treatment in a young patient who presented to the rheumatology department 12 years after the initial thrombotic event.

Case Presentation

A 33-year-old male patient, who works as a chef, is being treated in cardiology for CTEPH and was referred to rheumatology for Behçet's disease. He has a history of chronic venous insufficiency, diagnosed 12 years ago and having been re-operated twice. One year ago, the patient also underwent surgery for CTEPH. The patient has a smoking history of 15 pack years of cigarettes. The patient presented with two days of abdominal pain progressing to widespread epigastric tenderness and free fluid in the pelvic area one month ago. At the time of presentation, the patient was taking low molecular weight heparin (LMWH) enoxaparin 6000 anti-Xa IU/0.6 mL 2x1) with acetylsalicylic acid. The rheumatological examination showed no findings suggestive of Behçet's disease. The ophthalmological examination was normal.

During the consultation, the patient reported exertional dyspnea with an MMRC (Modified Medical Research Council) score of 1-2 and occasional wheezing. In addition, the patient had a history of cough and sputum production for the previous two days. Physical examination revealed decreased breath sounds. Oxygen saturation was 89%. He also had a venous stasis ulcer on his left leg due to venous insufficiency. His C-reactive protein (CRP) was 115 mg/L and he was thrombocytopenic. The peripheral blood smear showed a platelet count of 80 000 µLt with normal morphology and distribution of erythrocytes and no atypical cells or blasts.

In serological tests, antinuclear antibody was found to be positive with a granular pattern, anti-CCP (anti-cyclic citrullinated peptide) antibody was 147 U/mL, and complement 3 and 4 levels were 0.59 and 0.03 g/L, respectively. The electrocardiogram showed normal sinus rhythm at a rate of 100 beats per minute with T-wave inversions in leads V1-4. Transthoracic echocardiography showed an ejection fraction of 60%, grade 1-2 tricuspid regurgitation, pulmonary artery pressure of 70 mmHg, significant right ventricular dilatation, and a pulmonary trunk diameter of 36 mm. Lung CT angiography showed filling defects consistent with multiple emboli in the right main artery and a lobar branch to the left lower lobe. Enlargement and tortuosity of the lobar and segmental branches were also observed. The heart was enlarged and there was dilatation of the right ventricle. The lungs showed mosaic ground-glass opacities. Normal contrast filling and diameter were noted in the abdominal aorta and its main branches. There was evidence of a filter in the inferior vena cava and minimal free abdominal fluid.

He has been treated for CAPS with hydroxychloroquine 200 mg daily, warfarin 5 mg daily, and acetylsalicylic acid 100 mg daily. Three months later, the patient presented with swollen hands and a C-reactive protein level of 42 mg/dL. Methylprednisolone, 16 mg/day, was added to the treatment regimen, with a tapering schedule. After two months of treatment, the patient presented to the emergency department with dyspnea and cough of two days' duration. Physical examination revealed bilateral fine crackles at the bases of the lungs. Oxygen saturation was 86%. Chest CT showed minimal pleural effusion in both hemithoraces, more on the right, with consolidations and ground-glass opacities in both lungs. The blood tests showed CRP levels of 82 mg/dL and INR levels of 10, which led to hospitalization by the pulmonary disease department. The patient was preliminarily diagnosed with diffuse alveolar hemorrhage and pneumonia. The patient's TTE results showed an ejection fraction of 45%, mild global hypokinesis, and a dilated right ventricle with a systolic pulmonary artery pressure of 55-60 mmHg. Pleural effusion was present in both hemithoraces. Widespread pulmonary edema was compatible with preserved peripheral areas of ground-glass opacity. The vascular structures were observed to be prominent due to congestion. The treatment plan was adjusted. Warfarin was stopped, and LMWH, meropenem, moxifloxacin, and riociguat 7.5 mg/day were started. Following a 14-day stay in the intensive care unit (ICU), the patient returned to our clinic with complaints of generalized edema. Tests revealed a creatinine level of 2.4 mg/dL, CRP level of 23 mg/L, and detected proteinuria, leading to hospitalization for acute kidney failure. The 24-hour urine protein was 588 mg/day. The patient received 3 days of pulse steroids and 1 g of cyclophosphamide. Subsequent follow-ups showed improvements in creatinine and CRP levels. A renal biopsy was planned, but could not be performed due to the high INR (International Normalized Ratio) and thrombocytopenia of the patient. The patient refused further treatment and was discharged on a regimen of mycophenolate mofetil 2 g/day, hydroxychloroquine 400 mg/day, MP 32 mg/day, LMWH and ramipril 2.5 mg/day.

The patient returned to the clinic one month later with generalized edema. Both lower extremities were found to have widespread edema, desquamation, post-infectious hyperpigmentation, and xerosis on physical examination. There was petechiae on the right knee and a 2 cm superficial eroded area around the ankle and dorsal aspect of the left foot. The patient was given IV immunoglobulin 0.4 mg/kg for 5 days. As part of the treatment, the cardiology department also prescribed IV iloprost for 6 days. The edema was reduced after these procedures. The patient was discharged with creatinine at 1.6 mg/dL and CRP at 4.5 mg/dL.

Main Points

- Catastrophic Antiphospholipid Syndrome (CAPS) is a rare, life-threatening autoimmune disorder characterized by widespread thrombosis and multi-organ failure.
- A 33-year-old male with a history of chronic venous insufficiency and prior surgery for chronic thromboembolic pulmonary hypertension (CTEPH) developed CAPS with rapidly worsening clinical status.
- Despite receiving aggressive treatment including anticoagulation, corticosteroids, immunosuppressants, and intravenous immunoglobulin (IVIG), the patient's condition deteriorated.
- The disease led to complications such as diffuse alveolar hemorrhage, acute kidney failure, and recurrent thrombotic events, culminating in respiratory failure and cardiac arrest.
- This case underscores the high mortality risk of CAPS and emphasizes the need for early diagnosis, multidisciplinary management, and more effective treatment strategies.

Due to generalized edema, dyspnoea, and deterioration in general condition, the patient was readmitted two months later. On examination, scrotal edema, erythema, and edema from the knee to the foot were noted. There were intact bullae and 1 cm white exuding ulcers distally, consistent with cellulitis. Transthoracic echocardiography (TTE) revealed an ejection fraction (EF) of 55%, good left ventricular function, slight enlargement of the right chambers, mild tricuspid regurgitation, pulmonary artery systolic pressure (PASP) of 50-55 mmHg, and a dilated inferior vena cava (IVC). Laboratory values indicated creatinine at 2.9 mg/dL, CRP at 196 mg/L, procalcitonin at 11 µg/L, and pro BNP at 26,235 ng/L. The patient's condition worsened and he was admitted to intensive care for low oxygen levels. Treatment with broad-spectrum antibiotics and diuretic infusion was started. Hemodiafiltration was performed and the patient had intubation for respiratory failure. At a later stage, the patient suffered a respiratory arrest followed by a cardiac arrest and, despite extensive efforts, died after a period of 9 months.

Ethical approval was not required for this work because it contains retrospective data of the patient, and all treatment decisions were made prior to our evaluation. Written informed consent was obtained from the patient's mother who agreed to take part in the study.

Discussion

Catastrophic antiphospholipid syndrome is a rare and potentially fatal condition.[5] Patients with CAPS often present with acute renal failure, respiratory distress syndrome, diffuse alveolar hemorrhage, encephalopathy, and adrenal hemorrhage due to microvascular thrombosis.[6] The clinical manifestations of CAPS are variable and depend on the affected organ system.[7]

CAPS is frequently linked to multi-organ failure, with the lungs, brain, and kidneys being particularly affected. An analysis of 500 CAPS registry patients revealed that 4% exhibited lupus-like symptoms. Renal involvement was the most common manifestation, accounting for 73% of CAPS episodes, including renal failure (77%), proteinuria (29%), and hematuria (16%). Pulmonary complications were present in 60% of cases, with acute respiratory distress syndrome (36%), pulmonary emboli (26%), pulmonary hemorrhage (12%), and pulmonary edema (8%) being the primary issues. Cardiac problems were observed in 50% of CAPS episodes. Cutaneous complications were seen in 47% of episodes, including livedo reticularis (43%), cutaneous necrosis (26%), cutaneous ulceration (24%), and purpura (14%). In 37% of cases, the peripheral vascular system was affected, with 69% showing venous involvement and 46% showing arterial involvement. Hematological manifestations included thrombocytopenia (67%), schistocytes as a marker of microangiopathic hemolytic anemia (22%), thrombotic microangiopathy (14%), and disseminated intravascular coagulation (11%).[3]

Mortality rates were initially reported at approximately 50%, but have been reduced to around 30% with early diagnosis and aggressive intervention. CAPS is a severe manifestation of APS that leads to widespread small vessel thrombosis, potentially resulting in multi-organ failure.[8] Cerebral involvement, including stroke, hemorrhage, and encephalopathy, accounts for one-third of deaths and is the primary cause of the high mortality associated with CAPS. Cardiac complications and infections follow closely, reflecting the aggressive nature of this autoimmune disease.[9] Despite advances in therapeutic approaches, mortality remains significant, emphasizing the need for increased awareness and prompt management strategies. Early detection of CAPS is crucial in influencing treatment outcomes and patient survival rates. The complexity of the disease requires a multidisciplinary approach that combines aggressive therapies, including anticoagulation, corticosteroids, plasmapheresis, and immunosuppression, to reduce thrombosis and control the underlying autoimmune process. This strategy is crucial for improving the prognosis and reducing the high mortality rates associated with CAPS.

Informed Consent: Written informed consent was obtained from patient's mother who agreed to take part in the study.

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