



Catastrophic Antiphospholipid Syndrome: A Case Series

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Abstract

Catastrophic antiphospholipid syndrome (CAPS) is the rare but most severe form of antiphospholipid syndrome with multiple organ ischemia developing over a short period of time. CAPS should be considered when imaging suggests an acute and concurrent multiorgan ischemia, associated with positive antiphospholipid antibodies. As CAPS can have fulminant irreversible complications, its early recognition is important to initiate the treatment promptly. We present three patients of CAPS who were managed at our institution.

Keywords

- ▶ antiphospholipid syndrome
- ▶ CAPS
- ▶ catastrophic antiphospholipid syndrome

Introduction

Antiphospholipid syndrome (APS) is a multisystem autoimmune condition characterized by vascular thrombosis and ischemic events associated with circulating antiphospholipid antibodies¹ The rare but most severe and life-threatening form of APS is recognized as catastrophic antiphospholipid syndrome (CAPS) or Asherman syndrome, in which patients develop multiorgan failure over a short period, usually associated with microthrombosis.²

'Definite' and 'probable' CAPS have been defined based on certain diagnostic criteria; however, patients who do not fulfil these criteria can be encountered in clinical practice.³ Imaging can play a key role in raising the suspicion of CAPS. Hence, the radiologist must know this possibility to promptly suspect the disease, alert the clinician, and guide appropriate management.

Cases

Case 1

A 38-year-old female patient presented to the hospital with fever, shortness of breath, vomiting, and abdominal pain over 2 to 3 weeks. She had recent non-ST elevation myocardial infarction (non-STEMI) and was being treated elsewhere as a case of infective endocarditis. She had a history of deep vein thrombosis and had been started on warfarin, which was discontinued 3 weeks before the admission. A history of multiple blood transfusions for anemia was also noted. Physical examination showed pallor, pedal edema, basal lung crepitations, and tender hepatomegaly. Laboratory investigations indicated elevated white blood cells (WBC) of 18,500 cells/mm³, anemia (Hb 7.0 g/dL), thrombocytopenia (platelet count 70,000 cells/ μ L), altered liver profile (SGOT 72 U/L, SGPT:18 U/L, ALP 120 U/L, total bilirubin

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1.73 mg/dL), and altered renal profile (serum creatinine of 2.9 mg/dL).

Contrast enhanced CT scan (CECT) of the thorax showed acute pulmonary thromboembolism in the bilateral lower lobe segmental branches (R > L), patchy areas of ground glass attenuation/mosaic perfusion in bilateral lung fields, and dilated central pulmonary arteries, suggesting pulmonary arterial hypertension. CECT scan of the abdomen revealed hepatosplenomegaly with multiple hypodense nonenhancing areas representing multiorgan infarcts in the liver, spleen, both kidneys, and adrenals (→ Fig. 1). However, no thrombosis was noted in the visualized major arteries and veins. Serology evaluation showed positive anti cardiolipin IgG and IgM.

Based on the presentation and imaging features of the patient, a diagnosis of CAPS was made, and ICU admission was done for multi-organ support. The patient was started on anticoagulation, pulse-dose steroids, IV immunoglobulins, and plasma exchange. Five sittings of plasma exchange were done with fresh frozen plasma as a replacement fluid to reduce the pathogenic antibody levels and cytokines, and intermittent hemodialysis was done via the right IJV line. Empiric antibiotic cover with imipenem was also given. The patient was improving clinically, however, developed massive gastrointestinal bleed, needing repeat ICU admission, and no active bleeding point could be identified on OGD or CECT. She improved on supportive measures and withholding anticoagulation, and she was started on statin and hydroxy chloroquine. Serum antibodies were followed for treatment response, with drop in cardiolipin IgM and IgG.

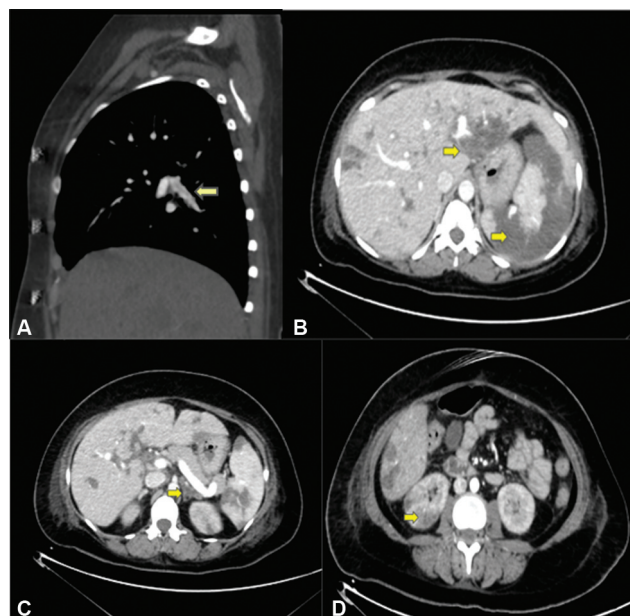


Fig. 1 Sagittal (A) and axial (B-D) sections of contrast CT thorax and abdomen of case 1 show (A) thrombus within the posterior basal segmental branch of left right lobe pulmonary artery (arrow), (B) multiple infarcts in the spleen and liver (arrows), (C) infarct in the left adrenal gland and (D) infarct in the right kidney - suggesting multifocal infarcts of various organs.

Case 2

A 45-year-old male patient presented with vomiting, abdominal discomfort, and cough for 2 days. He had no known comorbidities. Physical examination showed minimal epigastric tenderness. Initially, he was hemodynamically stable and was started on IV fluids, antiemetics, antitussives, and other supportive care, despite which he became increasingly hypoxic overnight, requiring intubation and admission to the ICU. On further evaluation, he was found to have severe metabolic acidosis, deranged renal parameters, and hyponatremia. He went into shock requiring multiple inotrope support and was also started on IV meropenem and IV teicoplanin.

CECT of the abdomen revealed multiple hypodense non-enhancing areas in the kidneys and spleen representing bilateral renal and splenic infarcts (→ Fig. 2). The patient was started on anticoagulation. Further evaluation showed low complement levels, significant transaminitis (-SGPT/SGOT > 4000 s), elevated D-dimer, and LDH levels. Autoimmune workup revealed high anti β -2 glycoprotein and antiphospholipid levels. He was given pulse steroid therapy and also underwent 10 cycles of hemodialysis. Gradually, he improved and was weaned off mechanical ventilation and extubated.

Five days later, the patient developed two episodes of seizures and was intubated and ventilated again in view of poor sensorium. The CT brain revealed subacute infarct in the right parietal region (→ Fig. 3). No hyperdense vessels were

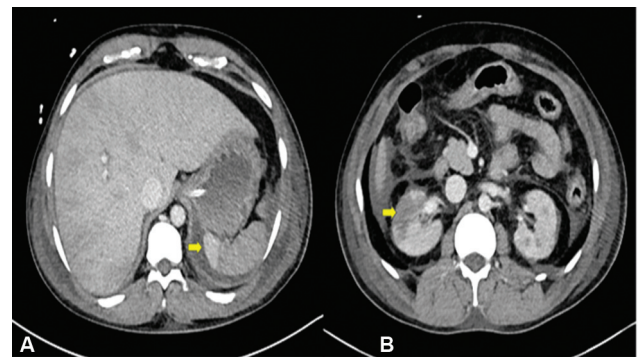


Fig. 2 Contrast CT axial sections of case 2 show (A) infarcts in the spleen (arrow) and (B) infarcts in right kidney (arrow).

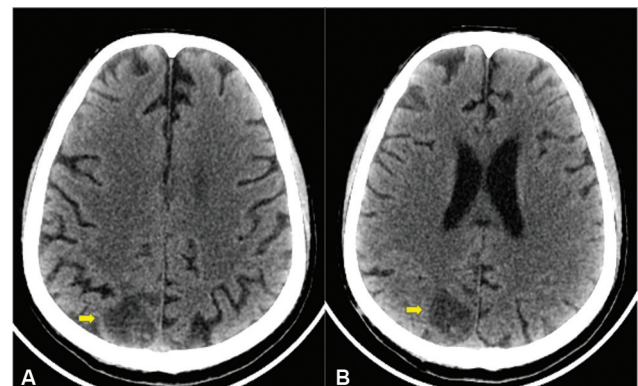


Fig. 3 CT brain of case 2 taken 5 days later shows infarct in right parietal region (arrows).

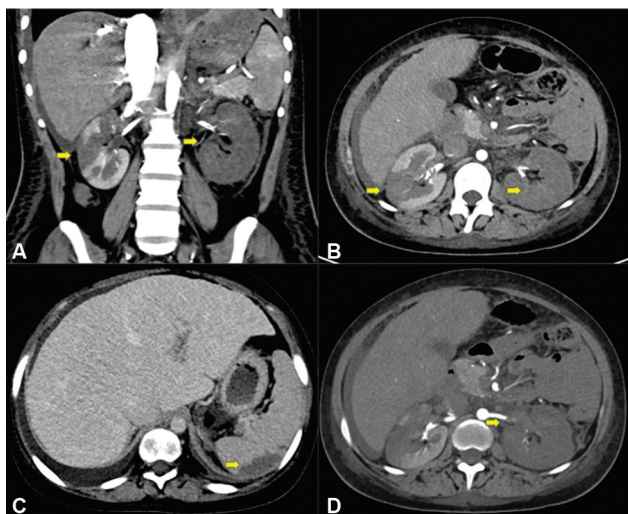


Fig. 4 Coronal and axial sections of contrast CT abdomen of case 3 show (A) (B) multiple wedge shaped infarcts in right kidney and global infarct of left kidney (arrow), (C) infarcts are seen in the spleen also (arrow), (D) thrombus (arrow) is noted in the left renal artery.

noted in the plain study to suggest large vessel occlusion. Contrast CT could not be done as his clinical condition deteriorated. Based on the serological and imaging findings, he was given a presumptive diagnosis of CAPS. After a multidisciplinary discussion, plasma exchange therapy was initiated. He was also given high-dose steroids. His sensorium and platelet count improved after 2 cycles of plasma exchange therapy, and steroids were tapered off. Repeat investigations showed improving trend, and the patient symptomatically improved.

Case 3

A 19-year-old female patient presented with vomiting, left loin pain radiating to the back, and shortness of breath. CECT abdomen was done, which demonstrated thrombosis of the left renal artery with near total left renal infarction, and scattered nonenhancing areas in the right kidney and spleen, suggesting multiple infarcts (►Fig. 4). The patient was

started on anticoagulants and supportive measures. However, on the fourth day of admission, she developed increasing breathlessness, and CT pulmonary angiography showed acute pulmonary thromboembolism involving the right and left pulmonary arteries and bilateral segmental and subsegmental branches, with features of right heart strain (►Fig. 5).

Serological investigations revealed positive lupus anticoagulant and she was given a probable diagnosis of CAPS. The patient was further started on a combination of immunosuppressive therapy with pulse-dose steroids and plasma exchange, following which she gradually improved.

Discussion

The catastrophic antiphospholipid syndrome is a rare life-threatening form of APS, in which widespread microangiopathy and intravascular thrombosis occur, resulting in multi-organ ischemia and failure. CAPS is the initial presentation of APS in almost half of the patients, while the remaining half has a prior history of APS.⁴

The unique characteristics of CAPS are:

- Rapid-onset thromboses resulting in multiple organ dysfunction;
- common association with other thrombotic microangiopathies;
- evidence of systemic inflammatory response syndrome;
- high risk of unusual organ involvement; and
- relatively high mortality rate despite optimal therapy.⁵

CAPS maybe accompanied by the systemic inflammatory response syndrome, likely to cause extensive tissue damage. In the majority of patients with CAPS, a precipitating factor such as infection, surgery, or medication may be identified.⁴

The serological hallmarks of CAPS are antiphospholipid antibodies such as lupus anticoagulant and antibodies against cardiolipin, β 2-glycoprotein I, and prothrombin. In addition, laboratory tests often reveal antinuclear antibodies, anemia, and thrombocytopenia.

Antiphospholipid antibodies act by stimulating endothelial cells, platelets, and immune cells, and causing a

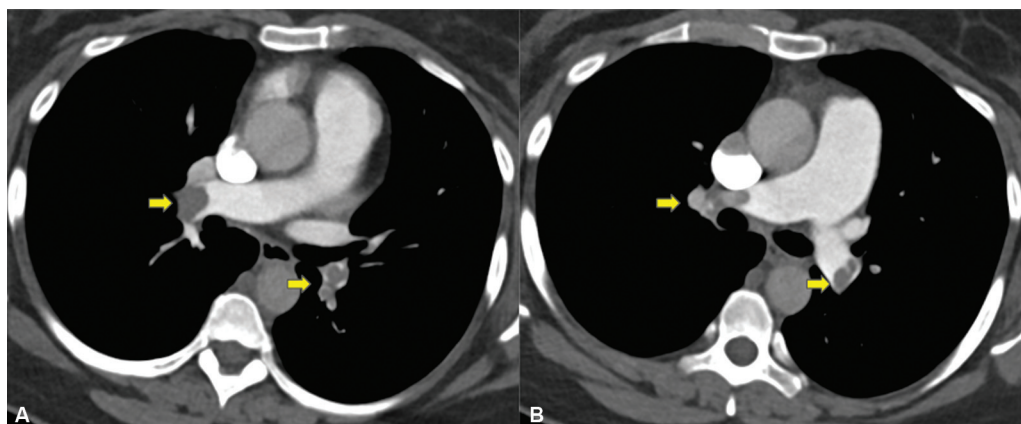


Fig. 5 Axial sections of CT pulmonary angiography of case 3 show (A) thrombi within the right and left pulmonary arteries and segmental branches (arrows).

proinflammatory and prothrombotic state in the body. These antibodies activate complements, impair fibrinolysis, and inhibit anticoagulants.⁴

CAPS diagnosis relies on the presence of antiphospholipid antibodies and the involvement of multiple organs in a microangiopathic thrombotic process with a close temporal association.⁶

The classification criteria for CAPS are³:

1. Evidence of involvement of three organs, systems, and/or tissues.
2. Development of the manifestations simultaneously or in less than 1 week.
3. Laboratory confirmation of the presence of antiphospholipid antibodies (aPL) (LA and/or anticardiolipin antibodies (aCL) and/or antibeta2-glycoprotein [anti-2GPI] antibodies) in titers higher than 40 UI/L.
4. Exclude other diagnosis.

Definite CAPS is defined as four criteria. Probable CAPS is diagnosed if there are only two organs involved, if laboratory testing could not be obtained, if criteria 1, 2, and 4 are fulfilled, or if 1, 3 and 4 are fulfilled. However, CAPS patients may present with multiple organ thromboses and/or thrombotic microangiopathies who do not fulfil these criteria, some without prior APS diagnosis or a history of aPL positivity.

Role of imaging:

The commonly affected organs in CAPS are the kidneys, lungs, central nervous system, and heart although a variety of tissues and organs can be affected.

The renal manifestations include renal arterial/venous thrombosis, renal infarction, APS nephropathy, and renal failure. The pulmonary manifestations of CAPS are⁷ pulmonary thromboembolic disease, diffuse alveolar hemorrhage, acute respiratory distress syndrome, pulmonary hypertension, thrombosis of large and small lung vessels, fibrosing alveolitis, or postpartum lung syndrome. The Neurologic manifestations comprise acute ischemic stroke, transient ischemic attack, and cerebral venous thrombosis. Other manifestations include cardiac manifestations such as infarcts or valvular thickening, abdominal involvement as in Budd–Chiari syndrome, mesenteric ischemia, and cutaneous manifestations (e.g., livedo reticularis, livedo racemosa).

In patients with vascular thrombotic events, various imaging modalities can be diagnostic. CECT and angiographic studies help identify the thrombotic process and ischemic effects, as in renal infarction secondary to renal vein or artery thrombosis, pulmonary infarcts with pulmonary thromboemboli or features of pulmonary hypertension, cerebral infarcts with large or small vessel occlusions, mesenteric ischemia, or thrombotic involvement of various large vessels. MRI scan of the brain helps identify the ischemic and infarcted regions in the brain, with underlying microangiopathy or vasculitis-like pattern seen as multiple sites of vascular narrowing and dilation or abnormal vessel wall enhancement, and MR angiography and MR venography help assess the location of arterial occlusions and cortical venous thrombosis, respectively. MRI of extremities can show bone infarctions due to microangiopathy and extensive

bone marrow edema. Cardiac MRI reveals subendocardial delayed enhancement and perfusion defects. Venous thrombotic events can also be diagnosed with Doppler ultrasonography or venography, which helps identify the thrombi and the extent involved.

The imaging features of CAPS are identical to the manifestations of classic antiphospholipid syndrome, except that multiple organ systems are involved acutely and concurrently. In addition, bleeding and infections can frequently complicate the disease course, directly affecting the prognosis.

Histologically, CAPS is characterized by intravascular thrombosis affecting predominantly microcirculation, and also involving large arteries, veins, or both.⁴ CAPS closely resembles other forms of thrombotic microangiopathies such as thrombotic thrombocytopenic purpura (TTP), hemolytic-uremic syndrome (HUS), disseminated intravascular coagulation (DIC), and sepsis, and has to be distinguished from them.⁸ This differentiation is challenging as HUS, TTP, DIC, and sepsis all share similar imaging features, and there is no specific imaging finding pertaining to CAPS. However, serological and hematological investigations can aid in this, such as aPL positivity in CAPS, low level of ADAMTS13 activity in TTP, culture or PCR positivity for *Shigella* in HUS, or abnormal coagulation testing and reduced fibrinogen in DIC.⁹ Patients with sepsis and CAPS can share the symptoms of systemic inflammatory response syndrome (SIRS) and because infection is a common triggering factor for CAPS, they can coexist.

CAPS is associated with high morbidity and mortality and requires an aggressive multidisciplinary treatment strategy. Anticoagulation, steroids, plasma exchange, cyclophosphamide, and intravenous immunoglobulin therapy are often used.¹⁰ The long-term mortality of catastrophic antiphospholipid syndrome is nearly 50%, and patients may develop further events of catastrophic antiphospholipid syndrome after the initial episode.

Hence, in patients presenting with acute and close temporal thrombotic involvement of multiple organs, the early suspicion of CAPS should be raised to initiate the treatment promptly and improve the prognosis. When relevant, an integrated approach to diagnosis and management with a multidisciplinary team of intensive care, rheumatology, hematology, nephrology, infectious disease, obstetrics, and plasma exchange team is vital for managing this complex and highly fatal disease.

Conclusion

CAPS is the most severe form of APS with multiple organ ischemia, usually accompanied with intravascular thrombosis and hematologic manifestations. The diagnosis of CAPS relies on the presence of antiphospholipid antibodies and involvement of various organs in a close temporal association. The clinical manifestations of CAPS may evolve gradually, commonly overlapping with other thrombotic microangiopathies, requiring a high index of clinical suspicion. CAPS is truly a rheumatologic emergency, requiring prompt recognition and diagnosis, as well as aggressive

treatment, to avoid the fulminant irreversible complications. Imaging can play a key role in raising the suspicion of CAPS, and the radiologist needs to be aware of this possibility to promptly suspect the disease, alert the clinician, and guide appropriate management.

Funding

None.

Conflict of Interest

None declared.

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