Catastrophic Antiphospholipid Syndrome in a Young Adult: A Case Report and Literature Review

Thomas Szewczyk, BS; Farzana Hoque, MD, MRCP, FRCP

ABSTRACT

Introduction: Catastrophic antiphospholipid syndrome (CAPS) is a rare, life-threatening variant of antiphospholipid syndrome marked by rapid multiorgan thrombosis. Early diagnosis remains challenging, especially in young adults.

Case Presentation: A 22-year-old woman with immune thrombocytopenia, Raynaud's phenomenon, and a recent cholecystectomy presented with headache, abdominal pain, and systemic symptoms. She developed thrombotic events in the brain, spleen, and kidneys. Laboratory testing demonstrated positive antiphospholipid antibodies, and renal biopsy confirmed thrombotic microangiopathy.

Discussion: CAPS was diagnosed in the context of evolving systemic lupus erythematosus. Treatment included corticosteroids, plasma exchange, anticoagulation, hydroxychloroquine, and rituximab. Despite delayed recognition due to overlapping autoimmune conditions, multidisciplinary management led to clinical stabilization.

Conclusions: This case highlights the diagnostic complexity of CAPS in young patients with autoimmune comorbidities. Early recognition and aggressive multidisciplinary treatment are essential for favorable outcomes.

INTRODUCTION

Catastrophic antiphospholipid syndrome (CAPS) is a rare, life-threatening variant of antiphospholipid syndrome (APS) characterized by widespread small-vessel thrombosis leading to multiorgan failure. First formally described in the early 1990s, CAPS affects fewer than 1% of patients with APS and carries a high mortality rate, historically ranging from 30% to greater than 50% despite advances in treatment.[1,2] The condition evolves rapidly, often within days, distinguishing it from classic APS, which typically involves thrombosis at a single site. The pathophysiology of CAPS is multifactorial and involves the pathogenic antiphospholipid antibodies (aPLs), including lupus anticoagulant, anticardiolipin, and anti-β2 glycoprotein I antibodies. These antibodies promote a prothrombotic state through endothelial activation, complement activation, and inflammatory cytokine release, culminating in systemic microvascular occlusion.[2,3] A widely accepted "two-hit" hypothesis suggests that an external trigger, most commonly infection, surgery, malignancy, or anticoagulation withdrawal, precipitates the catastrophic cascade in individuals with underlying aPL positivity.[2,4]

CAPS is frequently associated with autoimmune disorders, particularly systemic lupus erythematosus (SLE), which coexists in approximately 30% to 40% of cases.[5] The neurologic, renal, pulmonary, and cardiac systems are most commonly affected. Diagnostic criteria for CAPS include multiorgan involvement, acute symptom onset within 1 week, histopathologic confirmation of small-vessel thrombosis, and laboratory detection of aPLs.[3] Empiric treatment consists of "triple therapy": therapeutic anticoagulation, high-dose corticosteroids, and either plasma exchange or intravenous immunoglobulin (IVIG). In refractory cases, immunomodulatory agents such as rituximab and eculizumab have shown positive results.[2,6] Despite these interventions, prognosis typically remains unclear, underscoring the importance of early recognition and aggressive multidisciplinary management.[4,6]

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Author affiliations: Saint Louis University School of Medicine, St. Louis, Missouri (Hoque, Szewczyk).

Corresponding author: Farzana Hoque, MD, MRCP, FACP, FRCP, Department of Internal Medicine, Saint Louis University School of Medicine, St. Louis, MO 63104-1016; email farzanahoquemd@gmail.com; ORCID ID 0000-0002-9281-8138

CASE PRESENTATION

A 22-year-old woman with a complex medical history notable for immune thrombocytopenic purpura (ITP), Raynaud's phenomenon, rheumatic mitral valve disease, myopericarditis, and recent cholecystectomy (2 weeks before admission) was transferred to our institution for further evaluation of abdominal pain, intractable headache, nausea, and vomiting. She had previously been scheduled for an outpatient renal biopsy because of hematuria and proteinuria identified during a prior admission; however, she presented to the emergency department before the biopsy could be performed.

On initial presentation, the patient was found to have a malar rash, joint pain, easy bruising, and chronic headaches, a constellation of findings suggestive of an autoimmune disorder, in addition to abdominal pain, nausea, and vomiting. Physical examination revealed a murmur and right lower quadrant abdominal tenderness. She was hemodynamically stable and afebrile. Initial imaging revealed a right middle cerebral artery infarct on brain magnetic resonance imaging (MRI) (Figure 1) and a splenic infarct on abdominal computed tomography (CT) (Figure 2). Urinalysis demonstrated 2+ protein and 2+ blood, suggestive of a nephritic syndrome. Collectively, these findings, along with a new-onset rash, raised concern for a systemic autoimmune or thrombotic process.

Further serologic testing revealed positive lupus anticoagulant and elevated IgM anticardiolipin and IgM β2-glycoprotein I antibodies. Although her antinuclear antibody (ANA) and extractable nuclear antigen (ENA) profiles initially were negative, an ANA titer of 1:160 was later confirmed by immunofluorescence. Given the multiorgan involvement, including the central nervous system, spleen, kidneys, and heart, together with the serologic findings, a working diagnosis of CAPS was made. The rheumatology service also considered underlying SLE as a contributing autoimmune condition, although the patient did not meet full classification criteria at the time of diagnosis.

The patient's vital signs remained relatively stable throughout hospitalization. Blood pressure fluctuated between hypertensive and normotensive ranges during the first 10 days, with a peak measurement of 159/111 mm Hg on the hospital day 2. She never developed hypotension requiring vasopressor support. The patient remained afebrile throughout hospitalization, and no supplemental oxygen was required.

During admission, the patient experienced worsening cardiopulmonary symptoms, including pleuritic chest pain and elevated troponin levels. Serial echocardiograms and cardiac MRI demonstrated an ejection fraction of 47%, classified as mildly reduced according to contemporary cardiology guidelines, as well as new regional wall motion abnormalities consistent with recurrent myopericarditis. Cardiology attributed myopericarditis to underlying inflammatory activity rather than ischemic heart disease. Coronary angiography showed no evidence of thrombotic lesions.

Figure 1. Brain Magnetic Resonance Imaging of Patient Consistent With Right Middle Cerebral Artery Infarct

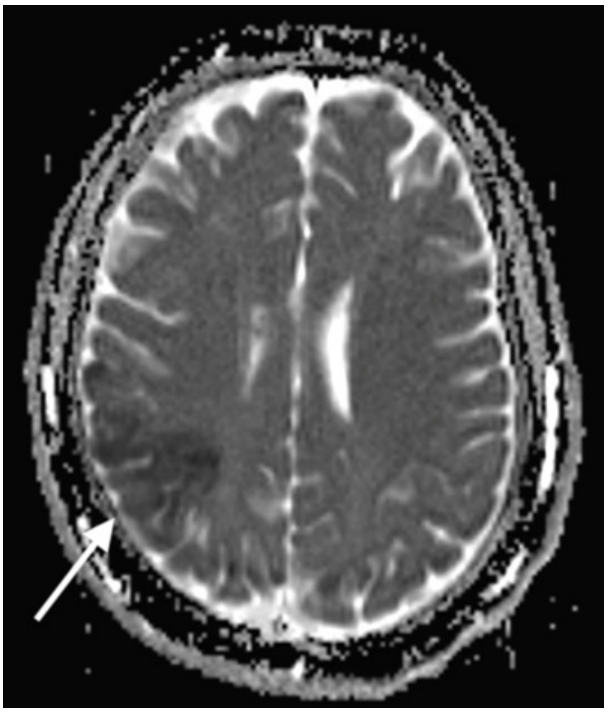
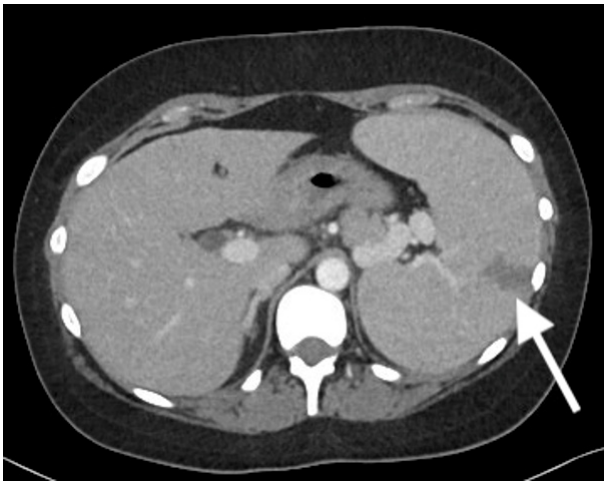


Figure 2. Abdominal Computed Tomography of Patient Consistent With Splenic Infarct



Colchicine and corticosteroids were administered for symptom control, and guideline-directed medical therapy for heart failure, including carvedilol and empagliflozin, was initiated. Renal biopsy demonstrated thrombotic microangiopathy with features of acute interstitial nephritis and acute tubular injury, findings consistent with renal involvement in CAPS. Unlike cerebral and splenic infarcts, no renal infarction or other renal abnormality was identi-

fied on imaging. Evidence of renal thrombosis was demonstrated only on biopsy. Significant laboratory findings are summarized in the Table.

Initial attempts at biopsy were delayed because of concerns regarding bleeding in the setting of chronic ITP and thrombocytopenia. A skin biopsy performed to evaluate a faint malar and reticulated rash demonstrated leukocytoclastic vasculitis. The cumulative clinical, radiographic, and histopathologic findings supported the diagnosis of CAPS. Anticoagulation was initiated with a heparin drip and later transitioned to therapeutic enoxaparin bridging to warfarin. Because of the known limitations of international normalized ratio (INR) monitoring in APS, the hematology and pharmacy teams recommended chromogenic factor X activity testing to guide anticoagulation therapy. The patient was discharged with a target factor X activity level of 20% to 30%, with outpatient INR correlation planned.

For immunosuppression, she received pulse-dose methylprednisolone (1 g intravenously daily for 3 days), followed by high-dose maintenance methylprednisolone and transition to oral prednisone, 60 mg daily, at discharge. Hydroxychloroquine was initiated, and the patient completed 5 plasma exchange (PLEX) sessions. She also received 2 doses of rituximab, 1000 mg each, administered 2 weeks apart. Trimethoprim-sulfamethoxazole (Bactrim) prophylaxis was initiated to prevent opportunistic infections during immunosuppressive therapy, with plans to consider alternative agents such as atovaquone or dapsone if needed.

Neurology remained involved because of persistent intractable headaches and for ongoing stroke management. Despite multiple therapeutic interventions, The headaches remained partially refractory, with only mild improvement following treatment with topiramate and gabapentin. Opioids gradually tapered during hospitalization. The patient's hospital course was further complicated by profound fatigue, anorexia, and weight loss, with clinical evidence of severe protein-calorie malnutrition. Nutritional supplementation and a gradual diet reintroduction were implemented under the supervision of the internal medicine team.

Following stabilization of her condition, improvement of symptoms, and completion of planned immunosuppressive and anticoagulation therapies, the patient was discharged home in stable condition on hospital day 30. She was instructed to follow closely with outpatient specialists in rheumatology, hematology, nephrology, neurology, cardiology, and gynecology. Follow-up appointments and laboratory monitoring, including repeat antiphospholipid antibody testing and chromogenic factor X assays, were arranged to ensure continuity of care.

Table. Significant Lab Results During Hospitalization

Lab Test	Days Collected	Peak/Key Value
Platelet count	Days 2–30	Lowest: 47 (day 3); improved to 161
White blood cell count	Days 2–30	Peak: 46.5 (day 22); improved to 16.4
Creatinine	Days 2–30	Peak: 1.29 (day 20); normalized to 0.89
Troponin I	Days 12, 13, 14, 23	Peak: 52,695 (day 14); elevated on days 12, 13, 14, 23
Urinalysis	Days 2, 10	Protein 2+, Blood 2+; Protein 2+, Blood 2+
Antinuclear antibody titer	Day 3	1:160
Lupus anticoagulant	Day 3	Positive
aCL IgM	Day 3	Positive
β2GPI IgM	Day 3	Positive

DISCUSSION

CAPS is a rare but life-threatening variant of APS, defined by rapid multiorgan failure due to widespread small-vessel thrombosis. This case of a 22-year-old woman demonstrates a diagnostically and therapeutically complex presentation of CAPS, made more challenging by comorbidities, including refractory ITP, nephritic syndrome, myopericarditis, and possible SLE. The patient's admission was initially prompted by gastrointestinal symptoms and severe headache but rapidly escalated into a systemic evaluation when imaging revealed infarctions in the brain and spleen. Renal biopsy showed thrombotic microangiopathy, with additional findings of acute interstitial nephritis and tubular injury. The diagnosis of CAPS was ultimately supported by the involvement of 3 major organ systems (brain, kidney, spleen), along with laboratory evidence of antiphospholipid antibodies (lupus anticoagulant positive, anticardiolipin IgM positive, β2-glycoprotein I IgM positive) and biopsy-proven microthrombosis. This constellation satisfies the international consensus criteria for definitive CAPS, which require evidence of small-vessel thrombosis in at least 3 organs occurring over a short period and the presence of antiphospholipid antibodies.[7] The lack of hypotension further supports thrombosis, rather than hypoperfusion, as the cause of organ injury. CAPS occurs in less than 1% of patients with APS, with a female predominance and an average age in the mid-30s, making this patient's diagnosis at age 22 relatively early.[8]

Neurological involvement is common in CAPS, with stroke being the most frequent manifestation, followed by seizures and cognitive dysfunction.[9] The patient's right middle cerebral artery infarct aligns with the neurologic manifestations commonly seen in CAPS. Though her persistent headaches were initially attributed to migraine, there was consideration of underlying cerebrovascular inflammation or vasculitis. However, repeat neuroimaging did not show progression of vessel irregularities, making progressive large-vessel vasculitis unlikely. Thus, microvascular thrombosis, a hallmark feature of CAPS, remains the most likely mechanism behind her infarct. Renal involvement in CAPS commonly presents as thrombotic microangiopathy or APS nephropathy,[10] and in this patient, the renal biopsy revealed hallmark features consistent with this pathology, including glomerular microthrombi. Her urine

protein-creatinine ratio improved from 0.88 to 0.57, and stable creatinine levels suggest partial response to therapy, although long-term outcomes remain uncertain. Cardiac complications in CAPS range from valvular abnormalities (including Libman-Sacks endocarditis) to myocardial infarction secondary to coronary thrombosis or microvascular disease.[11] The patient had prior mitral valve abnormalities suspected to be congenital, but worsening left ventricular function and wall motion abnormalities during the hospital course likely reflected CAPS-related myocardial involvement. Serial echocardiograms and cardiac MRI findings of hypomobility without fibrosis support this interpretation.

One of the significant hurdles in this case was distinguishing CAPS from other overlapping autoimmune syndromes. Despite systemic features consistent with SLE (including malar rash, photosensitivity, pericarditis, nephritic syndrome, and cytopenias), her initial autoimmune panel was largely negative. However, ANA later returned at a titer of 1:160 by indirect immunofluorescence assay, and skin biopsy confirmed leukocytoclastic vasculitis, raising strong suspicion for SLE. Whether the initially negative serologies reflected evolving disease or the effects of acute illness remain uncertain.[12] The literature recognizes that CAPS can either be primary or secondary to conditions such as SLE, and in up to 40% of cases, CAPS may be the first manifestation of APS or lupus.[13]

The coexisting diagnosis of ITP further complicated management. While thrombocytopenia is a paradoxical feature of a prothrombotic syndrome, it is frequently seen in APS and especially in CAPS, where platelet consumption is accelerated by ongoing microthrombosis.[4] This also delayed the renal biopsy and complicated anticoagulation decisions. Treatment of CAPS is multifaceted and often referred to as "triple therapy," consisting of anticoagulation, high-dose corticosteroids, and PLEX, with or without IVIG.[5] The patient received all three, plus rituximab, an anti-CD20 monoclonal antibody increasingly employed in refractory or overlapping CAPS/SLE cases.[14] The decision to escalate to rituximab was supported by the patient's poor response to thrombopoietin receptor agonists for ITP, suspected lupus activity, and evolving CAPS. The use of hydroxychloroquine further aligns with SLE management guidelines, and its potential antithrombotic benefit may aid in preventing recurrent thrombosis.[6] The patient's condition gradually stabilized following 5 sessions of PLEX, 2 doses of rituximab, and transition to warfarin with enoxaparin bridging. Given the complexity of CAPS management, shared decision-making with patients and families is critical to ensure understanding of the treatment goals, risks, and alternatives.[15] Discharge on prednisone 60 mg, hydroxychloroquine, aspirin, and a carefully titrated anticoagulation plan (monitored using chromogenic factor X activity assays because of potential lupus anticoagulant interference with standard coagulation testing), demonstrates adherence to tailored therapy recommendations in complex APS.[16]

At discharge, the patient was clinically stable but remained on substantial immunosuppressive and anticoagulation regimens. Her renal function had improved slightly, and her platelet counts were monitored without requiring platelet transfusions. Her headaches were managed with topiramate and gabapentin, and she was counseled on medication adverse effects and contraception due to potential teratogenic risk. Follow-up with hematology, rheumatology, nephrology, cardiology, and neurology was arranged.

CONCLUSIONS

This case demonstrates the diagnostic and therapeutic complexity of CAPS, particularly in young adults with overlapping autoimmune and hematologic conditions. The patient's rapid multiorgan involvement, including cerebral, renal, splenic, and cardiac manifestations, highlighted the importance of considering CAPS even in younger patients who fall outside the typical age range at presentation. Despite initially confounding features and negative serologies, the evolving clinical picture, supported by serologic and histopathologic findings, met diagnostic criteria for CAPS likely associated with evolving SLE. Early multidisciplinary collaboration and prompt treatment with high-dose corticosteroids, anticoagulation, plasma exchange, and rituximab were critical to disease stabilization and the patient's favorable condition at discharge.

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