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Case Report

Systemic Embolism Following Mechanical Thrombectomy for Acute Ischemic Stroke: A Case of Suspected Catastrophic Antiphospholipid Syndrome

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Objective: Catastrophic antiphospholipid syndrome (CAPS) is a disease characterized by a poor prognosis and a high mortality rate, leading to systemic thrombosis. Approximately two-thirds of CAPS cases are associated with conditions such as infections, malignancies, surgical interventions, and events linked to the disease activity of systemic lupus erythematosus (SLE). Herein, we present a case of CAPS with multiorgan ischemia following ischemic stroke.

Case Presentation: In this case report, a 33-year-old woman with a history of SLE and prolonged steroid use manifested impaired consciousness. Detection of the right internal carotid artery (ICA) occlusion led to successful ICA recanalization through endovascular thrombectomy. Postoperatively, she experienced pulmonary embolism and renal infarction. Although antiphospholipid syndrome (APS) was suspected, APS-related antibodies were negative. Anticoagulation therapy was initiated, presuming corticosteroid-induced thrombosis. However, she developed multiorgan thrombosis, culminating in multiple organ failure. Based on her clinical course, a diagnosis of CAPS was established. Intensive care and plasma exchange therapy were instrumental in her recovery, and she was discharged with a modified Rankin Scale score of 4.

Conclusion: When encountering multiorgan ischemia following ischemic stroke in a young adult patient with an autoimmune disease, the consideration of CAPS as a differential diagnosis is crucial, even if APS-related antibodies test negative.

Keywords ▶ catastrophic antiphospholipid syndrome, ischemic stroke, multiorgan failure, systemic lupus erythematosus

List of Abbreviations

APS = Antiphospholipid syndrome
CAPS = Catastrophic antiphospholipid syndrome
SLE = Systemic lupus erythematosus
aPL = Antiphospholipid antibodies
dRVVT = Dilute Russell viper venom test
MCA = Middle cerebral artery
DWI-ASPECTS = Diffusion-weighted imaging-Alberta Stroke Program Early Computed Tomography Score
AIS = Acute ischemic stroke
TIA = Transient ischemic attack
SN-APS = Seronegative antiphospholipid syndrome
MT = Mechanical thrombectomy
IgG = Immunoglobulin G
IgM = Immunoglobulin M
aCL = Anticardiolipin antibody
aβ2GPI = Anti-β2-glycoprotein-I antibody

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Introduction

Antiphospholipid syndrome (APS) is an autoimmune disease characterized by the presence of antiphospholipid antibodies (aPL), causing arterial and/or venous thrombosis as well as recurrent fetal loss. The estimated incidence

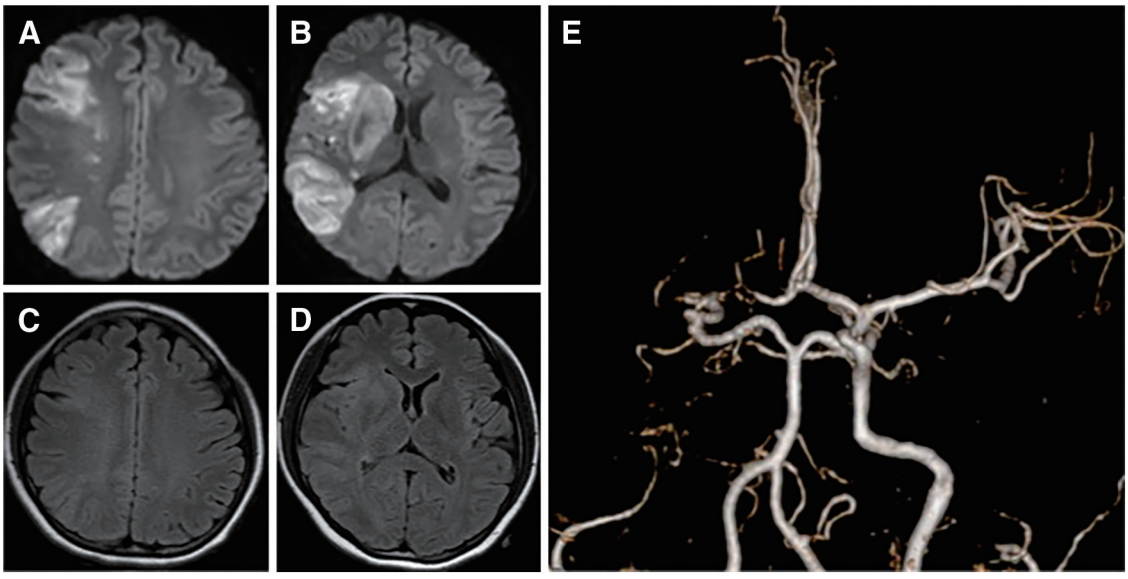

Fig. 1 Acute right hemisphere stroke detected by axial head MRI. Axial head MRI showing the acute phase of a right hemisphere stroke on a DWI, and the DWI-ASPECTS was 4 (**A** and **B**). The right hemispheric swelling shows slightly high intensity on FLAIR (**C** and **D**). MRA reveals occlusion of the right ICA (**E**). DWI: diffusion-weighted imaging; DWI-ASPECTS: diffusion-weighted imaging-Alberta Stroke Program Early Computed Tomography Score; ICA: internal carotid artery; MRA: magnetic resonance angiography; MRI: magnetic resonance imaging

of APS is approximately 5 cases per 100000 persons per year, with a prevalence of 40–50 per 100000 individuals.[1,2] This syndrome can manifest both with (secondary APS) and without (primary APS) an underlying systemic autoimmune disorder. Secondary APS is often associated with systemic lupus erythematosus (SLE), Sjögren's syndrome, and rheumatoid arthritis. Acute ischemic stroke (AIS) and transient ischemic attack (TIA) are common complications, representing the primary arterial pathology in APS.[2] The cumulative prevalence rates of AIS and TIA in patients with APS are reported to be 19.8% and 11.1%, respectively.[3] In addition, aPL may be detected in up to 13.5% of patients with stroke,[4] and the presence of aPL is a known risk factor associated with a 5.48-fold higher risk of thrombotic cerebrovascular events.[5]

Furthermore, serious thrombotic complications and fatalities among APS cases have been reported and termed catastrophic APS (CAPS).[6] CAPS is a rare occurrence, affecting less than 1% of all patients with APS, and until recently, only a few case studies were available. The CAPS registry, established in 2000, has facilitated the study of patient backgrounds and treatment modalities. CAPS predominantly affects women in their 30s and is associated with thrombosis in the kidneys, lungs, brain, and heart. Definite CAPS is defined as thrombosis in three or more organs within a week, microthrombosis in at least one organ, and persistent positivity for aPL. CAPS should be considered in young adult patients with recurrent multiorgan embolism, even in the absence of coagulation abnormalities or identifiable embolic sources. However, some patients are seronegative for aPL, making CAPS challenging to diagnose. In this report, we present a case of cerebral infarction followed by multiorgan embolism suspected to be caused by CAPS, and we discuss the associated pathophysiology and treatment.

Case Presentation

A 33-year-old woman diagnosed with SLE was discovered in a comatose state. The National Institute of Health Stroke Score was 27, as assessed 10 hours after the last check-up. Magnetic resonance imaging revealed right internal carotid artery (ICA) occlusion and extensive ischemic stroke in the right middle cerebral artery (MCA) territory (**Fig. 1A–1E**). The diffusion-weighted imaging-Alberta Stroke Program Early Computed Tomography Score (DWI-ASPECTS) was 4. A decision was made to perform an endovascular thrombectomy to salvage the penumbra. The procedure was conducted under local anesthesia, and an arterial sheath was inserted into the right femoral artery. A carotid angiogram displayed a contrast defect at the origin of the right ICA (**Fig. 2A**). A two-pass thrombectomy using a stent retriever and aspiration catheter achieved recanalization of thrombosis in modified

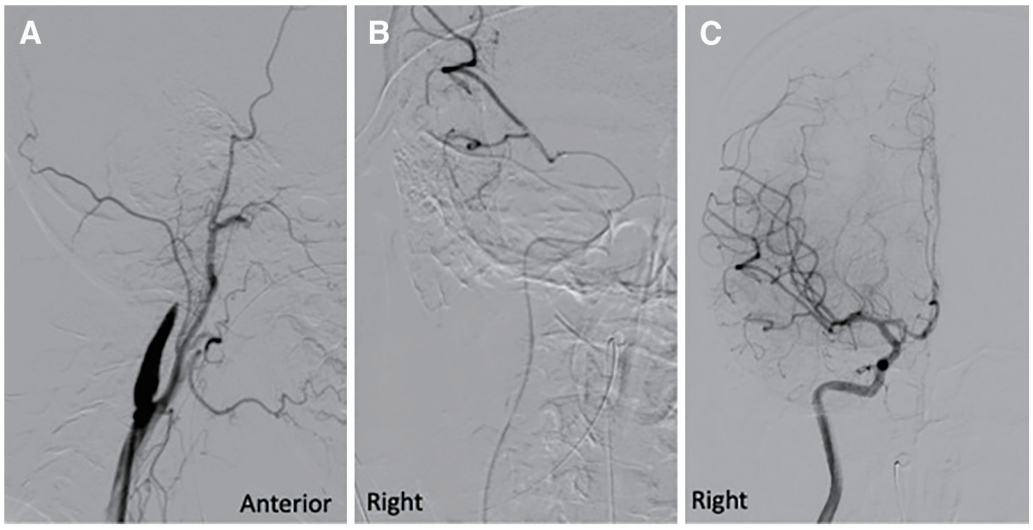

Fig. 2 Thrombectomy procedure for right ICA occlusion. Angiography of the right common carotid artery demonstrating occlusion of the right ICA (**A**). A microcatheter is advanced to the M1 segment of the MCA, and thrombectomy was performed with a Solitaire 6 mm × 40 mm stent-retriever (Medtronic Inc., Irvine, CA, USA) and Catalyst 6 aspiration catheter (Stryker, Kalamazoo, MI, USA) with two passes using the same technique (**B**). Recanalization of the ICA was achieved, except for one branch in the M3 segment (**C**). ICA: internal carotid artery; MCA: middle carotid artery

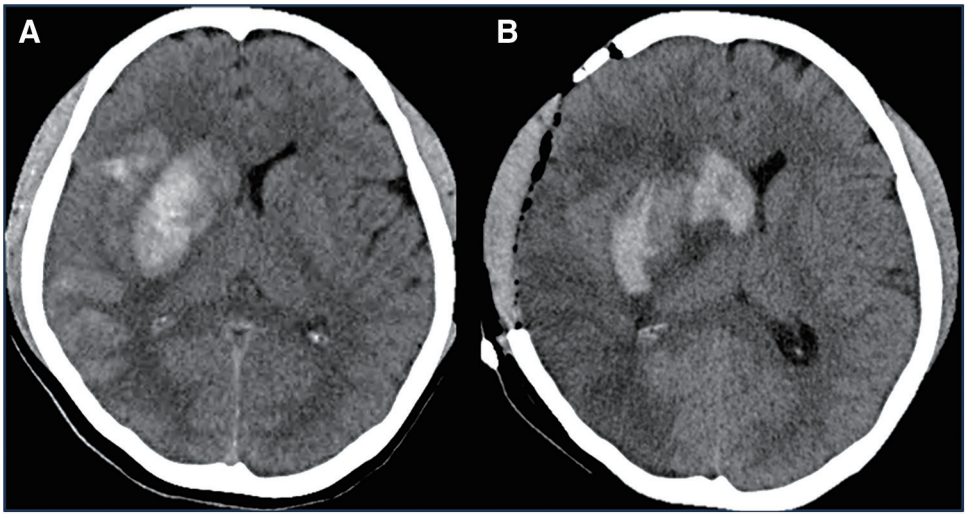

Fig. 3 Head CT scan revealed worsening edema and hemorrhage within the infarction (**A**). A decompressive craniotomy was performed under general anesthesia (**B**).

treatment in cerebral infarction grade 2B (**Fig. 2B** and **2C**). The patient regained consciousness on postoperative day 1, but a head CT scan revealed worsening edema and hemorrhage within the infarction (**Fig. 3A**). Consequently, a decompressive craniotomy was performed under general anesthesia the same day (**Fig. 3B**). Postoperative whole-body CT revealed a pulmonary embolism and renal infarction (**Fig. 4A** and **4B**). Although APS was suspected, laboratory tests for lupus anticoagulant (dilute Russell viper venom test [dRVVT]), anticardiolipin Immunoglobulin G (IgG) antibody (aCL), and anti-β2-glycoprotein-I antibody (aβ2GPI) showed negative results. The patient's prolonged use of steroids raised suspicions of corticosteroid-induced thrombosis. Anticoagulation therapy was started on day 5 with 10000 units of heparin/day and controlled to maintain an activated partial thromboplastin time of 60–70 s. Furthermore, after altering anticoagulation therapy to warfarin, a prothrombin time-international normalized ratio of 2.0 to 3.0 was maintained. On day 12, she developed acute myocardial ischemia and a deep venous thrombus in the left lower limb. Twenty-five days after the first event, she exhibited consciousness disorder attributed to a cerebral

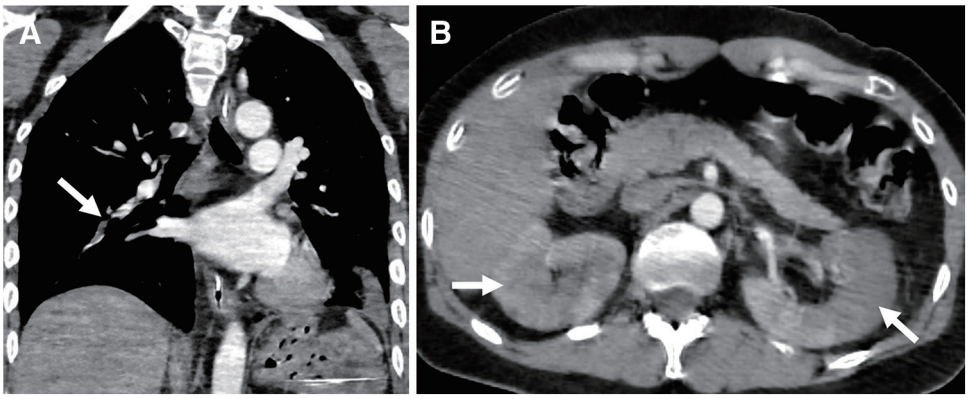

Fig. 4 CT after decompression surgery revealing pulmonary embolism (**A**) and bilateral renal infarction (**B**) (arrow).

Table 1 Preliminary criteria for the classification of CAPS (Asherson and Cervera[15])

1. Evidence of involvement of three or more organs, systems, or tissues.
2. Development of manifestations simultaneously or within less than a week.
3. Confirmation by histopathology of small-vessel occlusion in at least one organ or tissue.
4. Laboratory confirmation for the presence of antiphospholipid antibodies (lupus anticoagulation or anticardiolipin antibodies).

Definite CAPS: All four criteria.

Probable CAPS
- All four criteria, except only two organs, systems, or tissues are involved.
- All four criteria, except for the absence of laboratory confirmation at least 6 weeks apart because of the early death of a patient never previously tested for antiphospholipid antibodies before the catastrophic event.
- Criteria 1, 2, and 4.
- Criteria 1, 3, and 4, and the development of a third event in more than a week, but less than a month, despite anticoagulation.

CAPS: catastrophic antiphospholipid syndrome

infarction in the left parietal lobe. The patient developed multiple organ emboli over a short period, and the laboratory confirmed multiple organ failure. CAPS diagnosis was not confirmed, and there is a lack of evidence suggesting lupus anticoagulant or pathology of small-vessel occlusion (**Table 1**). However, due to the patient's history of SLE, young age, and lack of other triggers, it was considered reasonable to commence treatment for suspected CAPS. Intensive care and plasma exchange therapy were administered, leading to her recovery, and she was subsequently discharged with a modified Rankin Scale score of 4. Ethical approval was provided by our Institutional Ethics Committee, and written informed consent was obtained from the patient's family for the publication of this report.

Discussion

APS associated with SLE presents a spectrum of aPL and complications, ranging from severe arterial thrombosis to minor venous thrombosis.[7] In the Japanese population, cerebrovascular disorders account for the majority of arterial thrombosis in APS.[8] Individuals with SLE or those testing positive for aPL face an increased risk of thrombotic cerebrovascular events, with manifestations including large infarcts (22%), white matter changes (17%), small cortical infarcts (10%), and lacunar infarcts (9%).[9] The MCA (31%) is the most common site of occlusion, followed by the cerebellum (7%), posterior cerebral artery (5%), and thalamus (2%).[10] On the other hand, a study comparing APS-associated embolic stroke with cardioembolic stroke in patients with atrial fibrillation showed that APS-associated embolic stroke had a smaller infarct size and less relevant artery occlusion.[11]

A distinctive and rare manifestation, CAPS, is characterized by multiple organ emboli and a very poor prognosis. CAPS accounts for approximately 1% of APS cases and is prevalent in middle-aged women. This syndrome causes systemic thrombosis within a few days to a month, leading to multiple organ failure, often resulting in up to a 50% mortality rate. Predominantly affected organs include

the kidneys, lungs, brain, and heart.[12,13] About two-thirds of patients with CAPS experience episodes such as infections, malignancies, surgical interventions, and events associated with SLE disease activity.[12,14] The rapid progression of the disease, coupled with the positivity for APS-related antibodies, contributes to a CAPS diagnosis. The occurrence of three or more organ thromboses within 1 week is a key diagnostic criterion for CAPS[15] (**Table 1**). The presence of two organ thromboses within 1 week establishes a diagnosis of probable CAPS.[16]

In the presented case, three organ thromboses were observed within 1 week and five organ thromboses within 1 month. APS is typically characterized by the presence of aPL, including lupus anticoagulant, aCL, and/or aβ2GPI.[17] However, instances of CAPS with negative conventional APS-related antibody test results have been documented.[18] Seronegative APS (SN-APS) is a variant of APS in which thrombosis occurs in multiple organs despite an unclear thrombotic cause.[19] The diagnosis of SN-APS requires negative aPL results on at least two separate examinations. In addition, other potential causes of thrombosis, such as genetic factors, active cancer, trauma, major surgery, and prolonged bed rest, must be excluded.[20] On multiple examinations, Our patient tested negative for lupus anticoagulant (dRVVT), aCL-IgG, and aβ2GPI-IgG. The aPL outlined in the APS classification criteria (revised Sapporo APS classification criteria or Sydney criteria) include lupus anticoagulant, aCL-IgG, aCL-Immunoglobulin M (IgM), aβ2GPI-IgG, and aβ2GPI-IgM. However, until July 2020, insurance coverage in Japan only extended to IgG-type aCL, IgG-type β2GPI-dependent aCL, and dRVVT, excluding IgM-type antibodies. Consequently, tests without insurance coverage were not conducted. The rationale for classifying this case as probable CAPS with seronegative arises from the patient's rapid development of multiorgan embolisms within a short timeframe, despite her young age and the absence of embolic sources or coagulation abnormalities, except for SLE. It is speculated that the negative aPL results could be attributed to antibody consumption during the acute thrombotic episode.[21]

The fundamental treatment approach for CAPS involves a combination of anticoagulation and steroid therapy, with plasma exchange or intravenous immunoglobulin therapy also considered.[18,22] In this case, despite the commencement of heparin administration, the patient exhibited resistance to treatment (such as myocardial infarction and deep venous thrombosis), prompting the use of methylprednisolone, intravenous immunoglobulin, and plasma exchange due to suspected CAPS. Recent studies have explored the efficacy of eculizumab.[23] Endovascular thrombectomy has been reported to be beneficial in treating acute MCA occlusion with APS.[24,25] Although Japanese guidelines for mechanical thrombectomy (MT) are cautious for patients with Alberta Stroke Program Early Computed Tomography Score (ASPECTS) less than 7, the efficacy of MT for large ischemic lesions with ASPECTS 3–5 has been recently reported.[26] In this case, MT was considered based on the patient's age, angiographic findings, and the balance of risks and benefits. It is essential to be aware that surgeries or invasive procedures on patients with APS can potentially trigger CAPS, necessitating vigilance to prevent and treat ongoing thrombotic events and manage excessive cytokine storms. In this case, percutaneous thrombectomy and decompression craniotomy were performed before the diagnosis of CAPS, which may have contributed to the systemic embolism.

Conclusion

There are few case reports suggesting stroke due to CAPS,[27–29] with no instances found where MT was performed alongside anticoagulant and steroid therapies. Given the novelty of the CAPS concept, it may not be widely recognized or diagnosed. Despite its rarity, CAPS should be considered when a young woman with an autoimmune disease but poor vascular risk experiences a stroke, with careful consideration of the risk of progression to multiorgan ischemia. We emphasize that when multiorgan embolisms occur, the possibility of CAPS should be considered based on the clinical course and various antibody tests, and early initiation of treatment is crucial.

Disclosure Statement

The authors declare no conflicts of interest.

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