Case Reports

Massive Cerebrovascular Infarct Due to the Catastrophic Antiphospholipid Syndrome in a Patient With Idiopathic Thrombocytopenic Purpura

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Catastrophic antiphospholipid syndrome (APS) is caused by thrombotic vascular occlusions that affect both small and large vessels, producing ischemia in the affected organs as well as a systemic inflammatory response syndrome (SIRS). We report a case of a patient with idiopathic thrombocytopenic purpura (ITP) who developed massive cerebral ischemia due to this entity. Prompt and aggressive treatment may prevent and actually resolve lethal complications caused by this devastating syndrome.

Keywords: catastrophic antiphospholipid syndrome; idiopathic thrombocytopenic purpura; cerebrovascular infarct; systemic inflammatory response syndrome

Case Presentation

A 43-year-old man with idiopathic thrombocytopenic purpura (ITP) and prior splenectomy presented with headache and chills. The following day, he was found lethargic and febrile and was taken to the emergency room (ER). The patient was not taking any medication and he had not had any medical complication until this presentation. On arrival to the ER, the patient was noted to be febrile (39°C), tachycardic, and tachypneic with an oxygen saturation of 84% on a nonrebreather mask (NRB). On examination, he was lethargic and icteric. Neurologic examination did not reveal any focal deficits and his neck was supple. His chest exam revealed inspiratory crackles in both lung bases. The abdomen was distended, nontender and bowel sounds were decreased. The rest of his physical examination was unremarkable.

An arterial blood gas revealed a pH of 6.86, PCO₂ of 27 mm Hg and a Po₂ of 50 mm Hg on the NRB mask. The complete blood count showed a WBC of 55 cells/μL and hemoglobin of 2.8 g/dL. Platelet count was 220 000/μL. The electrolyte panel revealed a creatinine of 4.8 mg/dL. Liver function studies and coagulation profile were within normal limits. Amylase and lipase were highly elevated. Blood and urine cultures were sent and remained negative. The electrocardiogram was significant for sinus tachycardia. The chest x-ray revealed bilateral alveolar infiltrates. The patient was intubated for respiratory distress, hypoxemia, and lethargy.

Antibiotic therapy was initiated with ceftriaxone, azithromycin, and vancomycin for presumed pneumonia. Because of his severe anemia, a hemolysis panel was sent and showed a positive direct coombs test and warm anti–red blood cell antibodies (immunoglobulin [Ig] G). Methylprednisolone 1 mg/kg per day and immunoglobulin therapy (IVIG) were initiated for autoimmune hemolysis. Treatment with methylprednisolone was given for 7 days and IVIG...
for 5 days. A computed tomography (CT) scan of the head was performed showing no abnormalities. A lumbar puncture revealed normal cerebrospinal fluid. Intermittent hemodialysis treatment (IHD) was initiated for worsening renal function. A transesophageal echocardiogram (TEE) showed normal left and right ventricular function without valvular vegetations.

The patient continued on mechanical ventilation, being eventually liberated 4 days after intubation. He was able to communicate and was fully oriented. His oxygen saturation on oxygen nasal canula at 2 L/min was 96%. Twelve hours after extubation, he became hypertensive with systolic blood pressures in the range of 200 to 220 mm Hg, refractory to intermittent doses of intravenous antihypertensives. He was tachypneic and had an irregular respiratory pattern. His mental status deteriorated and he became progressively more unresponsive. He was re-intubated and a CT scan of the head was performed, showing no abnormalities. A transesophageal echocardiogram (TEE) showed normal left and right ventricular function without valvular vegetations.

Discussion

The catastrophic antiphospholipid syndrome (APS) was first described by Asherson in 1992. In this seminal article, 10 cases of catastrophic APS were described. Most of these patients presented with renal dysfunction and central nervous system involvement and 4 of them died despite receiving treatment. Catastrophic APS is caused by thrombotic vascular occlusions that affect both small and large vessels, producing ischemia in the affected organs as well as a systemic inflammatory response syndrome (SIRS). Common abdominal manifestations are renal disease, present in 70% of patients, adrenal insufficiency, mesenteric ischemia, and pancreatitis. Pulmonary complications involve adult respiratory distress syndrome (ARDS), pulmonary embolism, and hemorrhage. Neurological involvement is present in 60% of the patients and manifests as strokes, seizures, venous occlusions, migraine, transverse myelitis, chorea, and encephalopathy.
Cardiac events occur in 53%, with myocardial infarcts as the most common manifestation. Other features are livedo reticularis, testicular and ovarian infarction, and acalculous cholecystitis.

Thrombocytopenia is a usual finding, being present in 60% of the patients, while hemolysis is present in one third of the patients. Catastrophic APS presents with occlusion of small, medium, and large arteries. Elevated levels of antibodies directed against membrane phospholipids, such as anticytidiolipin (aCL), β-2 glycoprotein 1, or lupus anticoagulant are essential for the diagnosis. One study revealed the presence of IgG isotype of anticardiolipin antibodies (aCL) in 83% of the patients, IgM aCL in 38%, and lupus anticoagulant in 82%. In 2003, an international consensus was published which included criteria for the diagnosis of catastrophic APS. These criteria are (1) involvement of 3 or more organs or systems; (2) presence of manifestations simultaneously or within a week; (3) small vessel occlusion in at least 1 organ confirmed by histopathology; and (4) presence of lupus anticoagulant or anticardiolipin antibodies (antiphospholipid antibodies). This last criterion requires laboratory confirmation of antiphospholipid antibody detected at least 6 weeks apart from the 1 previously diagnosed. The manifestation of all 4 criteria defines “definite catastrophic APS” whereas the presence of 3 or 4 incomplete criteria (such as 2 organ involvement or absence of laboratory confirmation at least 6 weeks after a positive antiphospholipid antibody test) defines “probable catastrophic APS.”

When facing a possible scenario of catastrophic APS, it is crucial to investigate an identifiable trigger factor because the initial treatment involves its elimination. These triggers are most commonly infections, surgical procedures, trauma, malignancies, lupus flares, or warfarin withdrawal. Differential diagnoses of this syndrome include microangiopathic syndromes (TTP and HUS), disseminated intravascular coagulation (DIC), heparin-induced thrombocytopenia (HIT), HELLP syndrome, marantic endocarditis, and Sneddon’s syndrome. This last diagnosis is a noninflammatory occlusive arteriopathy of small- and medium-sized arteries. It involves the occurrence of neurological symptoms, hypertension, renal dysfunction, and livedo reticularis.

Although ITP and APS are well-defined entities, a study with 82 patients with ITP showed that 38% developed antiphospholipid antibody and APS. These findings suggest a possible association between ITP and APS.

The treatment of catastrophic APS is based on support of affected organs and specific therapies. Treatment includes intravenous heparin, corticosteroids, intravenous immunoglobulins, and plasma exchange. Immunosuppressive therapy with cyclophosphamide and rituximab has been described. Antiphospholipid syndrome carries a mortality of 50%, being cerebral involvement the most frequent cause of death.

In summary, we report a case of a patient who presented with lethargy and ARDS. His course was complicated by hemolysis, acute renal dysfunction, thrombocytopenia, pancreatitis, and, finally, massive cerebrovascular infarct due to catastrophic APS. A high index of suspicion is needed to diagnose this devastating entity. Prompt and aggressive treatment may prevent and actually resolve lethal complications such as those described in this unfortunate case.

References

