AMERICAN JOURNAL OF MEDICAL CASE REPORTS

ISSN 2374-216X

Catastrophic antiphospholipid syndrome: A rare but serious complication of antiphospholipid antibody syndrome

Sandhu VK*; Singh H

***Vaneet K Sandhu, MD**

Assistant Professor, Division of Rheumatology, Loma Linda University, 11234 Anderson Street, Suite 1521, Loma Linda, California 92354, USA

Abstract

Abdominal pain in young patients, particularly females in high-stress work environments, is often shrugged off as irritable bowel syndrome. We present herein the case of a young woman presenting with abdominal pain due to catastrophic antiphospholipid syndrome (CAPS). This case highlights the value of timely investigations when evaluating patients with abdominal pain, particularly given the risks of ischemic bowel and intestinal necrosis in antiphospholipid syndrome. Many aspects of CAPS remains unexplored, for which we recommend continued research with particular emphasis on diagnostic evaluation and treatment options.

Keywords

catastrophic antiphospholipid antibody syndrome (CAPS); antiphospholipid antibody syndrome (APS); antiphospholipid antibodies (aPL); thrombosis

Introduction

Antiphospholipid syndrome (APS) is an autoimmune disease characterized by both a tendency toward bleeding and thrombocytopenia as well as clotting in the presence of elevated antiphospholipid antibody titers [1]. The ability of APS to manifest in multiple organ systems urges increased awareness of the disease state, particularly in the setting of catastrophic APS (CAPS), which can progress rapidly to the point of imminent death. We present herein a case in which abdominal pain occurs as a result of multi-organ thrombosis, yielding the importance of timely diagnosis and intervention as a means to prolong survival.

Case Report

A 23-year-old nulliparous female with no medical history presented with a 6-month history of abdominal pain with bloating and constipation. She had numerous prior investigations, including upper and lower gastrointestinal endoscopies that were unremarkable, yielding a diagnosis of irritable bowel syndrome. After repeated follow-up with her gastroenterologist for persistent symptoms and an incidental finding of cholelithiasis, an elective cholecystectomy was carried out in an attempt to alleviate her pain.

One week post-op, the patient was readmitted for severe worsening of abdominal pain with

distension and bilious vomiting. There was no relationship with food intake, diarrhea, bloody bowel movements, pale-colored stool, jaundice, or pruritus. She had no fever, chills, vaginal discharge, dysuria, or frequency or urgency of urination. No recent sick contacts or history of travel was noted. Her menstrual cycle was regular.

On examination, vital signs were within normal limits and her surgical sites lacked signs of infection. Although abdominal examination was significant for guarding, the abdomen was soft and bowel sounds present.

Admission labs yielded normal complete blood count, comprehensive metabolic panel, pancreatic enzymes, negative pregnancy test, and negative serum antinuclear antibody. Abdominal ultrasound, esophagogastroduodenoscopy (EGD) and colonoscopy were unremarkable with the exception of post-operative changes from recent cholecystectomy on abdominal ultrasound. CT abdomen ruled out a bilious leak but revealed a thickened loop of jejunum. Small bowel capsule endoscopy confirmed small intestinal ulceration, raising concern for Crohn's disease. The patient was started on intravenous methylprednisolone and symptoms of pain and vomiting improved. A follow-up CT abdomen, however, revealed a wedge-shaped infarct of the left kidney (Figure 1). Cardiac echocardiogram was unremarkable. A hypercoagulable workup was initiated and the patient was started on intravenous heparin. Coagulation studies were significant for positive serum lupus anticoagulant with elevated serum anti-cardiolipin antibodies (aCL), yielding a diagnosis of antiphospholipid syndrome.

Within one week of the left renal infarct, abdominal pain recurred with increased severity in the left flank. Repeat imaging revealed a new splenic infarct (Figure 2) despite therapeutic anticoagulation. Her platelet count dropped, she had an episode of gastrointestinal bleeding, and, within days, the abdominal pain progressed to a surgical abdomen. An emergency laparotomy was done and the patient was found to have a perforated portion of small intestine accompanied by necrosis of multiple bowel loops, as well as liver infarcts and a cyanotic ovary. A large portion of the small bowel was resected and biopsy subsequently revealed mesenteric thrombosis. Immediately postoperatively, for the treatment of catastrophic antiphospholipid syndrome (CAPS), plasma exchange and rituximab were initiated in addition to continuing anticoagulation and steroids. After a complicated subsequent hospital course, the patient was stabilized and discharged on oral warfarin.

Discussion

Antiphospholipid syndrome (APS) is characterized by vascular thrombosis or pregnancy morbidity in the presence of persistent antiphospholipid antibodies (table 1) [1]. Less than 1% of patients with APS go on to develop CAPS, an accelerated subset characterized by clotting events involving multiple organ systems over a short period of time [2]. Because of the unusual and unpredictable clinical manifestations and associations of this disease, it was once dubbed as “syndrome of the Black Swan [3].”

With mortality rates ranging from 30-50%, early diagnosis and intervention in CAPS are important [4-6]. Diagnosis includes clinical and laboratory criteria (table 2) with correlative pathology [7]. However, despite the availability of these diagnostic criteria, laboratory data may not always be definitive. For example, the patient discussed in this case report had an IgM cardiolipin antibody that did not exceed the diagnostic cutoff of >40MPL. Her IgG cardiolipin antibody was within normal limits.

However, with a heightened index of suspicion for disease, the diagnosis must be made so that timely treatment is initiated.

Precipitating factors for CAPS may include infection, surgery, anticoagulation withdrawal or low INR, medications, obstetric complications, neoplasia, and SLE flares (as SLE may be associated with concomitant antiphospholipid syndrome) [4]. In this case, the patient likely developed CAPS as a result of her recent cholecystectomy.

Abdominal pain is a common presenting feature of APS, of which hepatic involvement is most common (nodular regenerative hyperplasia, cirrhosis, portal hypertension, autoimmune hepatitis), followed by thrombotic events involving different branches of the intestinal vasculature [4]. Additional gastrointestinal manifestations include mucosal ulcerations, portal vein thrombosis, mesenteric thrombosis and Budd-Chiari syndrome. Renal disease may occur in up to 70% of patients [8], but gangrene of the bowel is an infrequent occurrence. Nonetheless, APS patients should be thoroughly monitored for evidence of intestinal ischemia and, similarly, patients with intestinal ischemia should be evaluated for APS.

In our case presentation, while the infarcts resulted in acute abdominal pain, it is likely that her chronic abdominal pain was a result of recurrent bouts of mesenteric ischemia until the bowel relented to infarction. In retrospect, the patient later noted that her abdominal pain would also worsen with air travel, yielding more uncertainties to be addressed in further studies on the relationship of barometric pressure changes to clotting events.

The treatment of primary APS necessitates the use of only anticoagulation. However, additional disease-modifying treatment measures are indicated in systemic lupus erythematosus (SLE)-associated APS as well as CAPS due to concomitant manifestations and life-threatening disease state, respectively.

While the global rarity of disease incidence and prevalence limits studies on the treatment of CAPS, higher recovery rates have been associated with a combination of anticoagulation, steroids, and plasma exchange [6]. Current guidelines continue to support this combination as a foundation of therapy in all patients [9]. While cyclophosphamide did not imply significant benefit [6],rituximab in different combinations with anticoagulation, steroids, plasma exchange, and intravenous immune globulin (IVIG) has been studied and reveals lower mortality rates [10]. As seen in our case presentation, the patient exhibited a favorable response after treatment with rituximab, to which we call to update treatment recommendations in CAPS. Additionally, in refractory cases of CAPS, eculizumab– a monoclonal antibody inhibiting terminal complement – has yielded variable results [11-13]. We also endorse favorable effects in the use of eculizumabin a subsequent patient with refractory CAPS (unpublished data), though further studies are recommended.

Figures

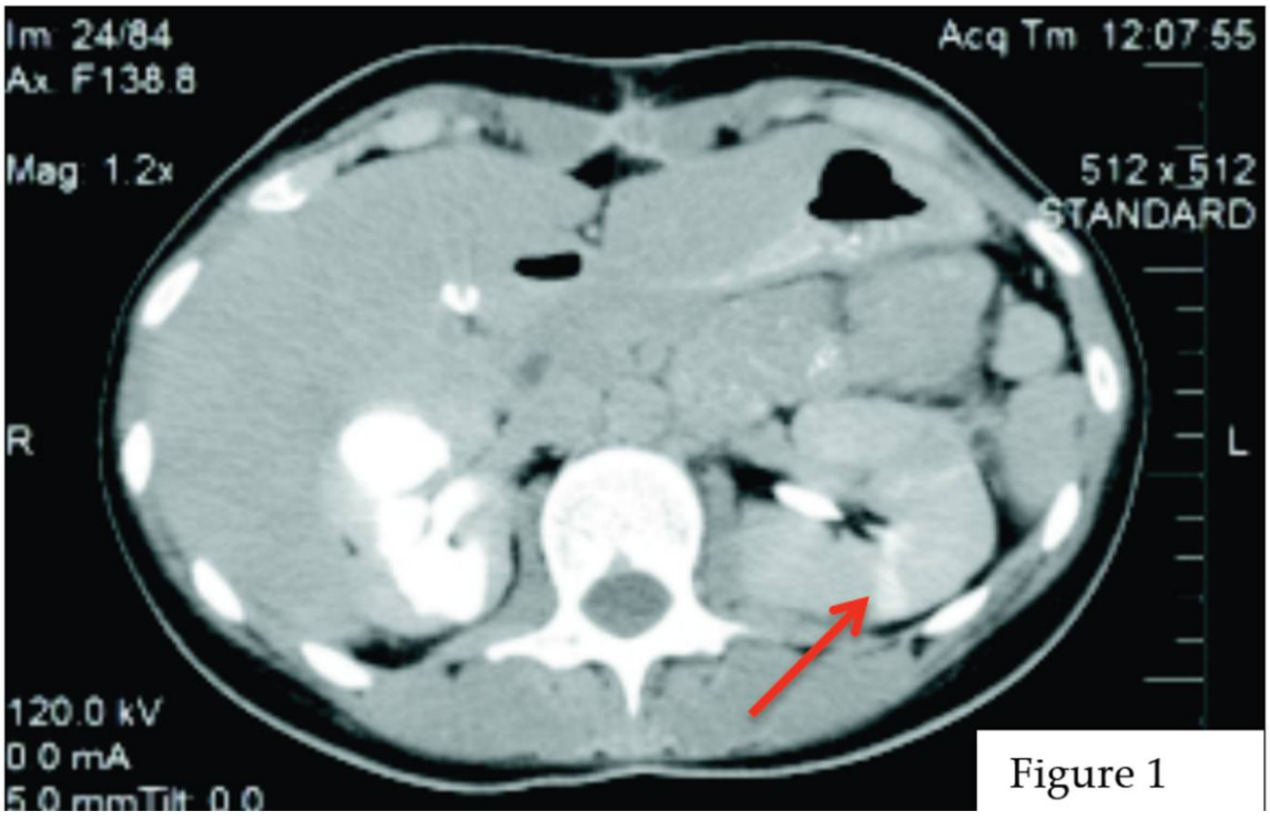

Figure 1: CT scan abdomen/pelvis, initial presentation: Left renal infarct

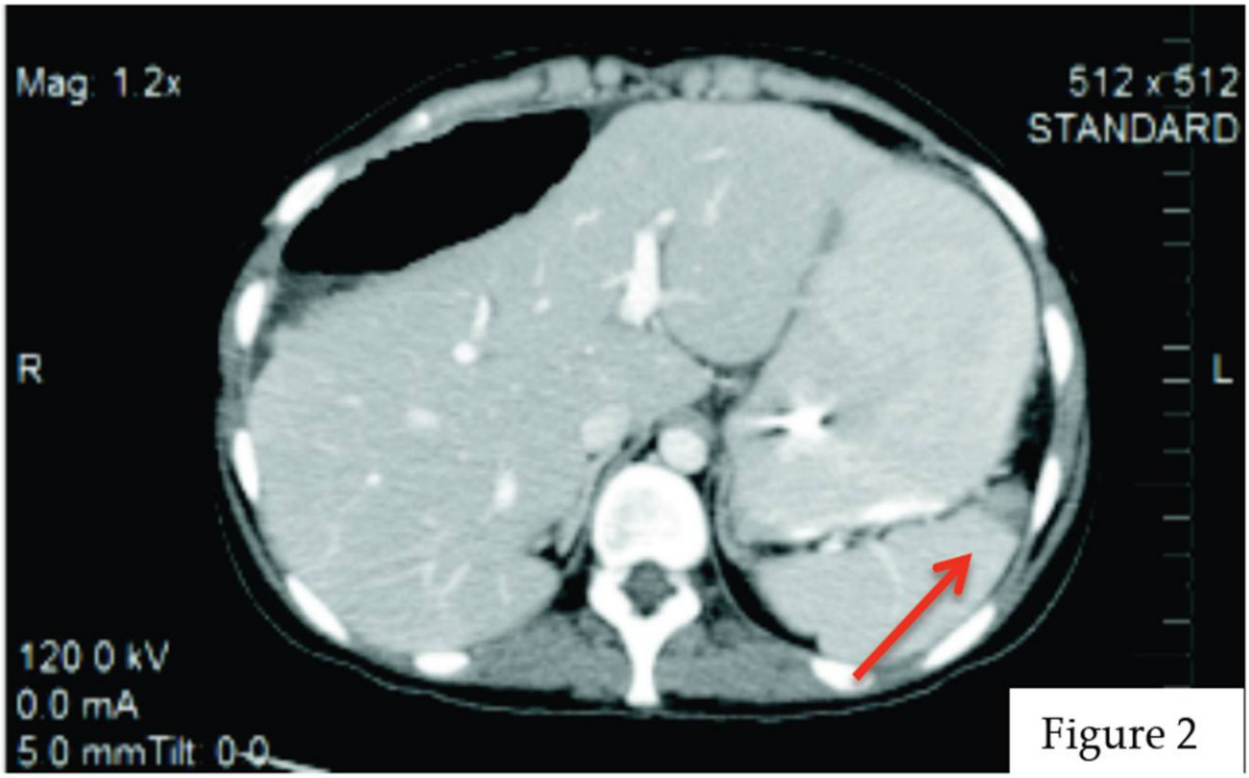

Figure 2: CT scan abdomen/pelvis, 2 days later: Splenic infarct

Tables

Table 1: 2006 revised Sapparo classification criteria for APS*[1]
*APS is present if at least one of the clinical criteria and one of the laboratory criteria that follow are met:
Clinical Criteria
1. Vascular thrombosis: ≥ 1 arterial, venous, or small vessel thrombosis 2. Pregnancy Morbidity (1) ≥ 1 fetal death at or beyond 10 weeks of gestation (2) ≥ 1 premature birth before 34 weeks of gestation due to eclampsia, severe pre-eclampsia, or placental insufficiency, or (3) ≥ 3 consecutive embryonic losses before 10 weeks of gestation
Laboratory Criteria
1. Lupus anticoagulant (LA) present in plasma on ≥ 2 occasions at least 12 weeks apart 2. Anticardiolipin (aCL) antibody of IgG and/or IgMisotype in serum or plasma, present in medium or high titre (i.e. > than 40 GPL or MPL, or > than the 99th percentile), on ≥ 2 occasions at least 12 weeks apart 3. Anti-β2 glycoprotein-I antibody of IgG and/or IgMisotype in serum or plasma (in titer > than the 99th percentile), on ≥ 2 occasions at least 12 weeks apart

Table 2: Diagnosis of CAPS*[2]
1. Evidence of involvement of 3 or more organs, systems, or tissues
2. Development of symptoms simultaneously or in less than 1 week
3. Confirmation by histopathology of small vessel occlusion in at least 1 organ or tissue
4. Laboratory confirmation of the presence of antiphospholipid antibodies (lupus anticoagulant or antiocardiolipin antibodies)
*Definite CAPS requires all 4 criteria. Probable CAPS requires all four criteria except for only 2 organs, systems and/or sites of soft tissue involvement, or all 4 criteria except for the laboratory confirmation at least 6 weeks apart due to early death of a patient never tested for antiphospholipid antibodies before the CAPS event or criteria 1, 2, and 4 or criteria 1, 3, and 4 and the development of a third event in more than a week but less than a month despite anticoagulation.

References

1. Gómez-puerta JA, Cervera R. Diagnosis and classification of the antiphospholipid syndrome. J Autoimmun. 2014;48-49:20-5.

2. Asherson RA. The catastrophic antiphospholipid (Asherson's) syndrome in 2004--a review.Autoimmun Rev. 2005;4(1):48-54.

3. Harris EN. Syndrome of the black swan. Br J Rheumatol. 1987;26(5):324-6.

4. Cervera R, Serrano R, Pons-estel GJ et al. Morbidity and mortality in the antiphospholipid syndrome during a 10-year period: a multicentre prospective study of 1000 patients. Ann Rheum Dis. 2015;74(6):1011-8.

5. Cervera R. Update on the diagnosis, treatment, and prognosis of the catastrophic antiphospholipid syndrome. CurrRheumatol Rep. 2010;12(1):70-6.