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**Clinical report**

# Mesenteric venous thrombosis in a patient with antiphospholipid syndrome and systemic lupus erythematosus

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***Background:*** Antiphospholipid antibodies (aPL) are associated with an increased risk of venous thrombosis and can occur in patients without any associated conditions, or in those with autoimmune disorders, such as systemic lupus erythematosus (SLE). Mesenteric venous thrombosis (MVT) is one of the clinical manifestations of antiphospholipid syndrome (APS), and it has rarely been reported in patients with SLE.
***Objective:*** To report a case of SLE complicated by APS and MVT.
***Method:*** A 28-year-old woman with a history of SLE and lupus nephritis was admitted with nonspecific abdominal symptoms. The working diagnosis was severe SLE and paralytic ileus because of primary peritonitis.
***Result:*** Nine days after she did not respond to symptomatic treatment, exploratory laparotomy revealed MVT and further coagulation work-up was diagnostic for APS. Despite treatment, she died because of complications of SLE and APS.
***Conclusion:*** Though rare, MVT should be considered in patients with SLE and/or APS. The diagnosis of MVT requires a high index of suspicion, and early aPL testing for SLE patients is highly recommended to reduce the morbidity and mortality associated with the condition.

***Keywords:*** Anticardiolipin antibodies, antiphospholipid syndrome, mesenteric venous thrombosis, SLE, systemic lupus erythematosus

Antiphospholipid syndrome (APS) is characterized by antiphospholipid antibodies (aPL), recurrent arterial or venous thrombosis (VT), and spontaneous abortions with thrombocytopenia. It can also be associated with a number of diseases as secondary APS, or occur in the absence of any associated conditions as primary APS [1]. The association of thrombosis with SLE is well-known [2] and patients with SLE and aPL or lupus anticoagulant (LA) have been shown to be at a higher risk of VT [3-5]. However, mesenteric venous thrombosis (MVT) or abdominal ischemia has rarely been reported in patients with APS [6-8]. We herein report a case of MVT in a 28-year-old female with SLE with nonspecific abdominal symptoms.

## Case report

A 28-year-old woman with a 1 year history of SLE (SLEDAI=10) and lupus nephritis presented with a 2 month history of abdominal distension and oliguria, 2 week history of dyspnea on exertion, abdominal pain, chills, and fever for 2 days, and inability to defecate. Her medications included prednisone and mycophenolate mofetil. Her temperature was 38.4°C; heart rate 102, respirations 23/min, blood pressure 118/58. Physical examination revealed a tense abdominal wall with rebound tenderness and moderate pitting edema of lower extremities.

Laboratory examination was significant for a white blood cell WBC count of $30.7\times10^9$/L with 93.5% neutrophils; hemoglobin 31 g/L; platelets $608\times10^9$/L, blood urea nitrogen 17.0, creatinine, 167 μmol/L, uric acid 623 μmol/L, serum CA-125, 153.63 U/ml, and human chorionic gonadotropin negative. Fibrinogen, prothrombin time, and activated partial thromboplastin time were normal. Computed tomography revealed paralytic ileus with irregular low-density signals, "target sign" and ascites. Paracentesis revealed bloody fluid with a WBC of $4.24\times10^9$/L.

An initial differential diagnosis included bacterial or tuberculous peritonitis, SLE mesenteric vasculitis, abdominal tumor, and MVT. A general surgeon was

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consulted and did not believe exploratory laparotomy was indicated. The working diagnosis was severe SLE and paralytic ileus due to primary peritonitis. Gatifloxacin and retention enemas using 0.9% saline and 20 mg Mosapride were administered. The patient's abdominal distension decreased; however, the pain persisted and no flatus or defecation occurred. Nine days later, an exploratory laparotomy revealed avascular necrosis in the ascending colon, ileocecal junction, and ileum, and MVT (**Figure 1**). Removal of a portion of the small intestine and right hemicolectomy was performed.

Postoperative laboratory studies revealed an elevated anticardiolipin IgG level. Her clinical condition improved with intensive supportive care that included low molecular weight heparin (LMWH; Fragmin) to treat the APS; however, heparin was discontinued because of a low platelet count ($44\times10^9$/L) and increased aPTT. The platelet count normalized after 4 days of treatment with Shuxuening, a Chinese herbal medicine that has been shown to inhibit platelet aggregation, reduce blood viscosity, and improve microcirculation [9]. Administration of LMWH was resumed.

Five days after the operation the patient developed lethargy, anxiety, and altered consciousness. CT of the brain showed cerebral atrophy and infarction, consistent with SLE central nervous system involvement. The patient was begun on 400 mg Depakine (valproate) intravenously once a day and 4 mg valproate via gastrostomy tube three times a day. After control of seizures and stabilization of vital signs, 17 days after the first operation, closure of the enterostomy was performed under epidural anesthesia.

Postoperatively she was begun on cefoperazone/sulbactam 3.0 g twice a day, tinidazole 800 mg/day, and fluconazole 200 mg/day along with supportive treatment and 5000 U LMWH subcutaneous once per day. However, she died as a consequence of respiratory and circulatory failure 39 days after admission.

Informed consent was obtained from the patient's father to report this case and publication was approved by our institutional ethics review board.

## Discussion

In the case presented, the differential diagnosis included bacterial or tuberculous peritonitis, mesenteric vasculitis secondary to SLE [10], or abdominal tumor. MVT and MVT were considered less likely and were diagnosed only at exploratory laparotomy.

MVT is an uncommon cause of intestinal ischemia, accounting for from 5% to 15% of all acute vascular events in SLE [11]. The condition is associated with mortality up to 50% because its nonspecific signs and symptoms result in a delay in diagnosis [11]. Patients typically present with vague, nonspecific abdominal pain that evolves over 7 to 10 days [11]. Most patients are not diagnosed until intestinal necrosis has occurred [12].

In patients with MVT, physical examination typically reveals a distended abdomen, guaiac-positive stool and peritoneal signs may be present. Laboratory studies may show hemoconcentration, leukocytosis, and metabolic acidosis [11]. CT scan may show an enlarged mesenteric or portal vein with sharp definition of the venous wall and low density within the vein and "target sign" because of thickening of the bowel wall. Paracentesis may produce bloody fluid. Previous abdominal surgery and hypercoagulable states are the 2 most common predisposing factors for MVT, though associations with other systemic disorders have been noted [13].

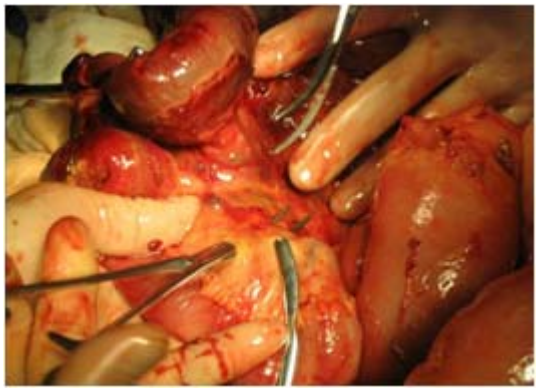

**Figure 1.** Exploratory laparotomy revealed mesenteric venous thrombosis and intestinal necrosis

In our case, MVT was the clinical manifestations of antiphospholipid syndrome (APS), a hypercoagulable state. APS is characterized by the presence of aPL, recurrent arterial or venous thrombosis or spontaneous abortions and thrombocytopenia. It can occur in association with other diseases, primarily autoimmune disorders (secondary APS), or in the absence of any associated conditions (primary APS) [1]. The diagnosis of APS is dependent on the presence of at least one clinical finding, such as vascular thrombosis or pregnancy-related complications (recurrent abortion, premature birth, stillbirth), and at least one laboratory finding, including a positive test for LA or high-titer IgG or IgM anticardiolipin antibody (aCL) [14]. In our patient, early aPL testing was not performed. This may have contributed to the delay in diagnosis of MVT.

APS associated with SLE has been reported in the literature [15-18]. In a report of 13 patients with myocardial infarction and aPL by Asherson et al. [15], 6 patients had SLE as defined by the revised 1982 criteria, three had "lupus-like" disease, and four patients had clinical and serological findings consistent with primary APS. In a long-term follow-up study of 128 APS patients, G mez-Puerta et al. [18] found that 11 (8%) patients developed SLE and only 3 patients developed anti-dsDNA antibodies after a median disease duration of 8.2 years suggesting that it is unusual to progress from primary APS to SLE or lupus-like disease. Tarr et al. [19] suggested that primary APS may be a forerunner of lupus, but it may also coexist with SLE as an independent autoimmune disorder. In their report, out of a total 362 SLE patients, 223 had antiphospholipid antibodies (aPL), of whom 110 met the criteria for APS. In 26 cases (7.2%) primary APS appeared an average of 5.5 years before the onset of lupus. The prevalence of deep venous thrombosis, stroke/transient ischemic attack, recurrent fetal loss, coronary heart disease and myocardial infarction was significantly higher in primary APS plus SLE patients compared with patients with SLE alone [19]. In our case, we did not know if the patient had a primary APS before lupus or if APS coexisted with SLE as an independent autoimmune disorder because early aPL testing was not performed.

The relative risk for venous thrombosis (VT) associated with aPL in SLE is high. Results of a meta-analysis [5] found that the odds ratios of the risk of VT related to LA summarized from 18 studies were 5.61 (95% [confidence interval] CI; 3.80-8.27) overall, 6.32 (95% CI; 3.71-10.78) for deep venous thrombosis and pulmonary embolism, and 11.6 [95% CI; 3.65-36.91] for recurrent VT after the first event. The odds ratios of the risk of VT related to aCL antibodies summarized from 14 studies were 2.17 (95% CI; 1.51–3.11) overall, 2.50 (CI; 1.51–4.14) for deep venous thrombosis and pulmonary embolism, and 3.91 (95% CI; 1.14–13.38] for recurrent VT after the first event. The above data indicate that patients with SLE and LA are at approximately six times greater risk for VT than patients without LA, and patients with SLE and aCL are at approximately two times greater risk for VT than patients without aCL [5]. Somer et al. [4] studied 678 patients with SLE and found that both LA and aCL were associated with an increased risk of VT.

However, it is rare to find a patient with SLE and concomitant MVT with or without APS. In a report of 177 SLE patients by Xu et al. [20], 39 (22.0%) had SLE-related gastrointestinal manifestations and only one case was complicated by superior MVT. Another article reported a 44-year-old woman with SLE who developed an infarction of the bowel and spleen after occlusion of the inferior mesenteric and splenic arteries, necessitating colectomy and splenectomy. Several bowel wall arteries and veins were occluded by fresh or organizing thrombi. She was found to have a prolonged partial thromboplastin time (PTT) LA and aCL in high titers, consistent with APS [21]. Medina et al. [22] reported 3 cases of MVT among 29 patients with primary APS. It is likely that the patient with superior MVT reported by Xu et al. [20] also had APS since MVT is not unusual in primary APS patients.

In summary, though rare, MVT does occur in patients with SLE and/or APS. The diagnosis of MVT requires a high index of suspicion and prompt treatment is necessary to reduce great morbidity and mortality associated with this condition. Early aPL testing is important.

The authors have no conflicts of interest to declare.

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