Systemic Lupus Erythematosus Associated Gastrointestinal System Vasculopathy in a Patient with Lupus Nephropathy

Lupus Nefropatili Bir Hastada Sistemik Lupus Eritematosusa Bağlı Gastrointestinal Sistem Vaskülopatisi

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ABSTRACT

Gastrointestinal system (GIS) manifestations are common in systemic lupus erythematosus (SLE) patients. The gastrointestinal vasculopathy of SLE is a unique clinical entity and reviewed infrequently but it should be kept in mind to give the necessary treatment with corticosteroids and other immunosuppressive agents and to avoid non-essential surgical interventions. Here we report a 33-year-old SLE patient that presented with surgical acute abdomen symptoms, was followed-up in a Nephrology Department, and was well managed with high doses of corticosteroids and cyclophosphamide after the diagnosis of GIS vasculopathy.

KEY WORDS: Lupus Erythematosus, Systemic, Vasculopathy, Abdominal pain

ÖZ

Sistemik lupus eritematosus (SLE) hastalarında gastrointestinal sistem (GİS) semptomları sıktır. SLE' ye bağlı GİS vaskülopatisi daha önce literatürde az bildirilmiş nadir bir klinik durumdur fakat kortikosteroidler ve diğer immünosüpresiflerle doğru tedavinin verilmesi ve gereksiz cerrahi uygulamalardan kaçınılması açısından akılda tutulması gerekir. Burada SLE tanısıyla Nefroloji Bölümünde takip edilen ve akut batın semptomlarıyla başvuran 33 yaşındaki hastanın GİS vaskülopati tanısı konulduktan sonra yüksek doz kortikosteroid ve siklofosfamidle tedavisi anlatılmaktadır.

ANAHTAR SÖZCÜKLER: Lupus eritematozus, Sistemik, Vaskülopati, Karın ağrısı

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Received : 19.01.2011
Accepted : 09.02.2011

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INTRODUCTION

Systemic Lupus Erythematosus is a chronic, complex, autoimmune inflammatory disease of unknown cause with a variety of presenting manifestations. It is the most prevalent autoimmune disease with an annual incidence of 60 per million population and a prevalence of 500 per million population (1,2,3). SLE is most prevalent in the 20-40 years age group with a female-male ratio of 9:1 (1). It can affect any system in the body.

We report a patient followed-u for lupus nephropathy who later developed severe gastrointestinal vasculopathy of SLE.

CASE REPORT

A 33 year-old woman referred to our Nephrology Department with malar rash, arthralgia, proteinuria (550 mg/day), and lymphopenia (800/mm^3), was diagnosed as SLE. Antinuclear antibody was positive with a titer of 1/3200 (using immunofluorescent staining) and anti-dsDNA antibodies were positive at a level of 11.7 IU/ml. Treatment with 32 mg prednisolone and 250 mg chloroquine was started. Three months later she was admitted to our department with chronic abdominal pain accompanied by diarrhea, nausea, vomiting and constipation episodes. She described intermittent episodes of similar symptoms in the last month occurring sporadically and resolving spontaneously in 3 to 4 days. Physical examination revealed diffusely sensitive, distended abdomen with guarding, rebound tenderness, and hypoactive bowel sounds. Laboratory studies showed an erythrocyte sedimentation rate (ESR) of 62 mm/h, elevated C-reactive protein (CRP) of 32

mg/dl, 2,6 mg/dl of albumin and 3.8 gr/day proteinuria. Renal biopsy was performed for increased proteinuria and showed class 2 lupus nephritis with mesengial proliferative changes, tubular atrophy and chronic interstitial inflammation. Complete blood count revealed lymphopenia and anemia (normochromic and normocytic anemia on the peripheral blood smear). Low C3 and C4 levels (C3: 0.384 g/L (0.9-1.8), C4: 0.0655 g/L (0.1-0.4)), and negative antiphospholipid antibodies (aPls) were also found. An ectopic pregnancy was excluded by negative serum beta-human chorionic gonadotrophin. A plain abdominal radiography showed multiple air-fluid levels (Figure 1), without free intraabdominal air. Ascites was found in the low abdominal quadrants by abdominal ultrasonography, and the ascite sample was characterized as transudate. Upper gastrointestinal endoscopy showed linear erosions in the esophagus. An oral and intravenous contrast enhanced computerized tomography scan showed dilatation of small and large bowels with wall thickening, ascites in the right upper quadrant, engorgement of mesenteric vessels and increased attenuation of mesenteric fat (Figure 2 A, B). She was diagnosed with GIS vasculopathy as a manifestation of SLE. In consultation with the general surgery department, oral feeding was stopped and bowel rest was instituted with placement of a nasogastric tube. Hydration was initiated with i.v. fluids. She was treated with intravenous methylprednisolone for 3 consecutive days (1 gr\day). Contrary to expectations, the abdominal symptoms persisted. Three days later, intravenous methylprednisolone, and intravenous cyclophosphamide 500 mg were administered and repeated every 2 weeks for 3 months. Azathioprine 2 mg per kg daily was initiated. Some abdominal symptoms such as nausea, dysphagia and constipation were started when she was taking azathioprine and prednisone. She suffered from chronic constipation despite regular use of laxatives and required repeated hospital visits for rectal enema. The azathioprine was switched to 750 mg MMF twice a day and oral prednisone 5 mg daily. She remained asymptomatic with complete resolution of GIS vasculopathy during 7 months of follow-up. However, she showed signs of recurrence of digestive symptoms while she was taking MMF 750 mg twice a day and prednisone 5 mg daily. Intravenous cyclophosphamide at a dose of 750 mg every 3 months for 12

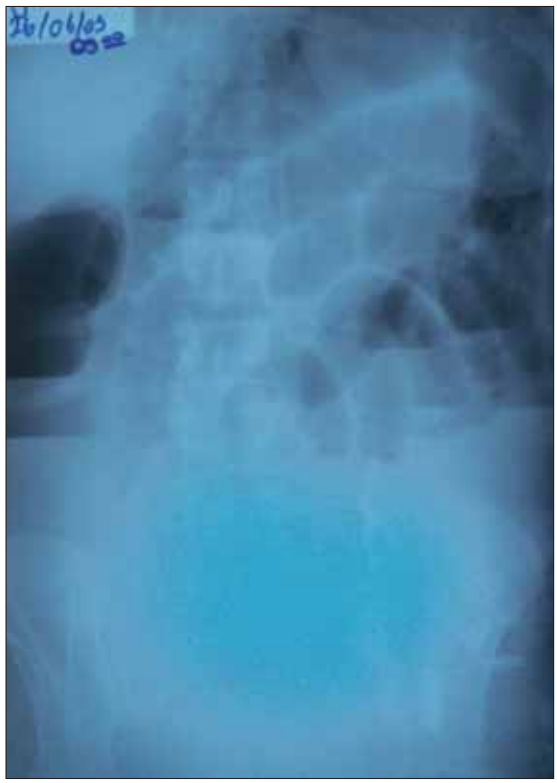

Figure 1: *Plain abdominal radiography revealing multiple air-fluid levels.*

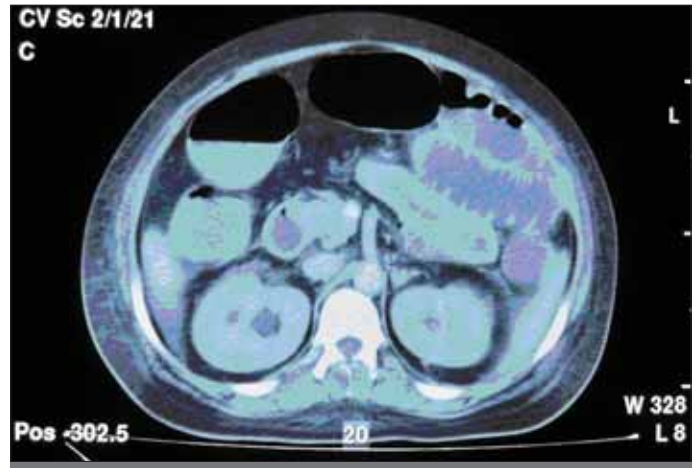

Figure 2 a

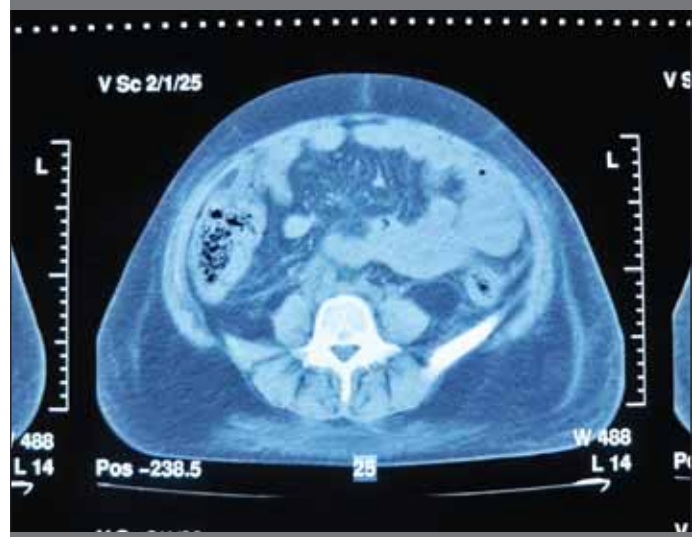

Figure 2 b

Figure 2A, 2B: *Oral and intravenous contrast enhanced abdominal CT. 2A CT demonstrates dilatation of small and large bowels with wall thickening and ascites in the right upper quadrant. 2B CT shows engorgement of mesenteric vessels and increased attenuation of mesenteric fat.*

months in addition to MMF 750 mg twice a day and prednisone 5 mg daily was initiated. She is still being followed up with complete remission of digestive symptoms.

DISCUSSION

Gastrointestinal complaints such as anorexia, nausea, vomiting, dysphagia, hematemesis, postprandial fullness, diarrhea and melena are present in 30-50% of SLE patients. Gastrointestinal symptoms may be due to side effects of medications, the vasculopathy of SLE, stress-related mucosal disease (gastritis) or any intercurrent illness (4,5,6).

Our patient presented with vomiting, abdominal pain, diarrhea and constipation episodes. All drugs used in the treatment of active lupus such as non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, hydroxychloroquine, azathioprine, methotrexate, mycophenolate mofetil and cyclophosphamide may cause such symptoms.

The gastrointestinal vasculopathy of SLE can be evaluated in two categories as thrombotic and inflammatory. The thrombotic form is caused by thrombosis of vessels secondary to a noninflammatory vasculopathy associated with circulating antiphospholipid antibodies (aPls) (7, 8). The inflammatory form is due to classic leukocytoclastic vasculitis secondary to immune complex deposition in vessel walls (9). Complement activation is the major mechanism in this form. Gastrointestinal system (GIS) SLE vasculopathy can develop from the upper to the lower GIS and small venous or arterial circulation of the GIS affected (10).

Clinical features of bowel ischemia can be explained by the degree of involvement of each of the bowel layers. The blood vessels most sensitive to ischemia are in the mucosa. The changes caused by bowel ischemia can differ according to the sensitivity of the blood vessels in the four different layers of the bowel wall. (11). These two types of microvasculopathy cannot be differentiated clearly by the clinical findings. Clinical findings might vary from a mild gastroenteritis to an acute abdomen with distension, guarding and rebound tenderness requiring urgent surgery for bowel infarction depending on the extent and duration of vessel inflammation. It commonly presents with symptoms of abdominal pain, nausea, vomiting and diarrhea (10). Our patient presented with rebound tenderness and abdominal muscle guarding. She was afebrile and had absent bowel sounds. aPls was negative whereas C3 was very low.

The incidence of clinically evident GIS SLE vasculopathy has been reported to be 0.2-2% in the literature (12,13). The majority of cases reported had findings of acute abdomen and high mortality. Medina et al. reported that the SLE disease activity index (SLEDAI) score can be useful for evaluation whether the abdominal complication was due to SLE or not . In the series of these authors, 51 patients presented with acute abdomen, the mean SLEDAI score was 15.4 which was higher than that of patients with evidence of active SLE but non-SLE related acute abdomen (SLEDAI score 8.2). (14). These authors reported that a SLEDAI score of below 5 was a strong indicator that the abdominal complication was not due to SLE. The SLEDAI score was 24 in our patient.

Bowel biopsy from affected patients are is always available and the diagnosis of GI SLE vasculopathy based on pathology can be difficult as well. Clinical symptoms, laboratory findings, plain radiography and bowel contrast studies are also of limited value for the diagnosis of GIS SLE vasculopathy (10). The use of CT for diagnosis of GIS SLE vasculopathy provides very helpful information to compensate for this lack of pathological information. We did not perform bowel biopsy. CT findings that are diagnostic of GI SLE vasculopathy include bowel-wall thickening, target signs, dilatation of intestinal segments, engorgement of mesenteric vessels and increased attenuation of mesenteric fat (10). Abdominal CT studies of our patient revealed dilatation of small and large bowels with wall thickening, ascites in the right upper quadrant, engorgement of mesenteric vessels and increased attenuation of mesenteric fat. An initial CT scan is not only useful to evaluate intra-abdominal vasculitis but also to exclude other intra-abdominal pathologies.

The mortality rate of intestinal vasculitis has been reported as 50-55%, particularly when a patient presents with an acute abdomen, showing the importance of early diagnosis and treatment (13,14).

Immediate and aggressive antiinflammatory immunosuppressive treatment should be initiated as the primary lesion in vasculitis is an occlusion that is inflammatory. We needed to use intravenous cylophosphamide in our patient although we had administered high doses of prednisolone for three days that has been reported to be a successful treatment.

In conclusion, GIS vasculopathy in SLE is a challenging diagnostic and therapeutic problem. It is important to diagnose intestinal vasculitis as a cause of abdominal pain in an SEL patient because of the high mortality potential, although it has a very low incidence. It should be kept in mind that the presence of other features of active SLE strongly suggests that the gastrointestinal symptoms are due to lupus, and abdominal symptoms and signs may be masked in patients who are already on high doses of corticosteroids. A careful history, clinical examination and appropriate use of investigations is the best approach to the evaluation for the GIS vasculopathy of SLE.

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