Lupus cystitis: An unusual presentation of systemic lupus erythematosus

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ABSTRACT

Lupus cystitis is a rare complication of systemic lupus erythematosus (SLE) and occurs in association with gastrointestinal symptoms. This rare disorder has been reported mainly from Japan. We report a 20 year old female who diagnosed as having SLE associated with paralytic ileus and chronic interstitial cystitis. Treatment with intravenous methylprednisolone, cyclophosphamide pulse therapy followed by oral prednisolone and azathioprine led to amelioration of manifestations. Later she developed lupus nephritis which was treated with mycophenolate mofetil.

Key words: Chronic interstitial cystitis, paralytic ileus, systemic lupus erythematosus

Introduction

Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by diverse clinical manifestations involving various organs systems and production of antinuclear antibodies (ANA). It may involve joint, skin, kidney, lung, heart, vascular system, gastrointestinal tract, central and peripheral nervous system and sometimes the bladder.

Interstitial cystitis can occur by itself or in conjunction with autoimmune diseases. Symptoms include dysuria, frequency, urgency and suprapubic pain. Repeated symptoms of urinary tract infection which do not show actual infection on testing suggest interstitial cystitis. It is most often diagnosed by cystoscopy (bladder examination under anesthesia) in which typical findings are low bladder capacity, Hunner's ulcer and petechial hemorrhages.

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We report an unusual presentation of SLE as lupus cystitis with paralytic ileus, who later developed lupus nephritis.

Case Report

A 20 year old female student presented in 2008 with features of recurrent episodes of cramping periumbilical abdominal pain, vomiting and constipation. Abdominal ultrasonography (USG) showed distended tubular appendix with a small amount of free fluid in the peritoneal cavity and focal wall thickening of bowl loops. A diagnosis of sub-acute appendicitis and colitis was made and appendicectomy was carried out. Histopathology examination revealed lymphoid hyperplasia of appendix. She recovered well in the postoperative period but pain again appeared. Straight Xray and USG of the abdomen showed features of sub acute intestinal obstruction and free fluid in the peritoneal sac. Ascitic fluid aspiration in November 2008 showed low serum ascitic fluid albumin gradient fluid with lymphocytic predominance. At this time she was treated with antitubercular drugs (rifampicin, isoniazid, ethambutol, pyrazinamide) and steroid from December 2008 to May 2009. She remained asymptomatic for 3 months following completion of therapy. Thereafter, abdominal pain recurred which was associated with vomiting and constipation. Upper gastrointestinal endoscopy, colonoscopy, bariummeal follow through and small bowel enema were normal.

Pain continued and she developed new symptoms such as arthralgia of small joints of hands and feet, Raynaud's

phenomenon, proximal muscle weakness, rash behind the left ear, photosensitivity, low grade intermittent fever, increased severity of abdominal pain and vomiting, and urinary frequency. On examination, she had mild pallor, cervical lymphadenopathy (2 cm × 1 cm, firm, mobile, discrete), oral ulcers and nonscarring alopecia with scaly erythematous discoid rash around left ear. On systemic examination, she had mild abdominal distension, diffuse tenderness all over abdomen, shifting dullness with bilateral tender renal angle and palpable left kidney.

Investigational workup showed a hemoglobin of 8.3 g/dl, erythrocyte sedimentation rate (ESR) of 38 mm in the first hour, a total leukocyte count of 8800/mm^3 with normal differential count, platelet count of 2.1 lakh/mm^3. Serum creatinine was 0.9 mg/dl with normal metabolic parameters and liver function test. Urinalysis showed Alb ++, without any active sediments. 24 h urine protein quantification was 2.08 g. Mantoux test, sputum for acid fast bacilli (AFB), tuberculosis polymerase chain reaction of whole blood, and IgM and IgG enzyme linked immunosorbent assays were negative. Lymph node biopsy revealed reactive hyperplasia. Serum ANA (Hep2) was 6.60 (strongly positive). Direct Coomb's test was positive with decreased C3 (38.90 mg/dl). Anti-double stranded deoxyribonucleic acid (dsDNA) was positive in significant titer. Contrast enhanced computed tomography of the abdomen did not reveal any mesenteric ischemia and any obvious gut abnormality. Repeat USG revealed distended gut loops with fluid sediment and thickened bowel wall, bilateral hydroureteronephrosis and free fluid in the peritoneal cavity. Intravenous ureterography revealed bilateral hydroureteronephrosis, and contracted bladder without any luminal obstruction. Urine was negative for AFB.

Figure 1 Intravenous Ureterography (IVU) showing bilateral hydroureteronephrosis, contracted bladder without any luminal obstruction.

Cystoscopy revealed small bladder with hyperemic mucosa. Histopathological examination [Figure 2] showed widespread edema in submucosal tissue with infiltration of mononuclear cells consistent with cystitis.

Patient was diagnosed as a case of lupus cystitis. She was treated with intravenous methylprednisolone and cyclophosphamide pulse therapy every 14 days for six cycles. Methylprednisolone had been given as 1 g/day for 3 days and cyclophosphamide (500 mg/day) for 1 day in each cycle. In between oral prednisolone was given. After six cycles patient was completely symptom free. Hydroureteronephrosis completely disappeared and 24 h urinary protein became normal. Thereafter patient was given azathioprine 100 mg/day as maintenance therapy. On follow up, her proteinuria decreased to 300 mg/24 h.

In February 2013, her proteinuria increased to 1.5 g/day. At that period her serum anti dsDNA titer was more than 1000 IU/L. Serum C3 and creatinine were 23.45 mg/dl and 0.8 mg/dl respectively. Hemoglobin was 10.2 g/dl, ESR 64 mm in the first hour with total leukocyte count 9600/mm^3; platelet count 3.8 lakhs/mm^3. USG showed normal sized kidneys and normal collecting system. Kidney biopsy was done. Out of 17 glomeruli, 2 showed segmental endocapillary proliferation with neutrophilic infiltrations, and thickened basement membranes. No necrotizing lesions, crescent, tubulointerstitial or vascular pathology were noted in the biopsy specimen. Immunofuorescence showed IgG (+3), IgM (+1), C3 (+3), C1q (+2) in the mesangium and capillary walls.

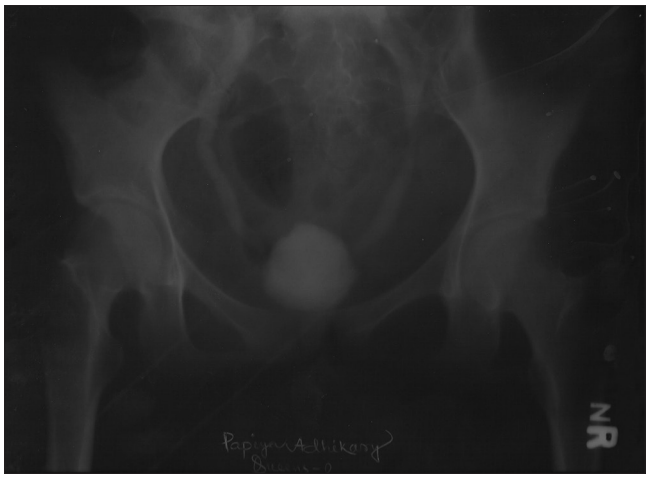

Figure 1: Intravenous ureterography showing bilateral hydroureteronephrosis, contracted bladder without any luminal obstruction

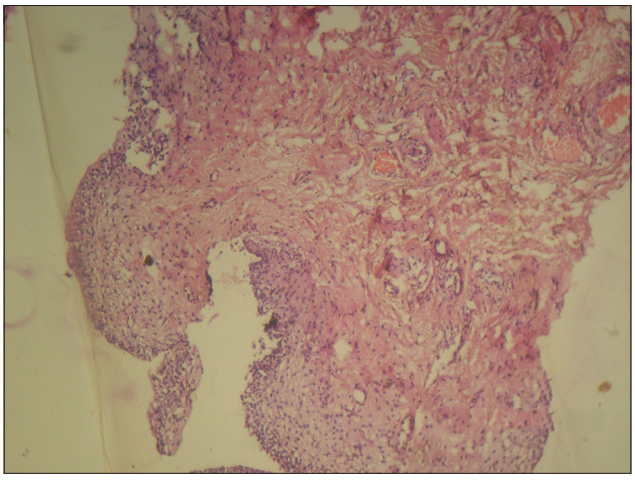

Figure 2: Cystoscopic guided biopsy specimen histopathology showing submucosal tissue edema with mononuclear cell infiltration

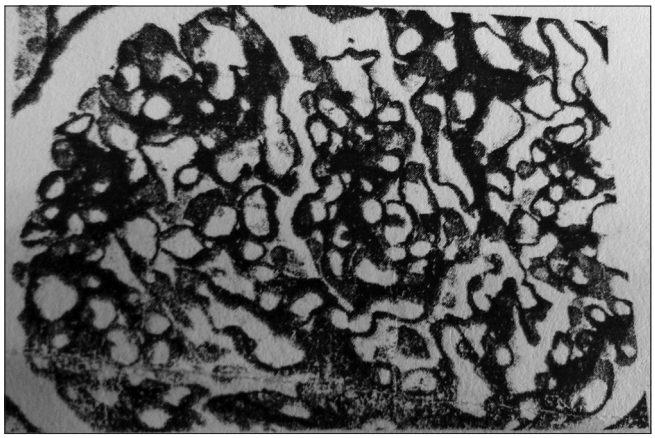

Figure 3: Kidney biopsy specimen (with periodic acidSchiff, silver, trichrome staining) showing two glomeruli with segmental endocapillary proliferation with thickened basement membrane and pinhole lesion

Figure 3 kidney biopsy specimen (with PAS, silver, trichrome staining) showing two glomeruli with segmental endocapillary proliferation with thickened basement membrane and pinhole lesion.

We started mycophenolate mofetil 1000 mg twice a day with regular monitoring of serum creatinine, potassium, C3, C4, anti-dsDNA titer which suggested improving course of the patient. On July, 2013 her 24 h urine proteinuria was reduced to 0.85 g/day. Patient is still on mycophenolate maintenance therapy and on regular followup.

Discussion

In our patient, the diagnosis of SLE was based on the both clinical manifestation and investigation. Interstitial cystitis was diagnosed on the basis of symptoms urinary frequency and cystoscopic finding of the bladder mucosa, which revealed small bladder with hyperemic mucosa and marked edema.

SLE cystitis is characterized by suprapubic pain, urgency, frequency and nocturia, reduction of the urinary bladder volume and hydroureteronephrosis with or without abnormal urine sediment and sterile urine.

Although the typical clinical manifestation of urinary tract in SLE is glomerulonephritis; interstitial cystitis has been reported.[1,2] An immune complex pathogenesis was suggested on the basis of immunoglobulin and complement deposition in the bladder vessels. A strong association of chronic interstitial cystitis and disease of the intestinal tract has been reported.[3] Abdominal pain, nausea, vomiting are noted in almost all patients with SLE cystitis.[3-5] Moreover, intestinal pseudoobstruction, bowel perforation, malabsorption, paralytic ileus with hydroureteronephrosis are described as well.[5,6] Common auto-antigens, present in both bladder and gastrointestinal wall, might play a role.[7,8] The pathogenesis of lupus cystitis is related to immune complex mediated vasculitis[2,6,9] and smooth muscle dysmotility.[2] In contrast to idiopathic cystitis, lupus cystitis is frequently associated (up to 92% of the cases) with hydroureteronephrosis,[10] which is usually due to distal ureteral obstruction at the uretrovesical junction because of inflammation and edema of the bladder and to detrusor muscle spasm secondary to inflammation.[11]

In our patient, initial manifestation were recurrent gastrointestinal symptoms such as abdominal pain, vomiting and constipation, which improved initially after oral steroid therapy, only to reappear after 3 months. Later she developed bladder irritation symptoms with hydroureteronephrosis. Subclinical interstitial cystitis is not rare in SLE patients.[12] Therefore, when a patient with SLE complains of gastrointestinal symptoms, even in the absence of bladder irritation symptoms, lupus cystitis should be suspected. Early diagnosis and treatment may prevent progressive bladder fibrosis, which may result in irreversible hydronephrosis and renal failure.[5,8]

In our patient, we treated her with pulse methylprednisolone and cyclophosphamide. She responded very well with gradually improving gastrointestinal symptoms, later which completely subsided. Her hydroureteronephrosis were also completely reversed to normal, evidenced by abdominal USG after completion of treatment. Increased proteinuria on subsequent visit with biochemical investigations suggestive of flair raised the suspicion of associated lupus nephritis, which was confirmed by kidney biopsy. Treatment with mycophenolate improved proteinuria with relief of symptoms.

In summary, we have presented a case of lupus cystitis with nephritis, an uncommon manifestation of SLE mainly reported in South Asians. This condition responds well to combination therapy with corticosteroid and cyclophosphamide. We hope that this report will draw our colleague's attention to the protean manifestation of SLE and its treatment.

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