Gastrointestinal Manifestations of Systemic Lupus Erythematosus

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ABSTRACT

Gastrointestinal symptoms are common in patients with systemic lupus erythematosus (SLE) and can be due to primary gastrointestinal disorders, complications of therapy or SLE itself. In this case report, we describe three different presentations and causes of gastrointestinal complaints in patients with SLE. Diagnostic and management problems are discussed.

Keywords: Systemic lupus erythematosus, bowel vasculitis, chronic intestinal pseudo-obstruction

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INTRODUCTION

Systemic lupus erythematosus (SLE) is a multisystem autoimmune inflammatory disease of unknown aetiology with a variety of presenting features and manifestations. It is characterised by exacerbation and remissions. Gastrointestinal symptoms such as anorexia, nausea, vomiting, diarrhoea and abdominal pain are common in the course of SLE and occur in up to 50% of cases[1-3]. Abdominal complaint in patients with SLE may pose difficult diagnostic challenge with the possible differential diagnoses of primary gastrointestinal disorders, complications of SLE on the gastrointestinal tract and side effects of therapy for SLE. We report three gastrointestinal complaints caused by different SLE associated complications on the gastrointestinal tract.

CASE REPORTS

Case 1

A 40-year-old Chinese lady was admitted with abdominal pain, nausea, vomiting and diarrhoea. She had been diagnosed to have SLE two years previously after her presentation with fatigue and joint pain and further investigations showed strongly positive ANA and anti-dsDNA. There was no visceral, renal or neurological involvement. Immunosuppression was started with oral steroid which brought the disease into remission and repeat anti-dsDNA six months later was negative.

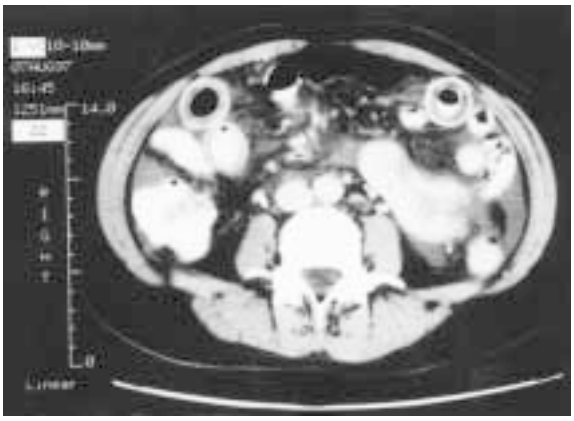

Fig. 1 Abdominal CAT scan showing small bowel vasculitis with oedema of the bowel wall.

She remained well for two years without any immunosuppressive therapy until her admission with epigastric pain and watery diarrhoea which was non-bloody. Clinical examination did not reveal any pallor, jaundice, vasculitic rashes or arthropathy. Abdominal examination did not reveal any distension or signs of peritonism.

Full blood count, liver and renal function tests were all within normal limits. CH50, C3, C4 were however depressed and ESR was 58 mm/hour. ANA was 1/400 with homogenous pattern while anti-dsDNA, anti-cardiolipin, ANCA and lupus anticoagulant were negative. Stool culture, leucocytes and occult blood were all negative. Plain abdominal radiograph and gastroscopy did not show any abnormality.

Abdominal CAT scan showed thickened small bowel loops with contrast enhancement consistent with small bowel ischaemia (Fig. 1). There was also ascites and interloop fluid collection. A barium meal and follow through did not show any mucosal lesions or intestinal obstruction. Duplex scan of abdominal vessels showed patent abdominal aorta, coeliac axis, superior and inferior mesenteric artery.

Diagnosis of lupus vasculitis involving the small bowel was made and the patient was treated with intravenous hydrocortisone followed by oral prednisolone. Her abdominal symptom resolved two weeks after steroid therapy. Prednisolone was

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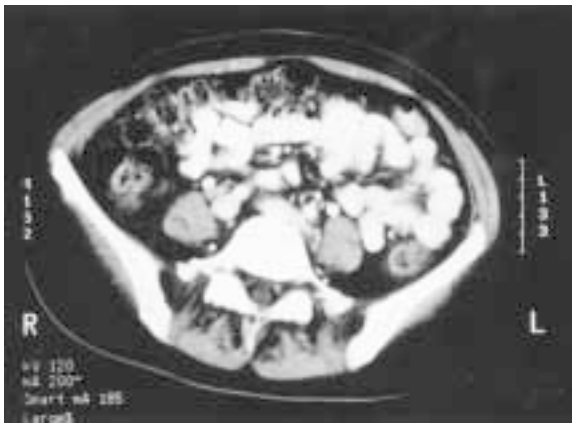

Fig. 2 Abdominal CAT scan of the same patient as in picture 1 with small bowel vasculitis. This CAT scan showed resolution of the oedema of bowel wall after steroid therapy.

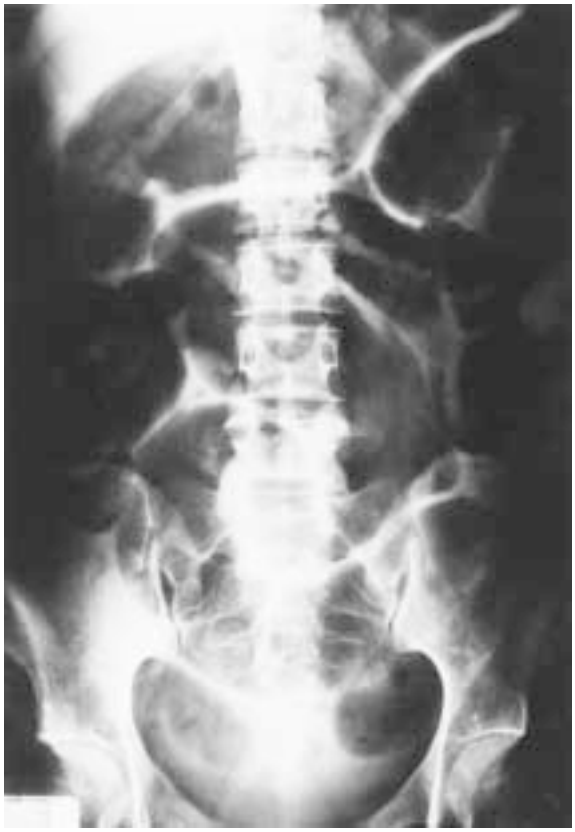

Fig. 3 Plain abdominal radiograph showing dilated intestinal loops in a patient with SLE complicated by pseudo-obstruction.

successfully tapered down and repeat CAT scan of abdomen two months later showed resolution of the small bowel oedema (Fig. 2).

Case 2

A 22-year-old Chinese lady presented with lower abdominal pain, diarrhoea and weight loss of 7 kg over the preceding three months. She looked cachetic and had alopecia and a distended abdomen.

Routine investigations showed normocytic normochromic anaemia with haemoglobin of 10.9 g/dl and ESR of 85 mm/hour. Renal functions and coagulation profiles were within normal limits. Liver function tests were normal apart from a low albumin of 30 g/L. ANA was positive at 1/640 with homogenous pattern, anti dsDNA was positive and C3 and C4 were both low. Twenty-four hour urinary collection showed proteinuria of 6.8 g/day. An abdominal radiograph showed dilated small bowel loops with air-fluid interface (Fig. 3). Abdominal CAT scan showed ascites and thickened small bowel loops with mixed attenuation of the mesenteric fat. There was concomitant dilated ureter and distended pelvi-calyceal system. Urinary bladder was contracted with irregular walls suggestive of tuberculosis cystitis. Intravenous urogram confirmed distended pelvi-calyceal and ureteric system with no obvious evidence of obstruction. Flexible cystoscopy showed mild cystitis and biopsy was negative for tuberculosis or malignancy. Small bowel enema showed dilated small bowel loops with markedly thickened wall; delayed transit time was noted. Diagnostic laparoscopy was unrevealing and ascitic fluid did not reveal acid fast bacilli on either smear or culture.

She was diagnosed to have SLE with intestinal pseudo-obstruction, obstructive uropathy and nephrotic syndrome. She was treated with a course of steroid and empirical anti-tuberculosis therapy for the possibility of superimposed tuberculous infection of urinary bladder and peritoneum. For the following six months, she required recurrent admissions with constipation, abdominal pain and distension consistent with chronic intestinal pseudo-obstruction. There was also progressive weight loss with body mass index of 15.7 (weight 30 kg) and serum albumin of 23 g/L. Repeat CAT scan showed persistently dilated small bowel loops after the initiation of prednisolone though there was improvement in the dilatation of the urinary tracts. Xylose absorption was decreased with urinary xylose of 1.3 mmol/L (5.3 - 10) at two hour and 6.2 mmol/L (10.0 - 17.3) at five hour. In view of the recurrent admissions with intestinal pseudo-obstruction and her poor nutritional state, she was placed on home total parenteral nutrition (TPN). Azathioprine was subsequently introduced as a steroid sparing agent.

After having home TPN for six months, both her weight and serum albumin increased to 44 kg and 42 g/L respectively. Home TPN was successfully phased out and her nutritional state has been well maintained with enteral nutrition for more than two years. Her SLE remains quiescent with long term azathioprine 50 mg and prednisolone 12.5 mg daily. However, she remains to suffer from chronic constipation despite regular use of laxatives and requires repeated hospital admission for rectal enema.

Case 3

A 24-year-old lady was admitted with generalised abdominal pain that was associated with vomiting and diarrhoea. She had been diagnosed to have SLE two years previously after her presentation with nephrotic syndrome. Serological markers at the time of diagnosis showed positive ANA, anti-dsDNA and decreased C3, C4 and CH50. She had been on immunosuppression with azathioprine 150 mg and prednisolone 10 mg daily. Investigations performed one week previously at outpatient review indicated quiescent SLE with normal complement levels and ESR of 34 mm/hour.

On examination, she looked cushingoid. Abdominal examination showed abdominal guarding with rebound tenderness. Bowel sound was absent. Erect chest radiograph did not show any free air under the diaphragm. She was diagnosed to have acute abdomen and emergency laparotomy was performed. The findings at laparotomy showed slightly turbid ascitic fluid and small bowel looked normal. Ascitic fluid culture did not reveal any growth. Post-operative period was uneventful and the dose of prednisolone was increased to 40 mg daily. She was discharged home well seven days after her laparotomy with the diagnosis of sterile serositis. She remained well at outpatient review four weeks later.

DISCUSSION

Our three patients presented with abdominal symptoms associated with different complications secondary to SLE. The cause of abdominal pain in the first patient was due to small bowel ischaemia secondary to vasculitis. The second patient presented with chronic intestinal pseudo-obstruction, a rather rare complication of SLE and the last patient presented with acute abdomen which was subsequently found to be sterile peritonitis from serositis.

Abdominal pain is a common symptom in SLE and it can be due to primary gastrointestinal disorders such as gastritis, peptic ulcer disease, pancreatitis and biliary tract disease. Other causes of abdominal pain are due to complications of the disease itself upon the gastrointestinal tract. Small and large bowel ischaemia due to either vasculitis or vascular occlusion associated with the antiphospholipid syndrome and peritonitis from serositis can manifest in abdominal pain and acute abdomen[1,3,4]. Intestinal vasculitis and serositis may present with severe abdominal pain and may masquerade as an acute abdomen leading to exploratory laparotomy[3,5].

The exact incidence of lupus vasculitis in the gastrointestinal tract is hard to determine but literature review indicates that clinically apparent bowel vasculitis occurs in about two percent of SLE patients[6]. However, the incidence may be higher as the condition may be clinically quiescent. Si-Hoe et al reported small bowel thickening in 30 out of 54 SLE patients who underwent abdominal CAT scan for a variety of gastrointestinal complaints[7]. It is the most feared abdominal manifestation as delayed recognition of this life-threatening problem may result in fatal bowel infarction and perforation. The outcome of intestinal perforation secondary to lupus vasculitis is extremely poor. In one series of 24 adult SLE patients with bowel perforations, two-thirds of the patients died[3] and another study showed mortality rate of 80%[4].

Other causes of mesenteric vascular insufficiency need to be considered before diagnosis of lupus vasculitis can be made with certainty. Thrombosis of mesenteric vessels associated with the anti-phospholipid syndrome can give rise to mesenteric ischaemia and bowel infarction. Other thrombo-embolic causes are valvular heart disease, cardiac arrhythmias and illicit use vasoconstrictive drugs such as cocaine[8].

It is important to make early and accurate diagnosis of mesenteric vasculitis as timely administration of steroid therapy will prevent bowel infarction. In patients who present with clinical picture that resembles 'acute abdomen', prompt diagnosis of mesenteric vasculitis as the cause of the clinical symptoms should prevent unnecessary exploratory laparotomy. However, the diagnosis of intestinal vasculitis is difficult to make as frequently only the small bowel is involved and it is inaccessible with standard endoscopes. Studies have shown that symptoms[9] and plain radiography[4] are of little diagnostic value in identifying patients with intestinal vasculitis. Mesenteric angiogram is usually not useful because the typical pathological changes are seen in the smaller vessels rather than the medium sized vessels of the mesentery[10,11].

CAT scan has been recently shown to be a promising investigation tool in the evaluation of gastrointestinal vasculitis. It offers direct observation of the thickness of intestinal wall and information about the mesentery and the mesenteric vessels[12]. Characteristic CAT scan appearance of small bowel vasculitis is of small bowel thickening with prominence of the mesenteric vessels[7,12]. However, small bowel thickening is not a specific finding for intestinal vasculitis as it may also be associated with hypoalbuminaemia, inflammatory bowel disease and gastroenteritis. Therefore small bowel series should be performed to exclude Crohn's disease and small bowel lymphoma. Nevertheless, the presence of small bowel thickening on CAT scan in a SLE patient should heighten the suspicion of small bowel vasculitis.

Vasculitis in SLE may involve any part of the gastrointestinal tract from oesophagus to colon though there is a tendency for the vasculitis to affect the distribution of superior mesenteric artery i.e. small bowel[13]. The severity of colonic involvement resulting from vasculitis may vary from mild colitis with diarrhoea, mucosal ulceration with haemorrhage, to intestinal infarction and perforation. Although less common than the involvement in the small bowel, colonic ulcers and perforation of the transverse colon, splenic flexure, sigmoid colon and rectum in SLE patients have been documented[14]. Acute pancreatitis from vasculitis have also been reported[11]. Gastrointestinal manifestation with vasculitis tends to occur during the flare or impending flare of the underlying disease. As shown by our first patient, she had not complied with her immunosuppressive therapy due to her clinical well being and at her presentation with gastrointestinal vasculitis, her complements levels were suppressed and ESR was elevated indicative of relapse of her SLE.

Immunosuppression with high-dose corticosteroids is the main therapy for lupus mesenteric vasculitis. Pulse therapy with intravenous cyclophosphamide may occasionally be required[6]. Our patient showed excellent response to intravenous hydrocortisone followed by oral prednisolone with resolution of the small bowel oedema as shown by her subsequent abdominal CAT scan.

Our second patient showed complications of chronic intestinal pseudo-obstruction (CIPO) and obstructive uropathy with cystitis. CIPO is a clinical syndrome of unknown pathophysiology and is characterised by ineffective intestinal propulsion. It can be caused by involvement of the visceral smooth muscle, the enteric nerves, or the visceral autonomic nervous system. CIPO is a rare complication of SLE[15]. In a series of five patients, Perlemuter et al[15] reported that the presenting symptoms were nausea, vomiting, diarrhoea or constipation. The majority of the patients had intestinal dilatation on plain abdominal radiographs. CIPO could be the presenting feature that led to diagnosis of SLE or it could occur as a complication. Gastric scintigraphy showed delayed emptying[15]. The manometric abnormalities in the small bowel were of intestinal hypomotility with reduced amplitude of contractions during phase III and infrequent contractions during phase II of the migrating motor complex (MMC). Similar findings of hypomotility have also been recently reported in patients with systemic sclerosis and related disorders[16]. The underlying cause for CIPO is unknown but postmortem examination on the only patient who died in the series reported by Perlemuter et al[15] showed normal innervation of the bowel wall but there was marked fibrotic process in the muscularis layer. These findings are suggestive of a myogenic type of CIPO. Generally, the cause of CIPO is difficult to establish as full thickness biopsy is required in order to study both the muscles and nerves. However, because the number of surgical interventions should be minimised in patients with pseudo-obstruction, a laparotomy with the sole objective of obtaining a full-thickness biopsy should not be performed to confirm a clinical diagnosis of pseudo-obstruction[17].

Urological manifestations of SLE are uncommon and are often associated with gastrointestinal disorders such as diarrhoea, vomiting, malabsorption, ascites and protein losing enteropathy[18]. CIPO is known to be associated with urological manifestations[19] and this association between cystitis and gut involvement in SLE appears to represent a distinct subgroup with poor prognosis despite aggressive immunosuppression[15,20]. The pathogenesis of lupus cystitis is believed to be due to immune complex mediated vasculitis[18]. The reduced bladder capacity seen in this complication could be due to obtrusor muscle spasm secondary to bladder inflammation. Other urological manifestations include bladder wall thickening and hydronephrosis.

As seen in our patient, corticosteroid may reverse the inflammatory cystitis[21], normalise bladder capacity and ureteric distension[15], and improve small bowel motility[15]. Oral feeding could be resumed and parenteral nutrition could be discontinued in all patients after immunosuppressive therapy[15]. The improvement in small bowel motility could be due to resolution of inflammatory changes in intestinal smooth muscle with immunosuppresive therapy but it would be difficult to confirm this hypothesis histologically without serial biopsies before and after therapy.

Our third patient presented with acute abdomen but during exploratory laparotomy, only ascites related to serositis was found. There was no evidence of bowel perforation or necrosis. Ascites in SLE patients may be related to coincidental nephrotic syndrome[22] but Ko et al showed that ascites was an infrequent finding in nephrotic patients[12]. It is more likely to be due to peritoneal serositis than hypoalbuminaemia of nephrotic syndrome[5,23]. Serositis can develop when SLE is inactive[24]. Similar to vasculitis, ascites and serositis resolves with high dose steroid therapy[12]. As judged from her clinical symptoms and inflammatory indicators, the disease in our third patient was quiescent when she developed her “acute abdomen” from serositis.

It is often difficult to ascertain whether the presentation of ‘acute abdomen’ is due to lupus vasculitis or that of surgical emergencies such as intestinal

perforation[25]. Laparotomy in this patient was carried without pre-operative CAT scan due to the signs of peritonism. The role of CAT scan prior to laparotomy in SLE patients with 'acute abdomen' and clinical signs of peritonism is unclear. It would seem reasonable to treat these patients for lupus associated bowel vasculitis or serositis with immunosuppression if there is no radiological evidence of bowel perforation on CAT scan. Laparotomy could then be undertaken if there is clinical deterioration. With the paucity of definitive tests, careful and repeated clinical assessment and abdominal palpation is required for deterioration as delay in surgery increases rate of mortality and morbidity[25].

Our three patients illustrate some of the myriads of abdominal complaints in SLE. It is important to be aware of intestinal vasculitis in patients with chronic abdominal pain. CAT scan looks to be a promising tool of investigation as the vasculitis commonly affects the distribution of superior mesenteric artery and is thus not easily accessible by standard endoscopic approach. Serositis and ascites can present with abdominal pain and as the presentation mimics acute abdomen, exploratory laparotomy may be carried out in order to exclude abdominal sepsis and intestinal perforation. Though uncommon, CIPO can be either the presenting or complicating features in SLE and if associated with urological involvement, may indicate a more severe course. The small bowel dysmotility is caused by myogenic inflammation. Both urological and bowel dysmotility may be reversible by high dose corticosteroids and parenteral nutrition but the long term outcome of patients with CIPO is unknown.

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