Lupus Enteritis: An Unusual Manifestation of Systemic Lupus Erythematosus

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ABSTRACT

Though gastrointestinal symptoms are common in Systemic Lupus Erythematosus (SLE), lupus enteritis remains a rare manifestation of the disease. The clinical picture may be non-specific but should be considered in patients with abdominal pain, as this disease entity can progress to intestinal necrosis and perforation if left untreated. This is a case report of a 37-year-old female who had multiple hospital admissions for abdominal pain, was diagnosed with lupus enteritis and showed excellent response to methylprednisolone.

CASE REPORT

SLE is a chronic inflammatory autoimmune condition with multi-organ involvement that is diagnosed by the European League Against Rheumatism (EULAR) and the American College of Rheumatology (ACR), EULAR/ACR criteria[1]. The first description of gastrointestinal symptoms of SLE in medical literature was in 1895 by Sir William Osler[2] and over the years, the most predominant of these symptoms were found to include nausea, vomiting, anorexia and abdominal pain[3]. Lupus enteritis, though not part of the EULAR/ACR diagnostic criteria, has been defined by the British Isles Lupus Assessment Group (BILAG) 2004 as either a vasculitis or inflammation of the small bowel with supportive imaging and/or biopsy findings[4]. However, the disease entity has been shown to affect anywhere along the gastrointestinal tract, from the oesophagus to rectum.

A 37-year-old female presented to Port-of-Spain General Hospital (POSGH) for recurrent episodes of abdominal pain, vomiting and diarrhoea. Her past medical history includes Systemic Lupus Erythematosus (SLE) diagnosed at the age of 12 with positive Rheumatoid Factor (RF) and antinuclear antibody (ANA) but had a negative double stranded DNA antibody (anti-dsDNA) at that time. She has been currently maintained on prednisolone 15 mg daily due to intolerance for azathioprine (AZA), mycophenolate mofetil (MMF) and methotrexate (MTX). Over a four-year period between ages 22 to 26, she has had multiple admissions to different tertiary institutions and specialties for this presentation. On each occasion, however, she was managed conservatively. During this period as well, an oesophagogastroduodenoscopy was performed with gastric and duodenal biopsies which

yielded no abnormality. Prior to her presentation to POSGH, she was hospitalized at San Fernando General Hospital for similar complaints. A lupus flare was diagnosed and was subsequently managed with prednisolone 40 mg once daily, intravenous fluids, anti-emetic dimenhydrinate 50 mg pro re nata (PRN) up to thrice daily and antibiotics. It was during this hospital admission where an abdominal computerised tomography (CT) scan was done, which showed jejunal thickening with inflammatory changes. Following this imaging, she was subsequently given outpatient gastroenterology clinic follow-up but defaulted; a diagnosis could not be ascertained at that time.

Her current presentation to POSGH was for abdominal pain, bilious vomiting greater than 10 times daily and non-bloody diarrhoea Bristol stool type 7 which was ongoing for over a month up to ten episodes per day. There was no elicited travel history or laxative use. Her current medication use was prednisolone.

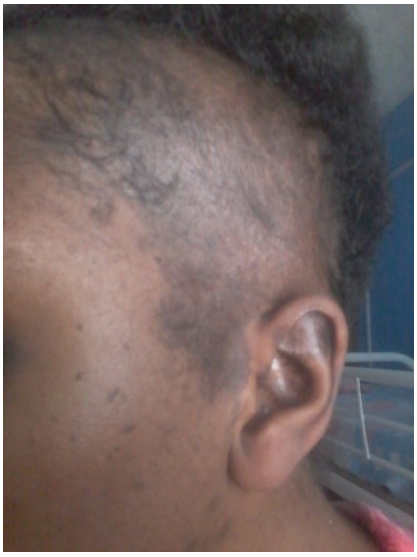
Admission vitals showed a blood pressure of 115/75 mmHg, pulse rate 105 beats per minute, respiratory rate 18 breaths per minute and temperature 36.7ºC. On physical exam, her mucous membranes were dry and skin turgor was decreased. Abdominal exam yielded generalized tenderness but there was no guarding or rebound tenderness and bowel sounds were normal. Of note, the patient had scarring alopecia shown in picture 1, swan neck hand deformities shown in picture 2 and a single oral aphthous ulcer, but the rest of her examination was unremarkable. SLE Disease Activity Index (SLEDAI) score of 6 on was in keeping with moderate disease activity.

Lab investigations yielded a haemoglobin (Hb) of 13.2 g/dl, white blood cell count 5.5 $x10^9$/L, platelet 233 x 10^9/L and a blood urea nitrogen (BUN) 12 mg/dl and creatinine 0.82 mg/dl with a C-reactive protein 8.52 mg/L (normal <5mg/L). Erythrocyte sediment rate (ESR) was 66 mm/1^{st} hour with normal liver function tests, normal amylase and lipase, a negative urine pregnancy test and a urinalysis with no haematuria or proteinuria. She was commenced on intravenous fluids, hydrocortisone 100 mg IV every 8 hours, anti-emetics and a nasogastric tube was inserted. Stool cultures were not collected as her diarrheal symptoms had quickly resolved.

Chest and abdominal X-rays were unremarkable. Despite her current management, abdominal pain and vomiting persisted after 3 days which was bilious in nature. Subsequently, an abdominal ultrasound was performed which showed mild to moderate free fluid but with normal liver, gallbladder, pancreas, spleen, and kidneys. Fluid in the pouch of Douglas and surrounding the ovaries prompted a pelvic ultrasound which was unremarkable apart from ascites. With ongoing abdominal pain and vomiting, a CT abdomen was done which showed moderate volume ascites with oedematous and thickened duodenal and jejunal walls up to 0.6cm, demonstrating the "target sign" (Figures 1 and 2).

Given the clinical scenario with the CT findings, this patient was ultimately diagnosed as lupus enteritis. After commencing pulsed methylprednisolone 1 g intravenously

Picture 1 Scarring Alopecia



Picture 2 Swan neck deformity

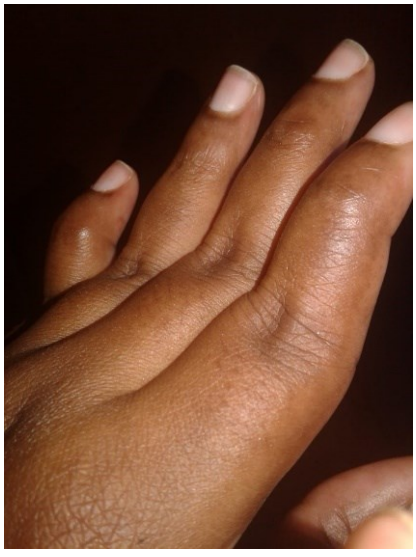


Figure 1 Small bowel wall oedema

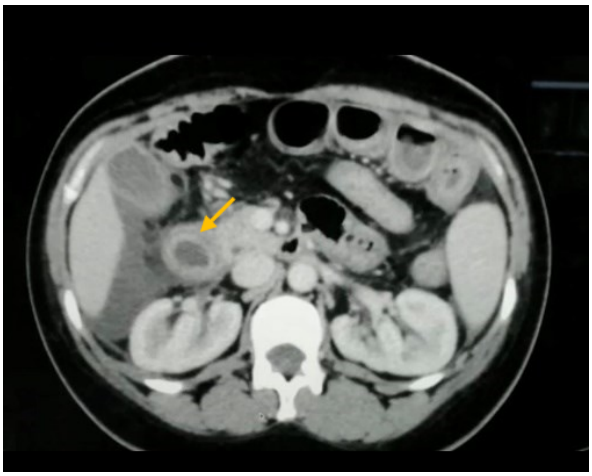
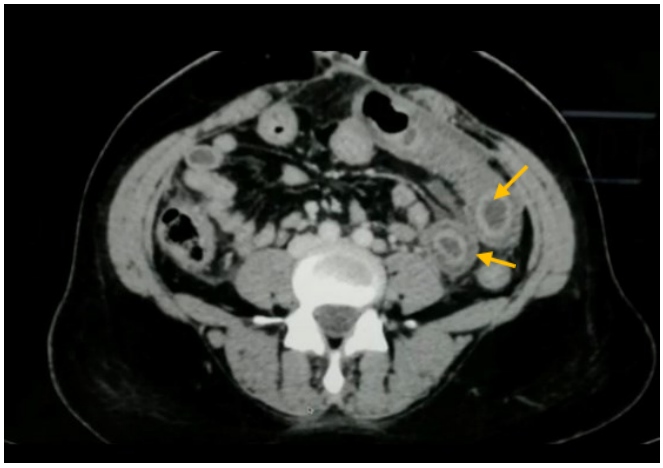


Figure 2 "Target sign"



daily for 3 days, her abdominal pain and vomiting completely resolved. The nasogastric tube was removed as she was tolerating oral intake. She was then discharged on oral prednisolone 60 mg daily with proton pump inhibitor coverage with a follow-up at rheumatology and gastroenterology clinics. Currently, the patient has remained symptom free for over 12 months with no further flares of her SLE.

DISCUSSION

Lupus enteritis complicates 0.2 to 5.8% of SLE patients[5] with a high female preponderance of up to 85% where the median age of onset is 34 years and occurs on average 34.3 months after SLE is diagnosed. This contrasts the highlighting case presentation whereby there were recurrent hospitalizations between ages 22 to 26 suggesting a much earlier onset of the disease entity. The proposed mechanism of lupus enteritis involves immune complex deposition with complement activation and subsequent endothelial cell and platelet activation proceeding to thrombotic events[6]. Intestinal involvement is largely confined to the jejunum and ileum, 83% and 84% respectively, followed by the colon (19%), duodenum (17%) and rectum (4%)[7]. The low incidence of rectal involvement is thought to be due to its collateral circulation as opposed to the jejunum and ileum which has end artery blood supply thus prone to ischemic injury. The frequency of the affected intestinal segments mentioned mimics our case whereby there were involvement of the jejunum and duodenum.

Janssens et al showed that the most common symptoms of lupus enteritis were focal or diffuse abdominal pain (97%), ascites (78%), nausea (49%), vomiting (42%), diarrhoea (32%) and fever (20%)[7], all of which were present in this patient except for fever. Abdominal contrast CT is considered the gold standard for diagnostic imaging of lupus enteritis whereby 98% of images show bowel wall oedema and 71% percent demonstrate abdominal bowel wall enhancement, termed the "double halo" or "target sign". Another 71% of images can show engorgement and increase visibility of the mesenteric vessels, termed Comb's sign. This target-sign was also mentioned by Byun et al[8] which has been demonstrated in the imaging study done on this patient.

Laboratory tests used as part of the diagnostic evaluation of lupus enteritis include ANA which has been positive in 92% of cases along with a positive dsDNA antibody in 74% of cases. Anti RNP, anti-SSA, and anti-Sm was positive in 28%, 26%, and 24% respectively[6]. Interestingly, the average C-reactive protein level was found to be 2.0mg/dl in the study population, unlike this case where the value was above 8 mg/dL. Furthermore, the presence of lymphopenia and hypocomplementemia has been shown to correlate with the incidence of lupus enteritis[9, 10]. It has become imperative the screen patients with lupus enteritis for concomitant nephritis as it has been observed to coexist in 65% of cases[11]. Screening was negative in this case as evident by a normal urinalysis in addition to renal function tests.

Given this patient's multiple hospital admissions between the ages 22 to 26 for abdominal pain along with her

recent admission to the San Fernando General Hospital, one can speculate the possibility of recurrent lupus enteritis. Lower cumulative dosage of prednisolone has been associated with a high recurrence rate of lupus enteritis of up to 23%[12] and since she has demonstrated intolerance to various disease-modifying anti-rheumatic drugs (DMARDS) she would have pen ultimately been on the lowest possible dosage of prednisolone to avert its long-term side effects, thus reemphasising this observation.

Given the lack of prospective studies on the treatment of lupus enteritis but an observed high steroid responsiveness, corticosteroids, either intravenous methylprednisolone or oral prednisolone, appear to be the first line treatment of the disease[7, 11] with preference to intravenous administration as there may be reduced absorption of oral medications[13]. Complete bowel rest is also advocated in the management of this condition. Additional immunosuppression with AZA or cyclophosphamide (CYC) has had success in some case reports[14] with one successful case report using the Euro-Lupus regime[15]. In resistant and recurrent forms, cyclophosphamide, MMF, AZA and rituximab have been successfully used.

This case brings to the forefront management dilemmas. Given intolerance to AZA and MMF, one can argue that after complete bowel rest and resolution of abdominal symptoms, reintroduction of these drugs could be done at a lower dose and up titrated in the absence of gastrointestinal side effects. We therefore recommend treatment to be individualized on a case-by-case basis, looking at benefits and risk with consideration of additional immunosuppression in concomitant organ involvement and pregnancy wishes.

CONCLUSION

Lupus enteritis, though a rare manifestation, should be considered in any SLE patient presenting with gastrointestinal symptoms where there should be a low threshold for CT imaging. The condition is typically steroid responsive and early diagnosis and treatment can affect morbidity and mortality. A local and regional registry should be established for SLE patients as it can add to medical literature and have an impact on management of the disease and its many complications.

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