Severe lupus enteritis, diagnosis and treatment journey: case report

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Abstract

Gastrointestinal system involvement is reported in a patient diagnosed with severe Systemic Lupus Erythematosus (SLE). Lupus enteritis is quite uncommon and characterized by presence of abdominal pain, nausea, vomiting and diarrhoea. The main pathological insult arises from inflammation of mesenteric vascular territories. Diagnosis of lupus enteritis is dependent basically on clinical, biochemical, serological and radiological features and one needs to rule out other differentials like infectious process or medications' side effects. The most critical step in management is to exclude acute surgical condition followed by supportive measures, antibiotics and immunosuppressive drugs. In this report, we will discuss a case of a patient diagnosed with SLE through the gate of lupus enteritis.

Keywords: Systemic Lupus Erythematosus, Lupus Enteritis, Gastrointestinal system, Female, Saudi Arabia

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Introduction

Systemic Lupus Erythematosus (SLE) is considered an immune complex mediated disorder characterized by relapsing and remitting phenomenon with an inflammatory autoimmune background[1]. It usually affects young, child bearing age women with a 9:1 female to male ratio[2].

SLE can attack different organs resulting in devastating complications if not diagnosed early and treated according to the organ affected[3]. Gastrointestinal complaints are frequently noticed in 40-60% of lupus patients and these symptoms could be related to either side effects of medications or attributed to infectious triggers or severe lupus activity. Lupus – related gastrointestinal symptoms occur in about 42.5% of patients diagnosed with lupus and there is a wide spectrum of manifestations that might present and affecting the prognosis of disease[4]. In this case report, we will describe a young female patient who presented with mainly gastrointestinal (GI) manifestations and labeled at the end as a case of SLE.

Case report

The patient was a 21 year old female, not known to have any medical illness before, she presented to the Emergency Room (ER) Department at King Fahad Medical City in Riyadh (KFMC) with a history of: diffuse abdominal pain that was moderate in severity, nausea and vomiting. The symptoms made the patient unable to tolerate oral food and liquids for the last four days. She was also complaining of diarrhoea which was watery in nature, moderate to large amount, the diarrhoea was not associated with fresh blood. Upon admission in (ER), the patient's vitals were; blood pressure 138/82, her heart rate 108, respiratory rate 19 and she was not febrile with core temperature 36^0C.

The patient was admitted under the internal medicine team for rehydration and further work-up. There was no history suggestive of any systemic symptoms like fever, fatigability or weight loss. No history of any cardiovascular or respiratory symptoms. Other systemic review including family history was completely unremarkable except for arthralgia which started two months earlier, the arthralgia was not associated with morning stiffness, not associated with certain activities and did not hinder the patient from carrying out her usual activity.

During the patient's admission, we were consulted for our opinion regarding her GI manifestations and arthralgia. Upon examination, the patient looked pale and sick with acceptable vital signs except for a high blood pressure reading of 150/92. No rashes were observed on the patient's face or body, she had no oral or nasal ulcers and there was no synovitis. Abdominal examination was performed and the patient had diffuse abdominal tenderness with positive bowel sounds. All other organ examinations were unremarkable.

Figure 1: This is CT- scan of abdomen and pelvis with contrast done for the patient upon her presentation to ED department: The blue arrow is showing bowel wall thickening indicative for inflammatory process while the arrow in the black colour showed an area of free fluid due to general pathological condition (Infections/Inflammatory process are differential diagnoses)

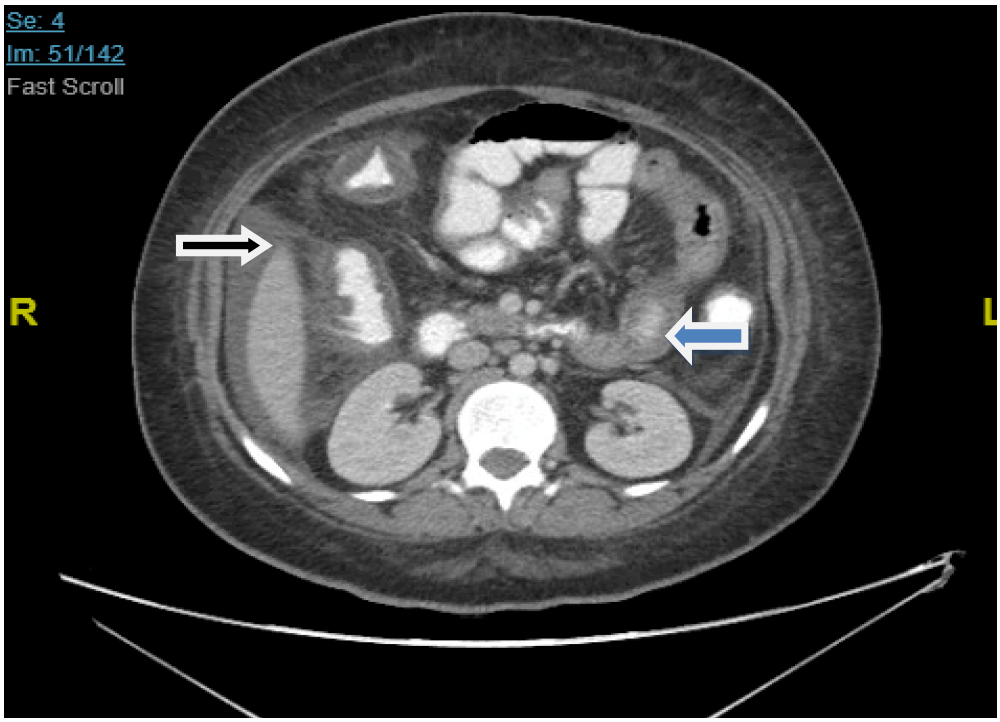

Table 1: Laboratory investigations done to our patient since her presentations and during the follow-up visits in our clinic

Labs	At presentation	After 3 months	After 6 months	After 9 months
Urea (mmol/L)	4 mmol/L	5.4 mmol/L	6.6 mmol/L	4.7 mmol/L
Creatinine (mcmol/L)	75 mcmol/L	54 mcmol/L	56 mcmol/L	60 mcmol/L
Proteinuria (g/day)	1.5 g/day (high)	0.14 g/day	0.30 g/day	0.20 g/day
*WBC	5.4 10*3/µL	4.18 10*3/µL	3 10*3/µL (low)	2.8 10*3/µL (low)
Platelets count	251 10*3/µL	291 10*3/µL	312 10*3 /µL	385 10*3/µL
Lymphocyte count	0.51 10*3/µL (low)	0.70 10*3/µL (low)	0.58 10*3/µL (low)	0.65 10*3/µL (low)
Haemoglobin	9.1 g/dl (low)	11.6 g/dl	12 g/dl	12.1 g/dl
*MCV	73.1 fl (low)	78.9 fl	80.9 fl	78.7 fl
*C3	0.65 g/L (low)	1.4 g/L	1.1g/L	0.60 g/L (low)
*C4	0.04 g/L (low)	0.3 g/L	0.2 g/L	0.14 g/L
*ANA	Positive			
*DsDNA	1325 IU/ml (high)	28.6 IU/ml (high)	21.2 IU/ml	19.1 IU/ml

*WBC= White blood cells, *MCV= Mean corpuscular volume, *C3,4= Complements
*ANA= Antinuclear antibody, *DsDNA= Anti double strand DNA

The patient underwent an extensive investigation which showed: Leucopenia of 2.9 10*3/µL with an anaemia of chronic disease 9.1 g/dl with a mean corpuscular volume of 73.1 fl and normal count of platelets. Renal and hepatic profiles were normal. Serum amylase and lipase values were also normal. Full septic screen ordered and cultures turned out to be negative without any evidence of infection. Urinalysis showed positive WBCs, positive RBCs and +2 protein. Also, Antinuclear Antibodies (ANA) were done and it was positive. Anti-double-stranded DNA antibody was elevated 1325 IU/ml while the complement (C3) value was low 0.65 g/L. ANCA test was negative. 24hour urine protein collection had shown proteinuria with 1.5 g/day.

CT-scan for abdomen and pelvis was arranged and it showed diffuse small and large bowel wall thickening suggestive for inflammatory process with mild-moderate free fluid. The gastroenterology team offered to do an upper and lower GI endoscopy but the family was hesitant to proceed for any endoscopic intervention. While we

were waiting for the result of remaining labs, the patient was managed by supportive measures such as: IV fluid, bowel rest, anti-emetics and proton pump inhibitors as advised by GI team.

Due to presence of proteinuria, the patient underwent a renal biopsy and the result was: Class III lupus nephritis, no crescents or interstitial fibrosis or tubular atrophy. Upon exclusion of infections, the patient was started on methyl prednisolone 60mg IV once a day and the patient was offered the choice between cyclophosphamide and mycophenolatemofetil (MMF), benefits and side effects and treatment regimen of both drugs were explained to the patient, the patient and her family both refused cyclophosphamide and opted for MMF which was started with the optimal dose gradually reached of 1.5gm orally twice a day. The patient was reviewed daily after starting this regimen and unfortunately the patient was still complaining of cramping abdominal pain with intractable vomiting that had led to multiple episodes of severe hypokalemia with potassium levels of 3.2 moll/L, 2.8 moll/L and severely reduced level of potassium 2.3 moll/L subsequently over a duration of two weeks. Given the seriousness of her hypokalemic episodes and the lack of significant improvement in her GI symptoms we re-discussed the importance of early and aggressive treatment of her condition and the ultimate decision of using cyclophosphamide was reached.

Intra venous cyclophosphamide (EUROLUPUS) protocol of 500 milligrams every two weeks for a total of six doses followed by maintenance therapy with MMF was started. The patient's vomiting episodes and abdominal pain improved within two days of the first cyclophosphamide dose and within one week the patient was discharged home on oral steroids with a tapering plan, hydroxychloroquine 400 milligram daily, lisinopril 5 milligram daily, calcium and vitamin D supplementations and follow up appointments in the Day Care unit and Rheumatology clinic. Upon follow-up as an outpatient, the patient's gastrointestinal symptoms had improved significantly and proteinuria levels were showing complete remissions.

Discussion

Lupus enteritis is a not uncommon sequela of SLE with worse prognosis arising from immune complex insult with activation of the complements' system leading to vasculitic injury and sub mucosal inflammation[5]. Gastrointestinal manifestations due to active lupus disease are wide and varied and this patterns can include: enteritis, vasculitis, pancreatitis, protein-losing enteropathy, intestinal pseudo-obstruction and peritonitis[6]. Gastrointestinal symptoms suggestive for lupus enteritis are non- specific as patients can present to emergency department with different vague presentations. So, the differentiation between various processes responsible for such symptoms is not an easy process as the differential diagnoses are broad and can include: adverse events from immunosuppressive drugs, or related to infectious organisms like bacterial, fungal or viral infections and if all these possibilities have been excluded; lupus enteritis will be the most suitable diagnosis.

There are many cases reported in literature about lupus enteritis and the most frequent symptoms noticed are abdominal pain followed by nausea, vomiting and diarrhoea[7].

The diagnosis of lupus enteritis is not dependent on tissue examination as in many conditions that biopsy will not be a feasible option and radiological imaging with Computerized Tomography Scan (CT scan of abdomen and pelvis) would be the gold standard for reaching the diagnosis[8]. There are three main radiological abnormalities reported to be correlated with presence of enteritis: (i) bowel wall thickening with edema > 3mm and this is called "target sign", (ii) engorgement of mesenteric vasculatures suggestive for vasculitis, (iii) change in enhancement of intra-abdominal fat. Moreover, other radiographic modalities can be utilized to clarify if there is any enteric inflammation like: conventional angiography and Magnetic Resonance Angiogram (MRA). Pathological examination can be done by requesting assistance from the gastroenterology team to do endoscopic intervention with biopsy that will show evidence of bowel wall mucosal hyperemia or ulceration noticed predominantly in jejunum, ileum followed by colon[9].

Severe gastrointestinal syndromes related to lupus occur mostly in the context of active general disease, but we cannot assume that for all cases as some patients can present with lupus - related GI complications with low (SLEDAI) based on contradiction noticed between different studies[10]. However, checking for other major organ involvement among lupus patients presenting with GI symptoms is desired to tailor the plan regarding which therapy should be administered. There is no single laboratory bio - marker that can be used to diagnose GI complications in lupus. Haematological abnormalities like: anaemia of chronic disease, leucopenia and thrombocytopenia all can be seen in these patients[11].

Additionally, lab tests for lupus activity such as: low complements level with an increment in the level of anti double-stranded DNA antibodies are noticed among patients diagnosed with lupus- related GI manifestations[12]. Positivity of anti-phospholipid antibodies is reported in 28% of individuals presenting with GI syndromes[13]. Ruling out other major organ involvement is paramount as nephritiscarditis and neuropsychiatric events might occur with gastrointestinal symptoms concomitantly[14].

There is no single therapeutic plan that can be followed for managing patients with lupus related GI symptoms. The most important step in management is to exclude surgical abdomen with a picture of bowel perforation before initiation of any immunosuppressive drugs[15]. The treatment mainly depends on supportive measures like: surgical team consultation, IV fluid, bowel

rest, antibiotics till the infections are ruled out then immunosuppressive medications can be initiated[16].

The mainstay immunosuppressive therapeutic agent is glucocorticoids therapy IV/ oral routes. Another immunomodulatory agent can be added like: Cyclophosphamide (CYC), Mycophenolate Mofetil (MMF), Azathioprine or Rituximab (RTX)[17,18].

Early discovery of lupus related gastrointestinal complication is essential as the initiation of steroid and immunosuppressive agents like intravenous cyclophosphamide will prevent unfavouarable outcome[19].

Lupus - related GI complications carry a higher risk for relapse especially among patients who have bowel wall thickening more than 9mm in (CT scan) and patients who received lower cumulative dose of glucocorticoids[20].

Alshehri *et al*[21] reported one case from Saudi Arabia diagnosed with SLE after her presentation with symptoms of abdominal pain and diarrhoea with picture of mesenteric involvement shown in CT-abdomen and pelvis.

Conclusions

Gastrointestinal symptoms among patients with lupus are frequently seen, however the symptoms related to (SLE) flare are associated with poor prognostic outcomes. The diagnosis depends mainly on the clinical picture with supportive radiological evidence after excluding other diagnoses like infections. The management of such complications has two components: The first is: IV fluid/ bowel rest after excluding worrisome conditions such as bowel perforation while in the second the treatment will encompass glucocorticoid therapy plus another immunosuppressive lines.

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