CASE REPORT

Isolated Gastrointestinal Symptoms as Initial Presentation in Systemic Lupus Erythematosus and Its Differential Diagnosis

Nurul Akmal Abd Latip[1], Azwanis Abdul Hadi[1], Mohd Nizamuddin Ismail[2]

[1] Department of Family Medicine, Kulliyyah of Medicine, International Islamic University Malaysia, 25200 Kuantan, Pahang, Malaysia.
[2] Department of Anaesthesiology, Kulliyyah of Medicine, International Islamic University Malaysia, 25200 Kuantan, Pahang, Malaysia.

ABSTRACT

Initial clinical presentation of Systemic Lupus Erythematosus (SLE) is varied as it affects various organs in the body. While the typical presentation of SLE is mucocutaneous, musculoskeletal and haematological manifestation, gastrointestinal (GI) manifestation is a rare initial presentation of SLE. We discuss the case of a 13-year-old girl who was diagnosed with SLE after she presented with isolated gastrointestinal symptoms. She presented with vomiting, diarrhoea, mild colicky abdominal pain and bilateral ankle oedema; and was treated as acute gastroenteritis. She returned after one week with worsening symptoms. Her full blood count showed bicytopenia; urinalysis had proteinuria and haematuria, and renal profile revealed acute on chronic kidney injury which triggered suspicions of a more serious disease rather than simple viral gastroenteritis. Further investigations of positive anti-nuclear antibody, low complements and positive Coombs's test supported the diagnosis of SLE. The diagnosis of SLE was confirmed when her renal biopsy reported crescentic lupus nephritis ISN/RPS Class IV. Additional investigation to investigate the cause of her gastrointestinal symptoms included an ultrasound abdomen which showed minimal ascites and bilateral renal parenchymal disease. She was planned for colonoscopy but due to the unavailability of paediatric endoscopy, colonoscopy was postponed. However, her symptoms markedly improved with intravenous Cyclophosphamide which supported the diagnosis of GI SLE. This case report is to highlight that a patient with symptoms of simple viral gastroenteritis might have a more serious underlying disease. Even though rare, SLE can present with gastroenteritis symptoms and is one of the differential diagnoses that should be considered.
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Corresponding Author:
Azwanis Abdul Hadi, M.Med (Family Med)
Email: azwanis@iium.edu.my
Tel: +609-5704000/ +6013 – 252 0466

INTRODUCTION

Acute gastroenteritis is the most common diagnosis made when a patient presents with diarrhoea. Similar to adults, typical presentations of SLE in childhood are mucocutaneous, musculoskeletal and haematological manifestations (1). Only 20% of the patient presented with gastrointestinal symptoms at the onset of the diagnosis of SLE (1). This case report is to highlight that SLE may present with GI symptoms as initial presentation and possible differential diagnosis of GI manifestation in SLE. Gastrointestinal abnormalities due to SLE are varied include Lupus Mesenteric Vasculitis (LMV), Protein-losing Gastroenteropathy (PLGE), intestinal pseudo-obstruction, pancreatitis and hepatitis (1,2,4).

CASE REPORT

A thirteen-year-old Malay girl initially presented with fever, vomiting, diarrhoea and lethargy for the past one week. It was low grade and intermittent fever which was relieved by Acetaminophen. Besides that, she also had nausea, vomiting and mild colicky lower quadrant abdominal pain. However, she had no abdominal distension, hematemesis, dysentery, melaena, recent travel history or taking antibiotics. She also had loss of appetite for one week. Before her first hospitalization, she had sought treatment from the emergency department, which treated her as acute gastroenteritis. She was prescribed antiemetics and oral rehydration salts, and then she was discharged home. No investigations were done. Pre-morbidly she was healthy, and this was her second visit to the emergency department and thus she was admitted due to persistent symptoms.

Upon the initial assessment, she looked pale, lethargic,

and dehydrated. Her vital signs and oxygen saturation were all normal except the temperature was 37.8 °C and the pain score was 2/10. There were no cutaneous signs suggestive of connective tissue disease. The abdomen examination was normal but there was the presence of pedal oedema up to bilateral mid shins. Other systemic examinations such as respiratory, cardiovascular, and joint examinations were normal. Due to acute gastroenteritis, she was infused with intravenous fluids and was given other symptomatic management.

Several baseline tests were ordered, including full blood count (FBC), renal profile, and urinalysis. Her FBC showed white blood cell was 4.0 x 109/L and haemoglobin was 8.8 g/dl while urinalysis revealed proteinuria 2+ and haematuria 3+, and her renal profile showed elevated serum urea 15.5 mmol/L and serum creatinine 182 umol/L. Her liver function test was normal except for low total protein (45 g/L) and low albumin (25 g/L). Urine protein creatinine index was moderately elevated (220 mg/mmol). Blood, urine and stool which were sent for culture and sensitivity showed no growth; and there was absence of ova and cyst in the stool. At this point, glomerulonephritis was considered as a differential diagnosis because of her haematuria, proteinuria and severe acute kidney injury which were not typical findings associated with acute gastroenteritis in a young healthy teenager.

We proceeded with several more specific investigations, and it showed positive anti-nuclear antibody, low complements C3 and C4 level (C3: 0.2 g/L and C4: 0.3 g/L) and positive Coombs's test. Both erythrocyte sedimentation rate (105 mm/H) and C – reactive protein (24.2 mg/L) were high which suggest ongoing active disease. She was further diagnosed with lupus nephritis when her renal biopsy showed diffuse global proliferative with 50% cellular crescents (crescentic lupus nephritis) ISN/RPS class IV with moderate chronic tubulointerstitial damage and mild acute interstitial nephritis activity index 12/24, chronicity index 6/12. Ultrasound abdomen showed bilateral renal parenchymal disease and minimal ascites which was not suitable for peritoneal tapping (Figure 1). Otherwise, the bowel was not thickened (1mm) and there was absence of multiple fluid levels in the bowel.

She was given intravenous (IV) Methylprednisolone 350 mg OD (10mg/kg/day) for 3 doses then converted to oral prednisolone 35 mg OD (1 mg/kg/day) with tapering dose 4 – 8 weeks. She also was started on oral Mycophenolate Mofetil (MMF) 1 g BD, Hydroxychloroquine 200 mg OD, Calcium Lactate 300mg OD, Calcitriol 0.25mcg OD and Hematinic 1/1 OD. Her condition improved and she was discharged. Unfortunately, she was not compliant to MMF and other medications leading to the reoccurrence of her symptoms. She was readmitted and was started on pulses of intravenous Cyclophosphamide 0.6 g (0.5g/m2) based on the National Institute Health

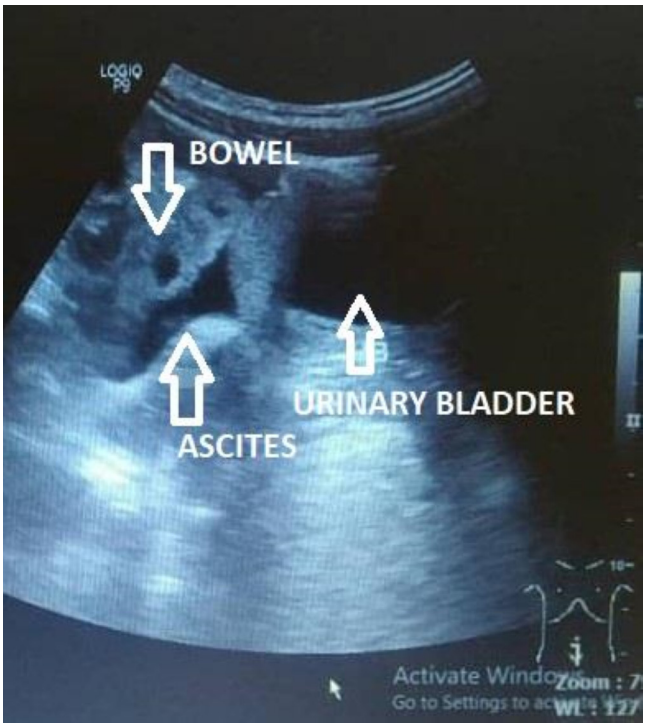

Figure 1: Ultrasound showed minimal ascites over the peritoneal region

regimen.

Because of her diarrhoea, colonoscopy was planned to investigate the possibility of GI SLE but due to the unavailability of paediatric endoscopy in our centre, the risk of bowel perforation in view of active disease and the patient already started on IV cyclophosphamide which is one of the treatments for GI SLE, endoscopy was postponed. Computed Tomography (CT) abdomen and angiography were scheduled as an outpatient appointment because IV cyclophosphamide already started and lack of resources in our centre. Patient's symptoms including diarrhoea improved with IV cyclophosphamide which made the diagnosis of GI SLE very likely. The patient was discharged and completed the induction cycle of cyclophosphamide as an outpatient.

She was restarted on MMF but became non-compliant due to the size of the tablet. She had another relapse with fever, diarrhoea, and generalised oedema. Clinically she was oedematous. Her urinalysis showed protein 3+ blood 3+; her creatinine of 161 worsened to 269, and she was losing albumin from 25 to 20. Just before the appointment for CT abdomen and angiography, her condition deteriorated with hypertensive crisis, acute pulmonary oedema and subsequently, she passed away in the Coronary Care Unit due to lupus pulmonary haemorrhage.

DISCUSSION

Since SLE affects various organs in the body, the clinical

manifestations are varied. Although SLE in children is fundamentally the same as it is in adults, it is well known that children with SLE have far more severe disease and earlier complications than adults with SLE (1). The most common presentation of childhood or juvenile-onset SLE is mucocutaneous manifestation which accounts for about 70% (1). This is followed by musculoskeletal manifestations (60%) and haematological manifestations (55 – 77%) (1). Only 20% of patients with SLE presented with gastrointestinal (GI) symptoms at onset (1).

Most GI symptoms in SLE are mild, but the few that are serious could be life-threatening with high fatality (2,3). Gastrointestinal abnormalities due to SLE are Lupus Mesenteric Vasculitis (LMV), Protein-losing Gastroenteropathy (PLGE), intestinal pseudo-obstruction, acute pancreatitis and hepatitis (1,2,4). One of the most common causes is LMV. A patient with LMV usually presents with abdominal pain which can be severe due to mesenteric ischaemia (2,4). Another common cause of gastrointestinal SLE is PLGE which typically presents with peripheral pitting oedema, hypoalbuminemia, nausea, vomiting, diarrhoea and abdominal pain but rarely symptomatic ascites or pleural effusion. The diarrhoea is watery and occurs frequently in a day (2). Our patient main GI symptom was diarrhoea. At the initial presentation, peripheral oedema was the only positive finding in clinical examination and her oedema worsened in subsequent presentations with concomitant severe hypoalbuminaemia. She could have been losing protein due to her underlying lupus nephritis, but her GI symptoms seem to be in keeping with the features of PLGE as well.

Diagnosis of GI SLE can be supported via several investigations such as endoscopy-guided biopsy, Computed Tomography (CT) abdomen or abdominal ultrasound (5). For LMV: endoscopy guided biopsy will show vasculitic changes; CT abdomen will have features such as intestinal wall thickening, target sign, intestinal dilatation, and abnormal mesenteric vascular filling; and abdominal ultrasound will show irregular thickening with wall oedema (2-4). All these investigations are non-specific but facilitate diagnosis (3), therefore it must be interpreted within the clinical context and other investigation results. For PLGE, diagnosis used to be made with low serum hypoalbuminemia and ruling out other causes of protein-losing disease such as abnormal liver function, or malabsorption (2). The diagnostic tool to rule out PLGE is Technetium-99m albumin scintigraphy (2,4) but it is expensive and not widely available, hence it is not commonly performed. For this patient, her ultrasound abdomen did not show features in keeping with LMV, rather the findings of ascites further support the possibility of underlying PLGE.

There are three other important GI diagnosis at initial onset that we should consider, which are intestinal pseudo-obstruction (IPO), acute pancreatitis and hepatitis, even though they do not fit this patient's case presentation. IPO's main presenting symptoms include abdominal pain, nausea vomiting, abdominal distension, and constipation (2). There will also be dilated fluid-filled thickened bowel and few fluid levels on radiological evaluation (2). While acute pancreatitis in SLE presents similarly to typical acute pancreatitis which includes abdominal pain with elevated serum amylase or lipase (2). Hepatitis is a common finding at diagnosis of childhood-onset SLE but usually, the patient is asymptomatic even though there was 2 to 3 times elevation of transaminases with the absence of other causes of hepatitis (1).

Advance investigations are often unavailable in smaller centres. The lack of effective and convenient diagnostic tools is an issue, which reduces diagnostic capability. However, GI SLE can also be clinically defined by improvement of symptoms after intravenous corticosteroids or immunosuppressants (3), which is seen in this case. Most GI SLE has a good therapeutic response to immunosuppressants, with corticosteroids and cyclophosphamide the most used therapies (2¬¬¬¬-4).

Cyclophosphamide or azathioprine were the immunosuppressive drugs of choice for lupus nephritis. Nowadays, MMF is widely used for paediatric lupus nephritis as it is as effective as cyclophosphamide and may be more effective as azathioprine; as well as MMF has a better safety profile (5). Since this patient was not adhering to MMF, cyclophosphamide is another treatment option for her. Cyclophosphamide is also a recommended treatment for most GI SLE in which this case diarrhoea improved after cyclophosphamide induction (2-4).

CONCLUSION

SLE with GI involvement should be considered as one of the possible differential diagnosis in a young female patient presenting with prolonged and unresolved gastrointestinal symptoms such as diarrhoea and/or abdominal pain. Basic investigations such as FBC and urinalysis may give initial clues towards the correct diagnosis. Prompt diagnosis is vital to ensure the early treatment to prevent further complications.

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