CASE REPORT

Protein Losing Enteropathy in Systemic Lupus Erythematosus

A Murali*, Denesh Narasimhan**, J Krishnaveni***, G Rajendiran****

Abstract
Systemic lupus erythematosus (SLE) is a chronic immunologic disorder that may affect multiple organ systems and present with myriad of clinical features. Gastro-intestinal (GI) manifestations are oral ulcers, dysphagia and abdominal pain caused by autoimmune peritonitis/intestinal vasculitis. Hypoalbuminaemia due to GI loss is uncommon. Protein losing enteropathy (PLE) is a group of clinical entities where there is loss of protein through GI tract. PLE due to SLE is rare but it can be the initial manifestation. Patients usually present with pedal oedema mimicking nephrotic syndrome clinically. It is diagnosed by excluding other causes of hypoalbuminaemia. Radio nucleotide labelled albumin scan is useful in confirming albumin loss through GI tract. Often there is a good response to corticosteroids and immunosuppressive drugs. Here we present two SLE patients whose presenting manifestation was protein losing enteropathy and both improved with corticosteroids.

Introduction

Systemic lupus erythematosus (SLE) is a multifactorial chronic inflammatory disease of unknown origin, characterised by the presence of auto antibodies and polymorphic clinical manifestations. Common clinical manifestations are oral ulcers, polyarthritis, pleuritis, pericarditis, seizures, psychosis and lupus nephritis.1 Gastrointestinal (GI) manifestations are rare in SLE. Hypoalbuminaemia in SLE is usually due to massive proteinuria. Protein losing enteropathy is a clinical entity characterised by hypoalbuminaemia secondary to excessive loss of serum proteins from gastrointestinal tract. It can be caused by many GI disorders like Menetriers disease, coeliac sprue, tropical sprue, intestinal lymphangiectasia, congestive cardiac failure and amyloidosis.2 The mechanisms of protein loss through GI tract include mucosal ulcerations, increase in mucosal permeability and lymphatic obstruction.3 The diagnosis of PLE is usually done by excluding other causes of hypoalbuminaemia.3 Histopathological changes in duodenum and colon are non specific. Protein loss through GI tract can be confirmed by Tc-99m albumin scintigraphy and stool alpha 1 antitrypsin clearance.4 PLE due to SLE is relatively uncommon and only less than 60 cases have been reported in the literature. PLE in SLE is usually diagnosed by excluding other causes of PLE. It is managed by corticosteroids and immunosuppressive agents with a good clinical outcome.3 We submit two SLE patients who had protein losing enteropathy, both of them improved with corticosteroids.

Case 1

45 year old female without any premorbid illness was admitted with one month history of fever, puffiness of face, abdominal distension, leg swelling, polyarthritis and breathlessness. Clinical examination showed anasarca, bilateral pleural effusion and ascites. There was no other evidence of malnutrition. Investigations revealed
25 year old female who had pulmonary thromboembolism six months prior to current admission came with intermittent high grade fever, polyarthritis, abdominal distension, leg swelling, breathlessness and puffiness of face for 2 weeks. Clinical examination showed pallor, bilateral pedal oedema, bilateral pleural effusion and ascites. Investigations showed anaemia (Hb - 8.1 g/dl), thrombocytopenia (26000/cmm) and no peripheral eosinophilia. Her renal, thyroid and lipid profile were normal. Liver function test showed hypoalbuminemia (Total protein – 3.4 g/dl, Albumin – 0.9 g/dl, Globulin – 2.5 g/dl) with normal enzymes. Serum Vitamin B12 and folate levels were normal. Her urine spot protein creatine ratio was 0.57. Serology for Hepatitis B, C and HIV were negative. Anti cardiolipin antibody and lupus anticoagulant were negative. Serum complements were low. Stool examination didn’t show any parasites and fat globules were negative. She was started on prednisolone 1 mg/kg/day, albumin infusion and supportive measures. She improved clinically and her platelet count increased to 92000 with her albumin being 2.2 g/dl at one month follow up.

**Discussion**

Systemic lupus erythematosus is a multi system auto immune disease with protein clinical manifestations. Gastrointestinal (GI) manifestations of SLE are though uncommon when compared to other systemic manifestations but can occur due to the complication of drugs or secondary to infections. The GI manifestations include mesenteric vasculitis, protein losing enteropathy, intestinal pseudo obstruction, pancreatitis, eosinophilic enteritis, autoimmune peritonitis and pneumatoce cystoides intestinalis. Clinically significant protein losing enteropathy due to SLE is uncommon. Al-Mogairen SM recently did a systematic review and reported that protein losing enteropathy due to SLE is more commonly seen with Asians. Tian XP et al reported that more than 50% of SLE patients had PLE as their initial presentation. On the contrary Gornisiewicz et al reported that PLE occurs in patients only with severe form of SLE. Our two patients had PLE as their initial presentation.

Diarrhoea is present in 40-50% of patients but our patients did not have any GI symptoms. Severe hypoalbuminaemia and hypocomplementaemia are the most common findings as seen in our patients. Kim et al reported that hypercholesterolaemia is common in SLE related PLE but neither of our patient had hypercholesterolaemia. The cause for SLE associated PLE is yet to be proven. But the probable hypotheses are being: 1. Non necrotising vasculitis of mesenteric vessels leading to increased vascular permeability to proteins. 2. Increased vascular permeability caused by vasodilatation due to intravascular activation and conversion of complement. 3. Cytokine or complement mediated vascular or mucosal damage. 4. Intestinal lymphangiectasia. The diagnosis of SLE associated PLE depends on the exclusion of other causes of hypoalbuminaemia and malabsorption syndromes. Colonoscopy is usually not diagnostic yet Al-Mogairen SM reported mucosal thickening in 44% of patients. On the other hand, intestinal histology either revealed mucosal oedema, inflammatory cell infiltrate, lymphangiectasia, mucosal atrophy or vasculitis in 80% of patients. Colonoscopy done in both of our patients was normal and histology showed only lymphocytic infiltration. We diagnosed thrombocytopenia (34000/cmm), increased erythrocyte sedimentation rate (ESR) - 115 mm/hr, no peripheral eosinophilia, normal renal, thyroid and lipid profile. Liver function test showed hypoalbuminemia (Total protein 4.2 g/dl, Albumin 1.3 g/dl, Globulin – 2.9 g/dl) with normal enzymes. Her 24 hour urinary protein excretion was 352 mg/day. Serology for Hepatitis B, C and Human Immunodeficiency Virus (HIV) were negative. Anti Nuclear Antibody (ANA) and dsDNA were positive. Serum complement levels were low. Serum Vitamin B12 and folate levels were normal. X ray chest PA view showed bilateral pleural effusion. Ultrasonogram (USG) of abdomen showed normal liver echotexture and ascites. CT abdomen didn’t show any bowel wall thickening. 2D echocardiogram was normal. Pleural fluid and ascitic fluid aspirates were found to be transudate. Upper gastrointestinal scopy (UGI) and colonoscopy were normal. Deep duodenal biopsy showed villous flattening and intraepithelial lymphocytosis and ileal biopsy showed lymphocytic infiltration. Antiendymysial antibody was negative. Stool examination did not show any parasites and fat globules were negative. She was treated with prednisolone 1 mg/kg/day, albumin infusion, haematinics and oral anti coagulants. She improved clinically and her platelet count was 138000/cmm and albumin was 2 g/dl at discharge.

**Case 2**

Tian XP et al
SLE related PLE in both of our patients as they did not have any other cause for hypoalbuminaemia, deep duodenal biopsy and ileal biopsy were negative for significant malabsorption findings and negative for anti endomysial antibodies. Tc-99m albumin scintigraphy is used as a diagnostic test as it is non invasive. Tc-99m labelled Human Serum Albumin is injected intravenously and serial scintigraphic images of abdomen are taken. We can localise the protein leakage through the GI tract. Stool alpha 1 anti trypsin clearance (A1AT) can also be used as an alternate diagnostic test. A1AT is a protein which has a molecular weight similar to albumin. It is synthesised in the liver, is neither actively secreted nor absorbed and does not undergo proteolysis or degradation in the gut. Hence estimation of 24 hour stool clearance indicates loss through GI tract. Normal A1AT clearance is ≤ 27 ml/24 h. The test should be cautiously interpreted in presence of diarrhoea, upper GI bleed and hyperacidity. We could not do both the tests due to non availability. The treatment is with corticosteroids and other immunosuppressive agents like azathioprine and cyclophosphamide can be added when there is no response or relapse. CC Mok et al reported that 88% of patients had good clinical recovery with high dose prednisolone for six months and then tapered with azathioprine. Our patients received high dose prednisolone alone with good clinical recovery.

References