Case Report

Chronic diarrhea unmasking systemic lupus erythematosus

Abstract

Gastrointestinal manifestation from lupus disease are uncommon, but recognized clinical syndromes include lupus enteritis, protein losing enteropathy, intestinal pseudo-obstruction, malabsorption syndromes, pancreatitis, Celiac Disease, and Inflammatory Bowel Disease. We report a case of a 60-year-old female with 11 weeks of painless diarrhea, recurrent fever, and pancytopenia. After extensive evaluation, a new diagnosis of SLE was established in conjunction with the Systemic Lupus International Collaborating Criteria. The patient showed rapid improvement on immunosuppressive agents. This case highlights the diagnostic complexity of SLE, and to our knowledge, records the first case of initial SLE presentation as a febrile chronic diarrhea.

Keywords: systemic lupus erythematosus, chronic diarrhea, fever of unknown origin

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Introduction

Systemic lupus erythematosus (SLE) is an autoimmune disorder characterized by multisystem inflammation, autoantibody formation, and immune complex deposition in nearly any organ system. Age of presentation is typically around the third decade, more likely in females of African, Hispanic, and Asian origin.[1] The most common initial symptoms include fever, arthralgia, and malar rash. Gastrointestinal tract involvement in SLE is characteristically related to adverse medication effects triggering nausea, vomiting, and anorexia, though disease related complications have been described.[2] Gastrointestinal manifestations range from the most life-threatening lupus mesenteric vasculitis, to lupus enteritis, protein losing enteropathy, intestinal pseudo-obstruction, malabsorption, pancreatitis, and associations with Celiac or Inflammatory Bowel Disease (IBD).[2,3] While SLE can present in a myriad of ways, to our knowledge, this is the first report of undiagnosed SLE manifesting as a constellation of chronic diarrhea, persistent fever, and pancytopenia.

Case report

A 60-year-old Asian female with a history of hyperlipidemia and a remote diverticulitis requiring right hemicolectomy presented with diarrhea for 11 weeks. Bowel movements were described as Bristol Scale 6, dark brown, with occasional hematochezia, and without mucous. Associated symptoms included weakness, several episodes of non-bilious, non-bloody vomitus and a 16-pound weight loss. The patient denied abdominal pain. Family history included gastric carcinoma. On hospital admission, physical examination was unrevealing. Laboratory investigations demonstrated leukopenia to 1.9K/µL, normocytic anemia of 9.1g/dL, thrombocytopenia of 120K/µL, hypoalbuminemia of 2.8g/dL, and elevated erythrocyte sedimentation rate at 50mm/hr. A contrast abdominal computerized tomography (CT) scan failed to reveal gastrointestinal abnormalities (Figure 1).

Early in the hospital course, the patient developed persistent fevers and tachycardia, with continued diarrhea. Stool cultures, ova and parasite microscopy, Clostridium difficile antigen and polymerase chain reaction, blood cultures, urine cultures, and chest radiographs were all negative. A bone marrow biopsy revealed mild hypocellularity, and did not elucidate a diagnosis. Considering a differential diagnosis of neutropenic sepsis as pancytopenia worsened, broad-spectrum antibiotics were initiated, though without response. Upper endoscopy and colonoscopy were both unremarkable with normal pathology on random biopsies. Evaluation of the small bowel with capsule endoscopy was also normal. Advanced investigations for a neuroendocrine origin of diarrhea exposed an elevated Chromogranin A level at 351ng/L, however further testing with Vasoactive Intestinal Peptide, Gastrin, 5-hydroxyindoleacetic acid, and Octreotide scanning were all negative. Concurrent rheumatologic studies revealed elevated titers for Antinuclear Antibody (ANA) at 1:80 and Anti-Double Stranded DNA (anti-ds DNA) of 675IU/mL, with decreased C3 complement level of 48mg/dL. Antibiotics were discontinued and patient was started on intravenous steroids for a presumed SLE flare. She demonstrated rapid clinical and laboratory improvement with complete resolution of diarrhea, pancytopenia and fevers within two days. The patient was transitioned to oral Prednisone and Hydroxychloroquine upon discharge with continued recovery.

Discussion

SLE can be diagnosed today using the Systemic Lupus International Collaborating Clinics (SLICC) criteria. This guideline defines seventeen SLE related clinical and immunologic phenomena, four of which, including one of each subtype, must be positive to meet diagnosis (Table 1).[4] Ongoing concerns with 1997 American College of Rheumatology (ACR) criteria for SLE diagnosis prompted this 2012 SLICC revision, with incorporation of chief immunologic tests such as complement levels and relevant clinical phenomena such as integument and nervous system manifestations.[4] In validation studies of the SLICC, sensitivity greatly outweighed the ACR at 97% versus 83% respectively, potentially allowing for earlier diagnosis and management.[5] Our case represents a unique subset of patients with not only more advanced age than usual, but also with atypical symptoms of presentation. SLE diagnosis would not have been established using the ACR criteria in this case, with only three of the eleven criteria met rather than the four required. However, leukopenia, thrombocytopenia, low complement levels, positive ANA, and elevated anti-dsDNA incited SLE diagnosis using the more sensitive SLICC criterion. Ultimately, this categorization and prompt management proved imperative to the patient's rapid recovery.

Table 1 Diagnostic criteria of SLE per ACR and SLICC Guidelines[4]

CR Criteria (4 of 11)	SLICC Criteria (4 of 17 Including at Least One Clinical Criterion and One Immunologic Criterion; or Biopsy-Proven Lupus Nephritis
Malar rash	Clinical criteria
Photosensitivity	Acute cutaneous lupus
Discoid rash	Chronic cutaneous lupus
Oral ulcers	Nonscarring alopecia
Arthritis	Oral or nasal ulcers
Serositis	Joint disease
Renal disorder	Serositis
Neurologic disorder	Renal
Hematologic disorder	Neurologic
ANA	Hemolytic anemia
Immunologic disorders	Leukopenia or lymphopenia
	Thrombocytopenia
	Immunologic criteria
	ANA
	Anti-dsDNA
	Anti-Smith
	Antiphospholipid
	Low complement
	Direct Coombs' test

Gastrointestinal complaints in SLE are frequent but are oftentimes related to the adverse effects of treatment rather than the disease itself. Diarrhea can be a presenting symptom of acute flare or associated pathologic conditions including lupus enteritis, protein losing enteropathy, celiac disease, malabsorption syndromes, and IBD.[2] Our patient, however, lacked the clinical symptoms, radiographic, and pathologic features which distinguish these conditions.

Lupus enteritis is defined as either vasculitis or inflammation of the small bowel with supporting imaging or biopsy findings. Typical symptoms include abdominal pain, diarrhea, and vomiting. CT scan is often the diagnostic test of choice. Imaging may show evidence of focal or diffuse bowel wall thickening, bowel dilation, abnormal wall enhancement or target sign, enlarged and increased number of mesenteric vessels, and fat stranding (Figure 1).[3,6]

The rare, but well-described entity of protein losing enteropathy also differs from our presentation. In this condition, a proposed cytokine and complement mediated damage to mesenteric vasculature and mucosa yields increased permeability and subsequent proteins loss.[3] It is thus manifested by marked hypoalbuminemia resulting in generalized edema, pleural and pericardial effusions, and ascites. Diagnosis is confirmed through Tc-(99m) albumin scintigraphy. Colonoscopy is often normal and thus nondiagnostic, although can demonstrate mucosal thickening. Up to 80% of patients have histological findings of mucosal edema, inflammation, lymphangiectasia, mucosal atrophy, or vasculitis.[7]

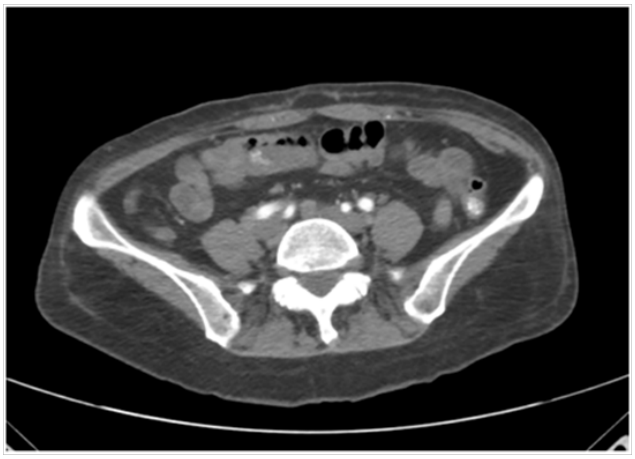

Figure 1 Abdominal CT scan showing normal small bowel and colon.

Fat malabsorption inducing diarrhea in SLE patients is thought to be a result of villi blunting from immune complex deposition.[2] Celiac autoantibodies, 24-hour fecal fat testing, and endoscopic biopsies can rule out this condition, all of which were negative in this case. Likewise, Ulcerative Colitis can be an associated autoimmune condition or a source of drug-induced lupus described in case reports.[3] This can be ruled out by the absence of colonoscopy findings.

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Conclusion

While diagnostically challenging, early recognition of SLE is possible by careful observation for distinctive immunological and clinical features. The SLICC criterion is a viable and useful tool which may allow for more prompt diagnosis. Though atypical, this case highlights a unique potential rheumatologic diagnosis when faced with the constellation of chronic diarrhea, persistent fevers, and pancytopenia in the absence of other infectious, inflammatory or malignant processes.

Acknowledgments

None.

Conflicts of interest

Authors declare that there is no conflict of interest.

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