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CASE REPORT | COLON

Colonic Involvement of Stevens-Johnson Syndrome/ Toxic Epidermal Necrolysis: A Rare Cause of Gastrointestinal Bleeding

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ABSTRACT

Stevens-Johnson syndrome (SJS)/toxic epidermal necrolysis (TEN) represents a spectrum of rare but severe mucocutaneous drug reactions. Gastrointestinal involvement of SJS/TEN is associated with high morbidity and mortality and often presents 2–3 weeks after the initial appearance of skin lesions. There are no evidence-based treatment algorithms for the management of SJS/TEN. We report a case of life-threatening gastrointestinal bleeding from colonic involvement of SJS/TEN and discuss potential therapeutic options.

INTRODUCTION

Stevens-Johnson syndrome (SJS)/toxic epidermal necrolysis (TEN) represents a spectrum of rare but severe mucocutaneous drug reactions based on the extent of epidermal detachment. SJS/TEN has an estimated annual incidence of 0.4 to 6 cases per million persons per year and mortality rates as high as 50%.[1] Cytotoxic T cells are thought to induce programmed cell death of the epidermis through various cytokines, including tumor necrosis factor-alpha (TNF-α) and mediators such as granulysin.[2,3] SJS/TEN is characterized by drug-induced necrotic epidermal sloughing and mucocutaneous involvement, most commonly of oropharyngeal, ocular, and urogenital surfaces. Although anal and esophageal involvement has been reported, colonic involvement is rare with only 13 cases described in the literature.[4–11] Intestinal SJS/TEN is characterized by severe diarrhea or delayed gastrointestinal (GI) bleeding, often occurring 2–3 weeks after the initial appearance of skin lesions.[4–11] There are no evidence-based treatment algorithms for management of SJS/TEN. Adjuvant therapies including intravenous immunoglobulin (IVIG), cyclosporine, and anti-TNF-α agents remain controversial.[2,12] We present a case of GI bleeding as a result of colonic involvement of SJS/TEN and its management.

CASE REPORT

A 71-year-old African American woman with type 2 diabetes mellitus, chronic kidney disease stage IV, hypertension, heart failure with preserved ejection fraction, chronic obstructive pulmonary disease, and gout was admitted to the burn intensive care unit with worsening maculopapular rash 1 week after starting allopurinol. This progressed to an erosive rash covering 25% of her total body surface area with ocular and oropharyngeal involvement. Skin biopsies were consistent with SJS/TEN. Her score of toxic epidermal necrosis (SCORTEN score) on admission was 4, corresponding to a 58.3% mortality rate.[13] The initial treatment consisted of IV corticosteroids followed by IVIG therapy. The course was complicated by respiratory failure requiring intubation, septic shock, ileus, and oliguric renal failure, necessitating continuous renal replacement therapy.

Three weeks into her hospitalization, the patient developed bloody diarrhea with a drop in hemoglobin from 10.3 to 6.5 g/dL despite transfusions. Infectious workup, including *Clostridium difficile* assay, was negative. Although an upper endoscopy showed only antral gastritis, colonoscopy revealed perianal skin breakdown consistent with epidermal SJS lesions, 2 nonbleeding 15–30 mm ulcers

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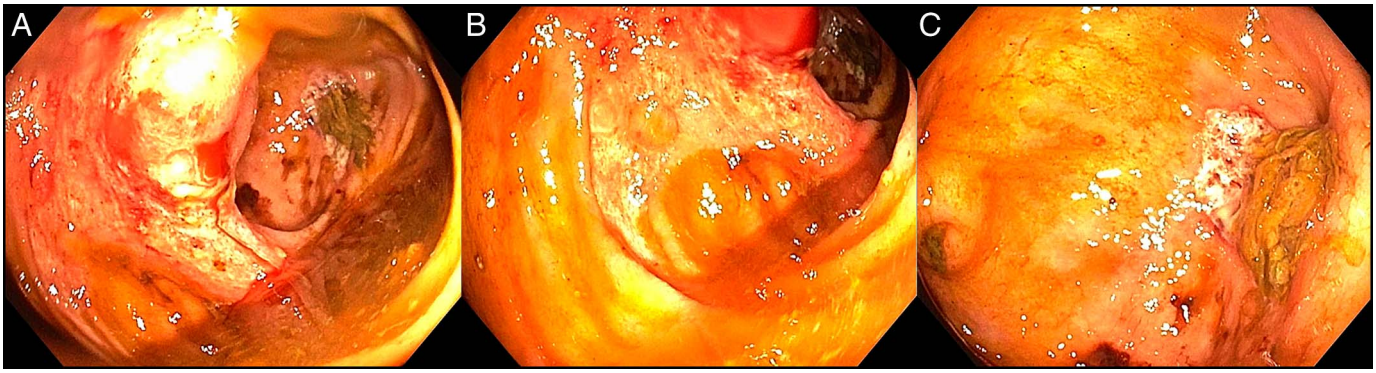

Figure 1. Endoscopic evidence of large ulcers in the cecum with surrounding friable mucosa.

of the cecum and ileocecal valve, and ulcerated, edematous mucosa in the ascending colon (Figure 1). Histologic examination of the mucosa demonstrated a nonspecific ulcerative pattern, consistent with the pathologic injury pattern of SJS and without the microcrypts typical of ischemic injury (Figure 2).

She continued to have hematochezia and transfusion-dependent anemia, requiring over 70 units of packed red blood cells through the next 4 weeks of her hospitalization. After repeated interventions including a colonoscopy and radiologic guided embolization were unsuccessful, an ileocecectomy was recommended; however, the patient's family declined surgical management given her high perioperative risk. High-dose steroid therapy with IV dexamethasone 100 mg daily for 3 days, followed by IV methylprednisolone 120 mg daily for 2 weeks, and a prolonged prednisone taper was implemented. A multidisciplinary conference discussed the utility of infliximab therapy in the management of colonic SJS/TEN. It was decided that the risks of further immunosuppression outweighed any benefits because her bleeding had not slowed in response to corticosteroid therapy. The patient ultimately died on hospital day 72 after developing septic shock refractory to vasopressors.

DISCUSSION

By contrast to the simultaneous presentation of epidermal, conjunctival, oropharyngeal, and urogenital lesions, individuals with colonic SJS/TEN have been reported to develop signs of GI bleeding 2–3 weeks after the appearance of skin lesions.[9] Owing to the high morbidity and mortality associated with colonic SJS/TEN, a prompt diagnosis is important, although an evidence-based treatment algorithm is yet to be defined. The offending agent should be discontinued and admission to the burn intensive care unit is recommended for wound management, monitoring of fluid and electrolyte balance, and nutritional support. Treatment with high-dose corticosteroids and IVIG should be considered, although monotherapy with systemic corticosteroids is not recommended because of the lack of evidence to support their benefit and potential risks including higher rates of infection and complications.[11,12]

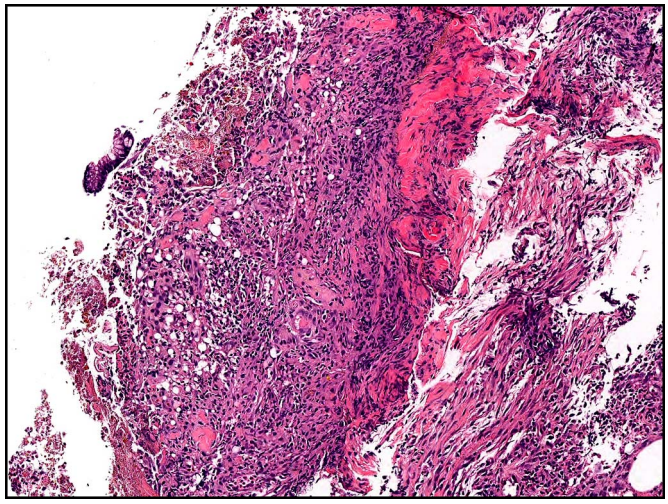

Figure 2. Histologic section showing areas of ulcerations accompanied by a background of unremarkable colonic mucosa, a pathologic injury pattern consistent with Stevens-Johnson syndrome (100×).

The use of adjunctive therapies targeting cytokines involved in the pathogenesis of SJS/TEN such as anti-TNF-α agents remains understudied.[12] A single randomized controlled trial evaluating the use of etanercept vs corticosteroids in the treatment of SJS/TEN showed that individuals treated with etanercept had shorter time to skin healing and a lower incidence of GI bleeding compared to the corticosteroid group (2.6% vs 18.2%, $P = 0.003$).[14] Because etanercept is an anti-TNF-α agent that is not effective in the treatment of GI conditions including inflammatory bowel disease, it is difficult to say whether the reduced incidence of GI bleeding is a result of TNF blockade vs increased risk of GI bleeding from corticosteroids.[14,15] Several case reports describe promising results with the use of infliximab as a therapeutic alternative for SJS/TEN, but its utility in management of GI complications is not known.[16,17] Although the same pathophysiologic mechanism presumably underlies the dermatologic and GI manifestations of SJS/TEN, it is difficult to advocate for the use of long-acting immunosuppression when the most common cause of death in patients with SJS/TEN is infection due to disrupted mucocutaneous barriers.[18]

Early surgical intervention in the setting of refractory GI bleeding with colonic SJS/TEN should be considered. Six individuals of similar age and comorbidity profile to our patient experienced life-threatening GI bleeding from colonic SJS/TEN. Three were managed exclusively medically with corticosteroids and IVIG, and 3 received corticosteroids before undergoing bowel resection for colonic SJS.[9,19] All 3 surgically managed patients survived to hospital discharge, but only one treated medically survived.[9]

Reports of colonic SJS in the literature reinforce its poor prognosis, particularly among patients with advanced age and comorbidities.[20] Our case provides a valuable example of the GI manifestations of SJS/TEN and a review of potential management options. Clinicians must maintain a high index of suspicion for GI involvement of SJS/TEN in individuals who develop diarrhea or GI bleeding several weeks after the appearance of SJS/TEN skin lesions. The use of anti-TNF agents in catastrophic hematochezia secondary to colonic SJS has not yet been evaluated, but surgical management of the bleeding lesions of colonic SJS may provide superior survival outcomes to current medical therapies.

DISCLOSURES

Author contributions: All authors contributed equally to this manuscript. KN Weaver is the article guarantor.

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Informed consent could not be obtained from the family of the deceased. All identifying information has been removed from this case report to protect patient privacy.

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