Noninfectious Colitides

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Abstract

Keywords

- ▶ diversion colitis
- ▶ neutropenic enterocolitis
- ▶ disinfectant colitis
- ▶ corrosive colitis
- ▶ salicylate-induced colitis
- ▶ toxic epidermal necrolysis

There are numerous etiologic and pathogenic mechanisms associated with colitis, ranging from infectious to noninfectious colitis. However, despite their different causes, their presentations are often similar making it difficult to formulate the correct diagnosis. This article describes the presentation, endoscopic and pathological findings of six different noninfectious colitides: diversion colitis, neutropenic enterocolitis, disinfectant colitis, corrosive colitis, nonsteroidal anti-inflammatory drug and salicylate-induced colitis, and toxic epidermal necrolysis. In addition, this article discusses the management and current treatment options for these six colitides.

There are several noninfectious colitides that the colorectal surgeon will encounter in his/her practice. It is important to recognize the clinical presentation of these entities and have an understanding of their unique pathophysiologies. Differentiating them from other diagnoses is key, and most importantly, it is crucial for the surgeon to have a strategy for diagnosis and treatment.

Diversion Colitis

The etiology of diversion colitis, also called disuse colitis, is thought to be a deficiency of nutrients (mainly butyrate and other short-chain fatty acids, SCFA) derived from bacterial fermentation of starch and proteins provided by the fecal stream. This is supported by the fact that daily instillation of SCFA results in improved endoscopic appearance of the diverted segment.¹

Diversion colitis is often asymptomatic, but when symptoms occur, rectal bleeding is the prominent symptom. Other symptoms include tenesmus, mucous discharge, and abdominal pain.

Endoscopic evidence of diversion (or disuse) colitis is present in 70 to 91% of the patients with fecal diversion. Findings include mucous plugs (scybalae), contact irritation,

erythema, and ulcerations.² In asymptomatic patients, endoscopic changes from diversion can include pallor of the tissue and friability. ▶ **Fig. 1** demonstrates these findings.

On pathological evaluation, biopsies of the diverted segment usually show acute and chronic inflammation with or without crypt architectural abnormalities. Lymphoid follicular hyperplasia is pathognomonic for diversion colitis.

Asymptomatic disease usually requires no treatment. In symptomatic patients or in whom diversion is permanent, twice daily irrigation of SCFA is recommended for up to 6 weeks. SCFA enemas require preparation at compounding pharmacies, and typically consist of sodium acetate (60 mmol), sodium propionate (30 mmol), and sodium *n*-butyrate (40 mmol) with additional sodium chloride (22 mmol). The solution has an osmolality similar to plasma at 280 to 290 mOsmol/L, and has a pH of 7.0 which is adjusted by using sodium hydroxide.³

The typical dose is 60 mL and is administered into the diverted rectum twice daily for up to 6 weeks. If symptoms improve, less frequent scheduling can be used. Other treatments that have been documented include 5-aminosalicylic acid (5-ASA) enemas and steroid enemas, and have only been used if the SCFA enemas are not well tolerated.⁴

Fig. 1 Endoscopic appearance of diversion colitis. (A) Images from a patient who had a long-standing ileostomy and rectal stump for chronic Crohn colitis. Note the pallor and fragility of tissue. (B) Linear ulceration without bleeding is noticed in the 2, 6, and 10 o'clock positions with gentle insufflations and endoscopic intubation. Note diffuse erythema and friability. (C) Tissues are prone to bleeding with such ulceration. (Photo credit: Anjali Kumar, MD.)

In the event where a patient is diverted for a long period of time (> 1 year), periodic endoscopic examination of the diverted segment for neoplasia is advised. Diversion colitis resolves once intestinal continuity is reestablished.

Neutropenic Enterocolitis

Neutropenic enterocolitis (NEC) is a potentially fatal condition that was initially recognized in patients with neutropenia as a complication of chemotherapy. However, this disease has been seen in any patient who has an absolute neutrophil count of less than 500 cells/mL,³ as seen in many patients with human immunodeficiency virus (HIV).⁵ The process has a predilection for the terminal ileum and cecum, but any segment of the bowel can be involved.

Common presenting symptoms are abdominal pain, fever, abdominal distention, nausea, vomiting, and diarrhea with or without blood. A tip-off is coexisting neutropenia in the at-risk patient population.

Computed tomography seems to be the most accurate method of diagnosis which reveals a thickened and inflamed terminal ileum and cecum.⁶ Endoscopy is generally contraindicated, but if performed will show a diffusely friable and hemorrhagic mucosa.

While adult NEC tends to be focused at the terminal ileum, neonatal NEC presents more diffusely. ►**Fig. 2** demonstrates the radiographic findings of NEC in a neonate with late stage disease, including pneumatosis and resulting portal venous gas.

The management of these patients remains challenging. Bowel rest, intravenous fluids, and broad spectrum antibiotics with parenteral nutrition are the cornerstones of treatment. Patients are usually too sick to withstand endoscopy. As the leukopenia resolves, often the patient improves. Surgery is reserved for perforation or peritonitis, or failure to respond to conservative measures.⁶ Surgical intervention consists of resecting the necrotic segment and creating a stoma. On pathological evaluation, significant edema in the submucosa and loss of the mucosa is evident. Clinical outcomes are unpredictable. In the adult population, coexisting morbidities can often take precedence over the septic insult.

Disinfectant and Corrosive Colitis

Disinfectant and corrosive colitis are two entities that have similar etiologies, as well as endoscopic and pathological findings. Commercially available endoscope disinfecting solutions can cause colonic damage if allowed to contact the mucosa.⁷ Hydrogen peroxide bases and glutaraldehyde formulations are commonly used for endoscopic cleaning. A 2% solution of glutaraldehyde is widely used as a disinfectant because of its broad spectrum of action against acid and alcohol-resistant bacilli, hydrophilic viruses, and spores. Despite the thorough rinsing of scopes, residual formulation may reach the mucosa and may cause irritation of the mucosa, the appearance of which has been referred to as pseudolipomatosis.^{8,9} Formalin injury can occur in the intestine in two ways. First, it is applied to the rectal mucosa as a treatment for

Fig. 2 Images from a neonate with neutropenic enterocolitis. (A) Plain film anterior posterior note pneumatosis of the small bowel in the right upper quadrant. (B) Lateral film showing pneumatosis and air in the portal venous system. (C) Computerized tomographic scanning confirms diffuse portal venous gas and bowel distension. (Photo credit: Muhammad Khan, MD, and Nabil Safdar, MD, of Children's National Medical Center.)

patients with bleeding because of radiation injury. Second, when biopsy instruments come in contact with formalin as specimens are placed in formalin fixing containers (► **Fig. 3**), they may not be adequately washed; formalin is then introduced by the instrument and comes in contact with the mucosa.

Symptoms appear 24 to 48 hours after endoscopy and range from mild pain to significant tenderness with fever and bloody diarrhea.^{10,11} Other causes of pain after endoscopy should be ruled out such as colonic perforation. Often, radiographic studies will help rule out colon perforation. Endoscopic findings appear as slightly raised whitish plaques, sometimes similar to pseudomembranous colitis. The damage is typically seen in endoscopy when areas that were noticed to be relatively normal on introduction of the scope are surprisingly abnormal on withdrawal. Pathological evaluation will demonstrate empty spaces within the lamina propria.

Most patients have a resolution of symptoms without any intervention. Thorough rinsing and forced air drying of the endoscopes will help prevent this type of colitis.¹²

Nonsteroidal Anti-Inflammatory Drug and Salicylate-Induced Colitis

The capacity of nonsteroidal anti-inflammatory drugs (NSAIDs) and salicylates to produce ulcerative effects in the gastroduodenal mucosa is well known. In addition, NSAIDs may produce colonic mucosal injury, colonic stricture formation, perforation, and hemorrhage.¹³ These drugs are also associated with the reactivation of quiescent inflammatory bowel disease. Presenting symptoms are often diarrhea, rectal bleeding, and abdominal pain, along with a history of NSAID usage.

Endoscopic findings range from patchy erythema and granularity to severe, extensive mucosal ulcers.¹⁴ Often the clinical and endoscopic features are indistinguishable from idiopathic colitis.

Treatment involves discontinuing NSAID and salicylate use as well as administering 5-aminosalicylic acid (ASA) and steroid medications. At times, inpatient therapy is required. Relapse is common and chronic colitis may require surgery.¹⁵

Fig. 3 (A) When biopsy forceps are repeatedly dipped into a specimen container with formalin to release a piecemeal resected specimen. (B) If they are not adequately rinsed, it could introduce formalin into the scope channel which can cause corrosive colitis. (Photo credit: Anjali Kumar, MD.)

Toxic Epidermal Necrolysis

Toxic epidermal necrolysis (TEN), commonly, but mistakenly regarded as Stevens–Johnson syndrome (SJS), is the most severe among a spectrum of mucocutaneous exfoliative diseases (SJS is a distinct entity which is less severe). The criteria for diagnosing TEN include involvement of at least 30% of the total body surface area, which typically involves at least two mucus membranes. At the cellular level, TEN is mediated by a cytotoxic immune process. Activated T cells induce apoptosis of keratinocytes and mucosal epithelial cells via FAS-ligand cell–cell interactions and by secretion of granulysin and necrosis follows.¹⁶

The most common sites of pathology are the oropharynx, conjunctiva, genitalia, anus, and gastrointestinal (GI) tract. Patients begin with a prodrome of fever and malaise. Often they will have a recent history of phenytoin or sulfonamide antibiotic use as an inciting, precipitating event. Symptoms include bloody diarrhea or protein-rich exudative diarrhea.¹⁶ Next, patients present with the appearance of an erythematous confluent eruption that rapidly evolves into exfoliation of the skin at the dermal–epidermal junction, resulting in large sheets of necrotic dermis, as seen in **Fig. 4A**.

Diffuse ulceration of the mucosal surface may occur anywhere along the GI tract. The endoscopic appearance may resemble severe ulcerative or pseudomembranous colitis; however, pathologic biopsies show extensive necrosis and lymphocytic infiltration without crypt abscesses or neutrophils. Interestingly, the muscular layer remains intact. The mucosal sloughing of the bowel may result in melena, segmental ischemia (**Fig. 4b**), or intestinal perforation.

Not all portions of the GI tract are affected equally or at the same time within the course of the disease. For instance, the oral mucosa sloughs early, the esophagus only occasionally forms strictures, and pathology of the lower GI tract may happen concurrently with skin lesions or after the cutaneous manifestations have cleared. Colitis may be an entity in and of itself or the sequelae of an overwhelming septic response. The scant number of cases of lower GI pathology may reflect a true rarity or a difficulty in diagnosis.¹⁶

Sepsis, GI hemorrhage, leukopenia, fluid and electrolyte imbalance, and renal insufficiency are the major complications that contribute to the high mortality rate. Patients with TEN are very ill and require hospitalization in an intensive care unit, where patients can receive supportive care of fluid

Fig. 4 Patient with toxic epidermal necrolysis who needed to be taken to the operating room for acute abdomen. (A) Preoperative diffuse dermatologic presentation. (B) Patchy intestinal necrosis noted in the small bowel on exploratory laparotomy. (Photo credit: Philip Fidler, MD, and Sarah Pradka, MD.)

Table 1 Types of noninfectious colitides

Type of noninfectious colitis	History	Endoscopic appearance	Histopathology	Treatment	Unique features
Diversion colitis	Disused segment	Mucus plugs, erythema, and friable mucosa	Lymphoid follicular hyperplasia	Short-chain fatty acids enema; Restore bowel continuity	Lymphoid follicular hyperplasia short-chain fatty acids enema
Neutropenic enterocolitis	Chemotherapy or other immunosuppressive diseases	Diffusely friable, hemorrhagic mucosa	Loss of mucosa, significant edema in the submucosa	NPO, IVF, broad spectrum Abx surgery	Affects mostly terminal ileum and cecum
Disinfectant colitis	Recent endoscopy	Plaque-like lesions	Pseudolipomatosis	Supportive	Lesions present on scope withdrawal
Corrosive colitis	Formalin use or self-induced material	Plaque-like lesions	–	Supportive	Formalin use or self-induced enema
NSAID and salicylate-induced colitis	Heavy use of NSAID	Ulcerations, patchy erythema	–	Discontinue NSAID, topical (5-ASA) or steroid	May reactivate quiescent IBD
Toxic epidermal necrolysis	Skin manifestation of SJS	Severe ulceration and bleeding	Extensive necrosis and lymphocytic infiltration without crypt abscesses or neutrophils	Multisystem approach, surgery	Epidermal necrosis and exfoliation; No crypt abscess on pathology

Abbreviations: Abx, antibiotics; ASA, aminosalicylic acid; IBD, inflammatory bowel disease; IVF, intravenous fluids; NPO, nil per os; nothing by mouth; NSAID, nonsteroidal anti-inflammatory drug; SJS, Stevens–Johnson syndrome.

resuscitation, enteral feedings, and peptic ulcer prophylaxis.¹⁶ Surgical resection is often required because of necrosis.

Conclusion

Noninfectious colitides are rare. They present with a wide range of symptoms, from minimal abdominal pain to severe life-threatening colon perforation. It is imperative for colorectal surgeons to be able to diagnose and treat these conditions. ► **Table 1** summarizes what we have covered in this review as high-yield facts.

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