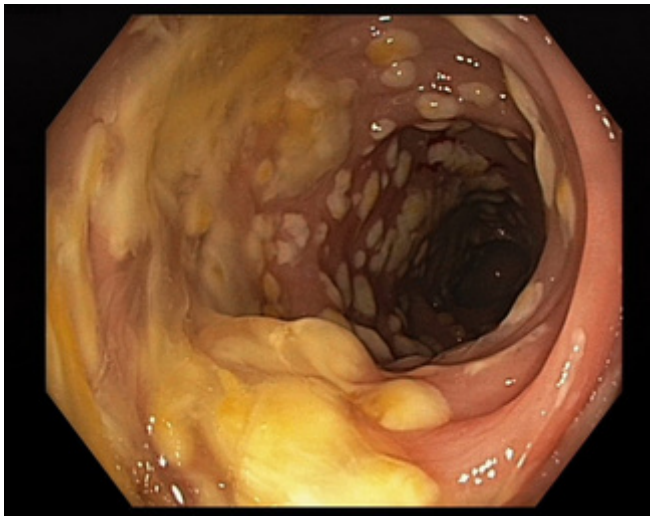
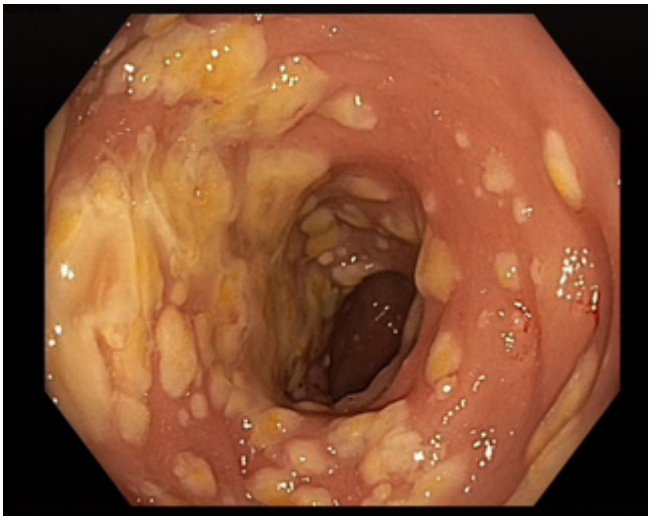
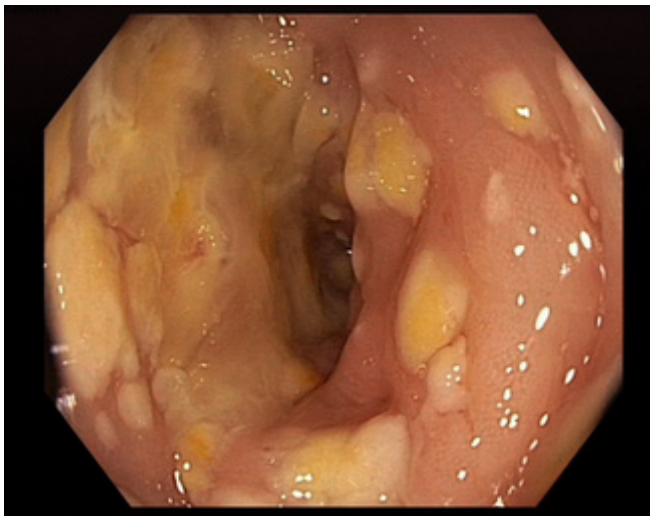
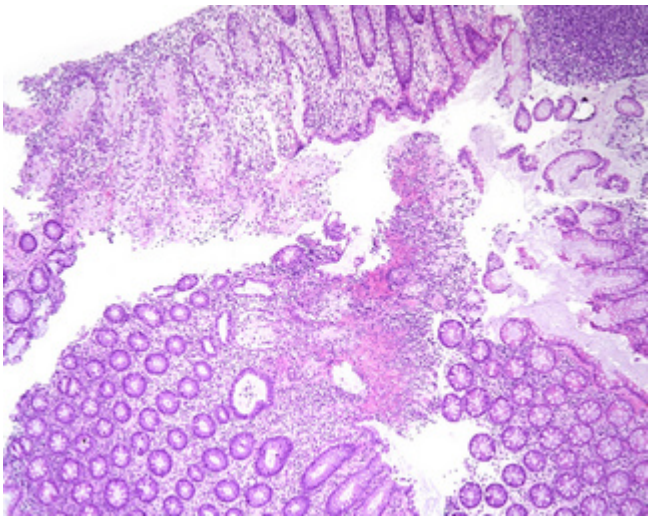
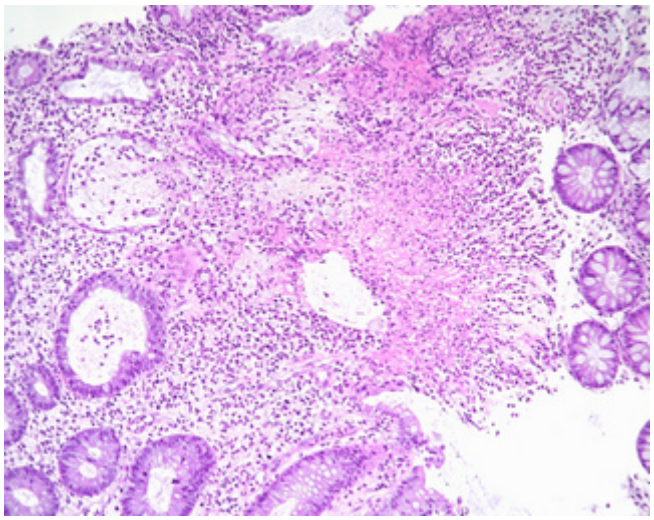
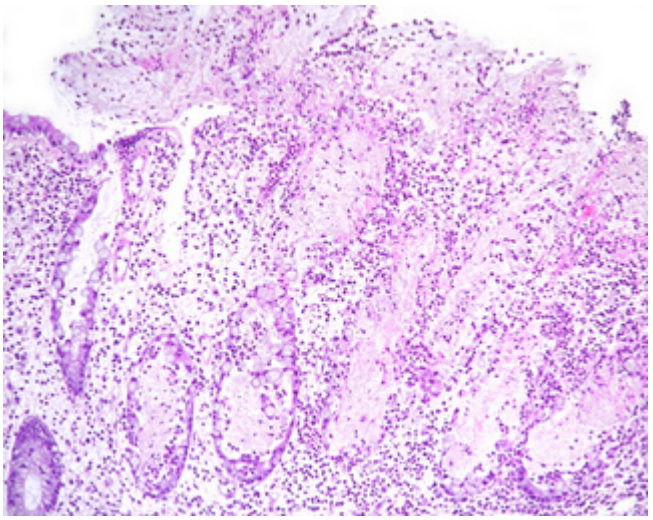
May 2018

42 year-old female with history of diffuse large B-cell lymphoma (DLBCL) and patches of white to yellow exsudates within the colon.

What is your diagnosis?

Diagnosis:

Pseudomembranous colitis.

Comment:

A 42 year-old female with history of diffuse large B-cell lymphoma (DLBCL; diagnosed eight months previously) received prophylactic antibiotic treatment during abdominal surgery (for reasons not related to the malignant disease). During the postoperative course, unspecific abdominal symptoms including mild diarrhoea developed. Laboratory investigation revealed leucocytosis of 20.5 (normal: 4.4-11.3 10^9/L) and increased CRP of 178.8 (normal: <5 mg/L). Abdominal computed tomography showed diffuse thickening of the large bowel wall with punctum maximum within the descending colon (12 mm). Upon colonoscopy, patches of white to yellow exsudates were identified scattered throughout the mucosa (predominantly left colon), focally coalescing into large swatches (Panels A-C).

Biopsies were taken, which disclosed two well-defined foci of dilated glands giving rise to a “volcano-like” shaped pseudomembrane composed of necrotic debris, fibrin, mucin and neutrophils (Panel D). Affected crypts were denuded and filled with mucin and neutrophils (Panel E). Sloughed degenerated goblet cells were also present in the lumen (Panel F). A final diagnosis of pseudomembranous colitis related to the infection with Clostridium difficile was made.

Within the large bowel, pseudomembranous may be associated with different causes, including infections, ischemia and drug-induced injury. The term “pseudomembranous colitis” should however be restricted to cases with Clostridium difficile infection, which occurs predominantly in hospitalized patients and/or after antibiotic exposure. There is a broad range of clinical presentations from mild diarrhoea to fulminant colitis and toxic megacolon. Tests for Clostridium difficile generally include stool culture, PCR or antibody-based assays. Endoscopy is not routinely recommended and should be avoided when severe disease is suspected, but can be helpful in cases with negative laboratory testing or treatment failure. Upon endoscopy, the disease is characterized by yellow-white pseudomembranes that can either involve the entire colon or be patchy or segmental.

Histologic features vary according to time course of the disease as well as disease severity. Early lesions show focal superficial inflammation (often with with micropapillary projections) of the interglandular surface epithelium, developing into microerosions that are covered by small exsudates of fibrin, polymorphs, and epithelial debris. As lesions grow larger, we find usually well demarcated foci (as in our case) of disrupted glands distended by mucin and polymorphs, flanked by normal mucosa. The crypt epithelium appears withered or thinned (“atrophic”) and ultimately undergoes necrosis. Grading was proposed by some authors (Price and Davies, 1977) but cannot be recommended for routine use. The presence of signet-ring-like cells within the disrupted crypt epithelium should not be mistaken for carcinoma (when in doubt, p53, ki67 and e-cadherin immunohistochemistry can help).

Ischemia (including lesions related to NSAIDs-associated mucosal damage) represents the most important differential diagnosis. According to Dignan and Greenson (1997), atrophic-appearing micro-crypts, lamina propria hemorrhage, full-thickness mucosal necrosis, and a diffuse microscopic distribution of pseudomembranes were significantly more common in ischemia than infection with Clostridium difficile.

Metronidazole and vancomycin are the mainstays of treatment, but recurrence is seen in as many as one half of the cases.

For further reading:

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- Wu ML, Natarajan S, Lewin KJ. Peculiar artifacts mimicking carcinoma. Arch Pathol Lab Med. 2001; 125 (11): 1473-6.
- Damiani S, Campidelli C. Pseudomembranous colitis with signet-ring cells. Histopathology. 2002; 41 (2): 176-7.
- Wang K, Weinrach D, Lal A, Musunuri S, Ramirez J, Ozer O, Keh P, Rao MS. Signet-ring cell change versus signet-ring cell carcinoma: a comparative analysis. Am J Surg Pathol. 2003; 27 (11) : 1429-33.

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