Case history:

A 50 year old female presented with mild alternating constipation and diarrhea; her past medical history included recurrent painful nodules on bilateral lower extremities with biopsies that showed vasculitis, suggesting Behçet's disease. The patient was recently started on colchicine as part of the treatment of her vasculitis. In view of her gastrointestinal symptoms, a colonoscopy was obtained. A single sessile 4 mm non-bleeding polyp of benign appearance was found at 12 cm, which proved to be a hyperplastic polyp. The rest of the colonic mucosa appeared normal; the photos below are from the normal appearing mucosa.
What may have caused the above histologic changes?

A. Graft versus host disease
B. Colchicine toxicity
C. Behçet’s disease
D. Radiation colitis
E. Ischemia

Answer: B. Colchicine toxicity

Colchicine, an anti-inflammatory drug best known for its efficacy in the treatment of gout, may be associated with adverse gastrointestinal symptoms such as diarrhea, nausea, and vomiting. Colchicine acts by arresting the cell cycle in metaphase; this effect causes characteristic ring-form mitoses and abundant apical mitoses in the colonic crypts that can be appreciated histologically. The ring mitoses are often
accompanied by prominent epithelial apoptosis and pseudostratification in the deep colonic crypts. In addition to the colon, the stomach and duodenum are common sites affected by colchicine. Colchicine associated histologic changes in the GI tract are usually associated with clinical colchicine toxicity such as diarrhea, nausea, vomiting, and abdominal pain.

A. In graft versus host disease there is increased epithelial apoptosis in the regenerative compartment of the gland or in colonic crypts, approximately four times that of negative controls. When apoptotic bodies are well developed, they contain intra-cytoplasmic vacuoles filled with nuclear dust and have been described as “exploding crypt cells”. Florid changes include clusters of apoptotic epithelial cells in crypt lumina, crypt drop-out and epithelial sloughing. While mitoses can be abundant in regenerating crypts, these mitoses are histologically normal. Ring-mitoses are not seen. See Human Pathology 2009; 40: 909 – 917.

C. Behçet’s disease may manifest as vasculitis in the gastrointestinal tract, which is not typically seen on endoscopically obtained mucosal biopsies. Secondary mucosal ischemic changes may be appreciated.

E. Ischemic injury in colonic mucosal biopsies manifests as superficial crypt dropout which results in the ‘withering crypt’ pattern with stromal hyalinization, regeneration of deep crypts, edema and congestion of the lamina propria. It does not cause ring form mitoses.

D. Radiation can cause mucosal necrosis and fibrosis, epithelial and stromal cell atypia and hyalinized capillaries. It however, does not cause increased mitoses or ring-form mitosis.

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References: