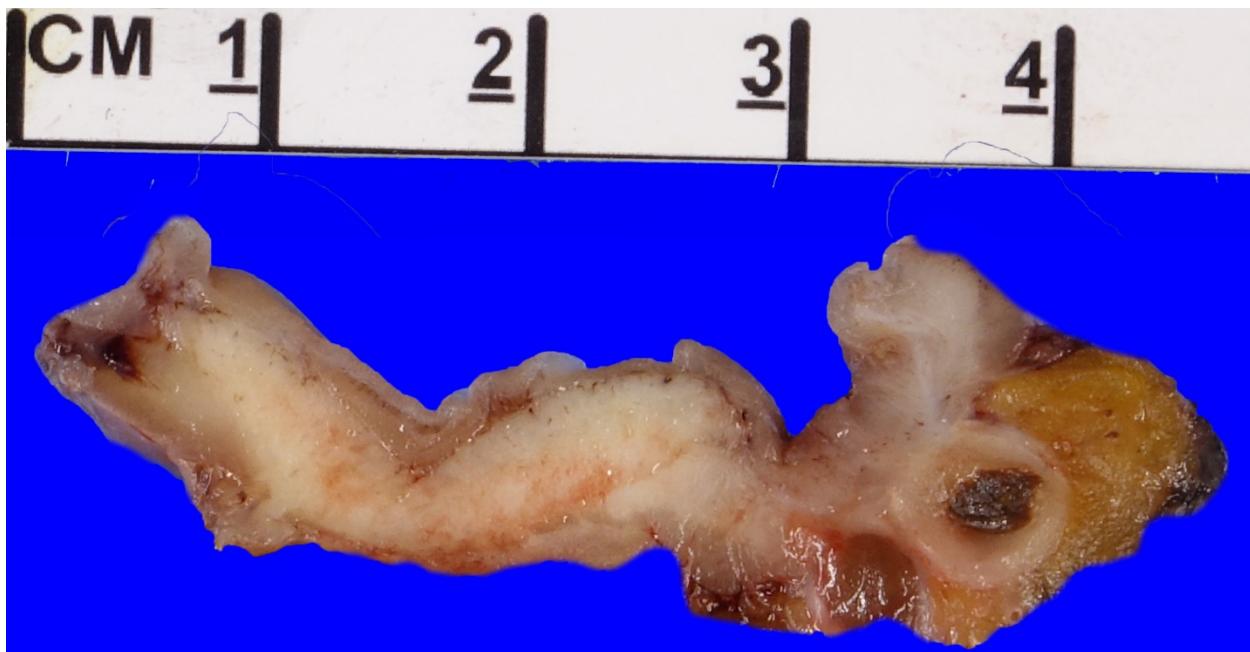
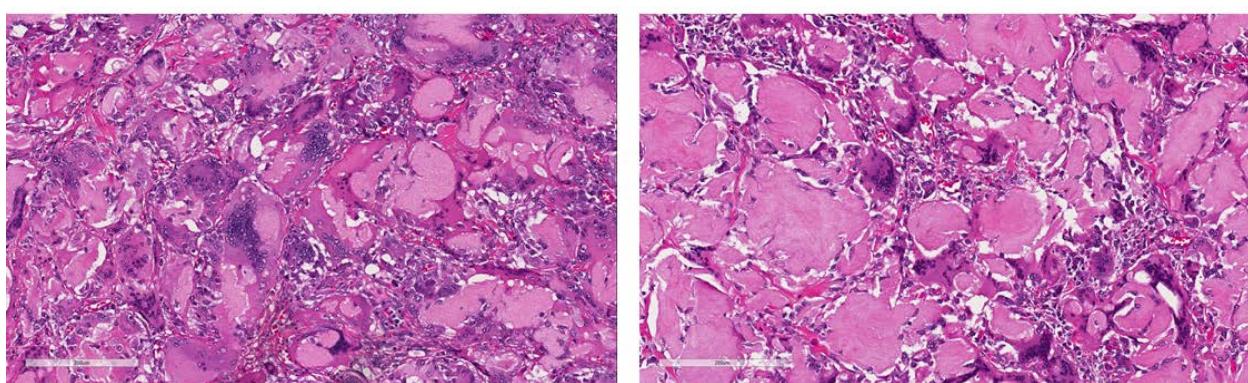


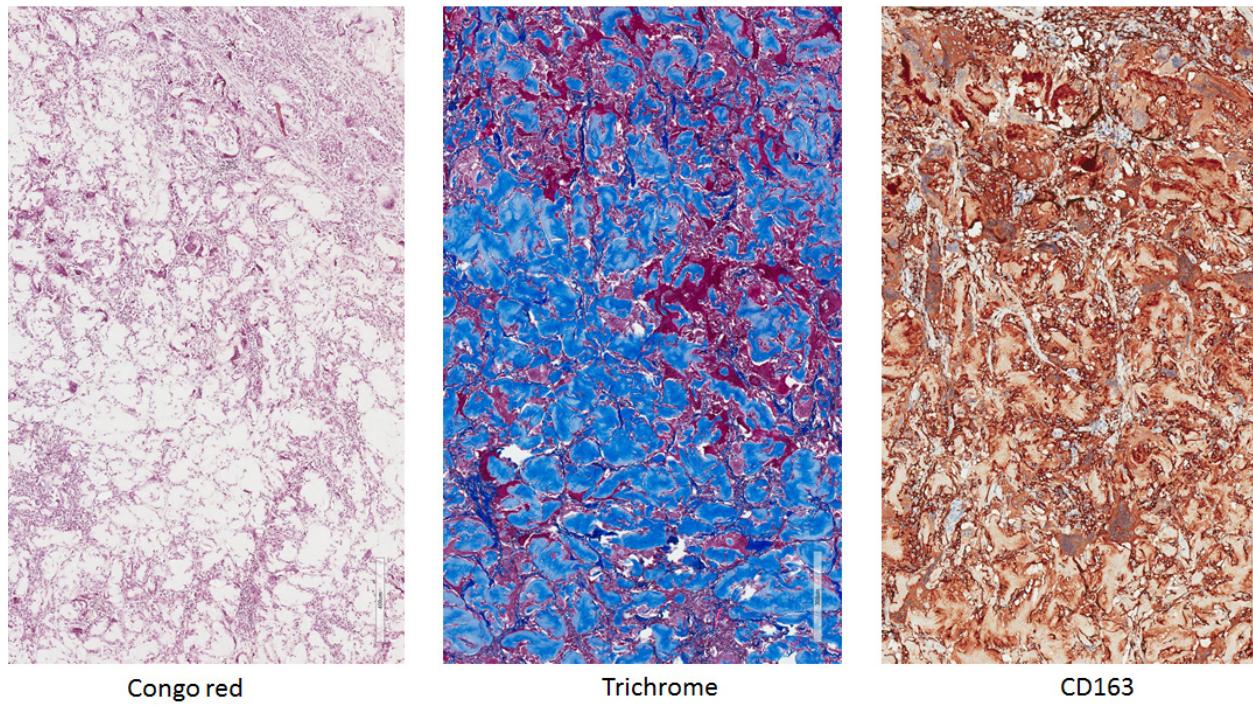
A 72-year-old man who presented for screening colonoscopy was found to have a 15 mm sessile polyp in the mid-sigmoid colon. Biopsies of the lesion revealed a tubulovillous adenoma with high-grade dysplasia and at least intramucosal carcinoma. The area was tattooed and an endoscopic polypectomy was attempted, but complete excision of the lesion was unsuccessful due to technical reasons. A week after the initial procedure, the patient underwent resection of the sigmoid colon. Gross evaluation revealed a residual polyp in the vicinity of the tattooed area, diverticula, and a submucosal indurated area. Sections of the residual polyp showed tubular adenoma without evidence of invasion. Sections of the indurated area are depicted below.



**Figure 1. Gross appearance**



**Figure 2A. H&E microscopic appearance of the submucosal lesion**



**Figure 2B. Special studies and immunohistochemistry.**

**What is your diagnosis?**

- A. Pulse granulomata
- B. Amyloidosis
- C. Injectable polymer reaction
- D. Acellular mucin

**Correct answer: C. Injectable polymer reaction (Orise)**

Endoscopic mucosal resections and endoscopic submucosal dissections are commonly performed to remove broad-based colorectal polyps that may not require colectomy. Both procedures entail injection of the submucosa with saline, norepinephrine, polymers, or other substances for the purpose of lifting the mucosa where the polyp is located. Injection essentially elevates a sessile polyp such that the snared tissue includes the base of the lesion as well as a portion of the submucosa. In addition, submucosal expansion by injection of these substances prevents injury to the muscularis propria. For many years, the submucosal lift was achieved by injection of saline-based solutions that adequately elevated the polyp but rapidly diffused into surrounding tissues, making it difficult to adequately excise the lesion in some cases<sup>1</sup>. Two products have recently received FDA approval for submucosal injection: Elevate and Orise, both of which are water-based solutions that contain sodium chloride, bulking agents, emulsifiers, and oils. These compounds appear as amorphous, eosinophilic deposits often accompanied by an exuberant giant cell-rich inflammatory response identical to that present in the current case. These deposits stain blue with a trichrome stain and are negative with a Congo red stain. A CD163 immunohistochemical stain demonstrates the presence of numerous multinucleated foreign body giant cells and macrophages surrounding these deposits.

A. Pulse granulomata:

As a result of mucosal damage, perforation or aspiration, exogenous hyaline material derived from the edible seeds of legumes (pulses) may be encountered in several sites including the mesentery, gastrointestinal tract, lungs, and oral cavity. This material forms hyaline ribbons or rings surrounded by foreign body granulomata, granulation tissue, dystrophic calcifications, and other food particles<sup>2,3</sup>. When rounded, the hyaline material may be confused with vascular amyloid deposits or parasitic ova. The extent of the tissue reaction depends on the evolution of the lesion: early deposits are associated with scant inflammation while those that have been present for several days elicit an intense inflammatory response with abscesses, lymphoplasmacytic-rich inflammation, foreign body type granulomata, and a sclerosing mesenteritis type fibroblastic reaction. The hyaline material of pulse granulomata is shaped as distinctive ribbons and/or rings which differ from the amorphous eosinophilic deposits present in this case. They are negative for the Congo red stain.

B. Amyloid deposits:

Amyloidosis is an umbrella term encompassing a number of heterogeneous disorders characterized by deposition of misfolded, insoluble peptides with a  $\beta$ -sheet structure. These deposits are faintly eosinophilic, homogeneous, and amorphous in routinely stained sections, and assume an orange-brick color with the Congo red stain<sup>4</sup>. Polarization of Congo red-stained sections shows apple-green birefringence. Gastrointestinal involvement is usually present in patients with either primary or secondary systemic amyloidosis. The localization of amyloid deposits within the gastrointestinal wall depends on their nature: mass like deposits in the

muscularis mucosa, submucosa and muscularis propria are frequent in patients with AL amyloid, while perivascular deposits in the lamina propria and submucosa predominate in patients with AA amyloid. Localized amyloid deposits (amyloidomas) unaccompanied by a systemic disease are extremely rare<sup>5</sup>. Similar to the present case, these deposits may elicit a foreign body type reaction. However, at variance with the Orise deposits, amyloid deposits have a waxy, homogeneous appearance and react positively with Congo red stain.

D. Acellular mucin:

Acellular mucin may be seen in a variety of benign and malignant conditions involving the gastrointestinal tract. Diverticula, fistulous tracts, colitis cystica profunda, misplaced epithelium (pseudoinvasion), previous biopsy sites, mucinous tumors of the appendix, and neoadjuvantly treated adenocarcinomas may show acellular mucin within and outside the intestinal wall. The “watery”, loose, slightly basophilic features of acellular mucin are quite different from the eosinophilic deposits present in this case. Acellular mucin-like material has been described in some cases after ORISE, but it stains negatively with periodic acid-Schiff with diastase digestion<sup>6</sup>.

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