## **Clinical History**:

A 69-year-old female with a history of adenomatous polyps and a family history of colon cancer presented for a repeat colonoscopy. A 2 cm sessile polyp at the base of the cecum was removed and submitted to pathology.

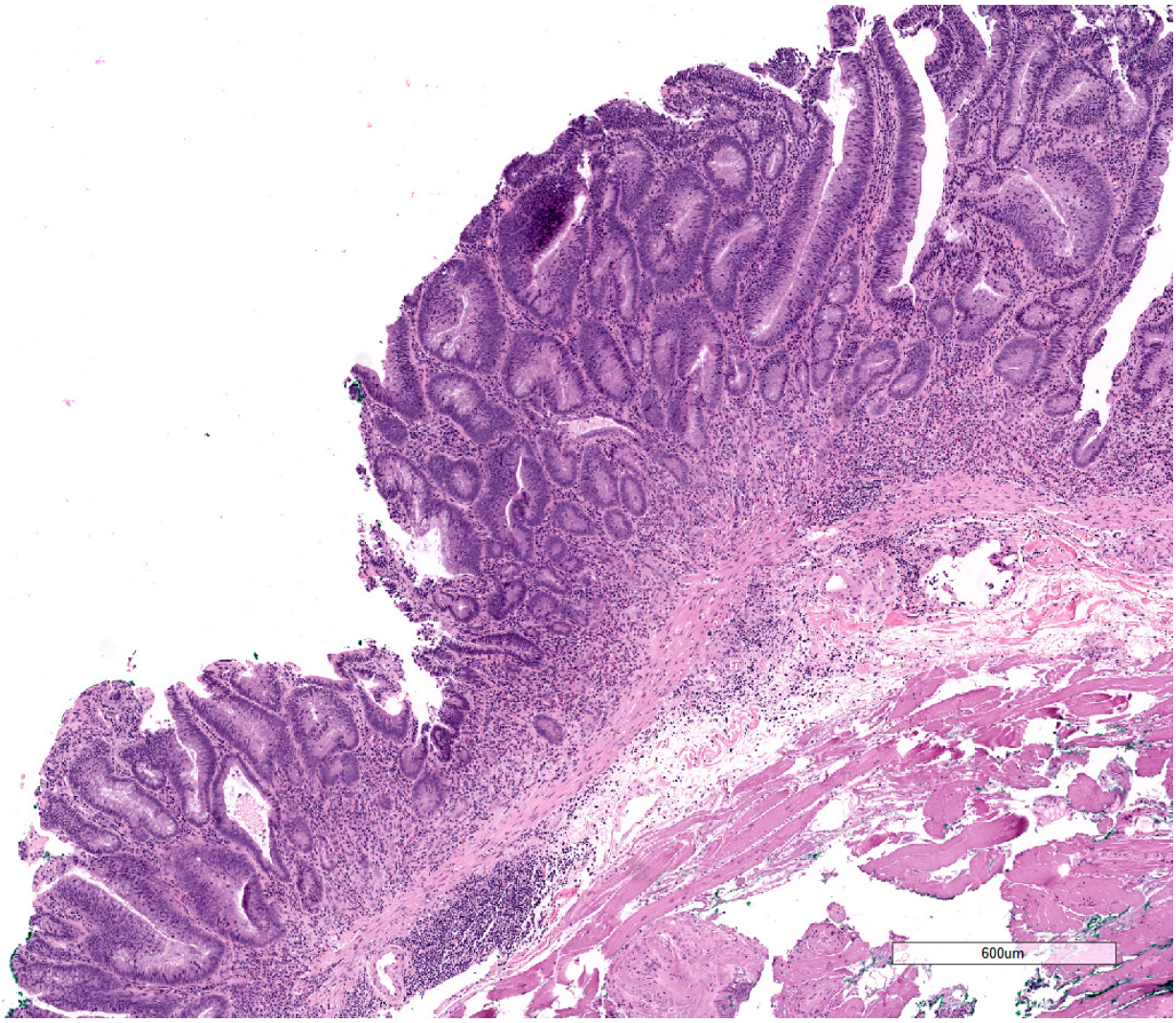


**Figure 1.** H&E

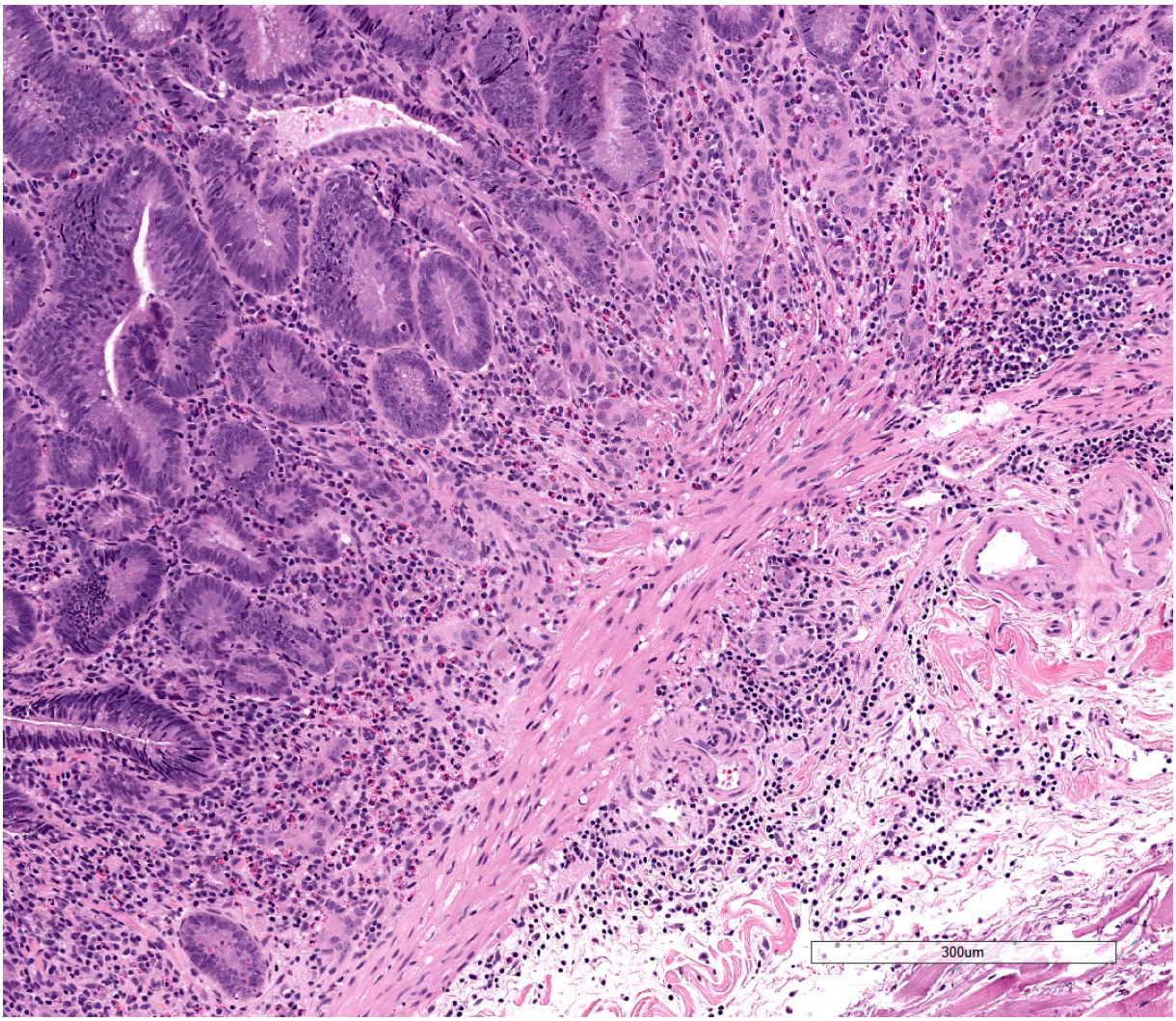


**Figure 2**. H&E

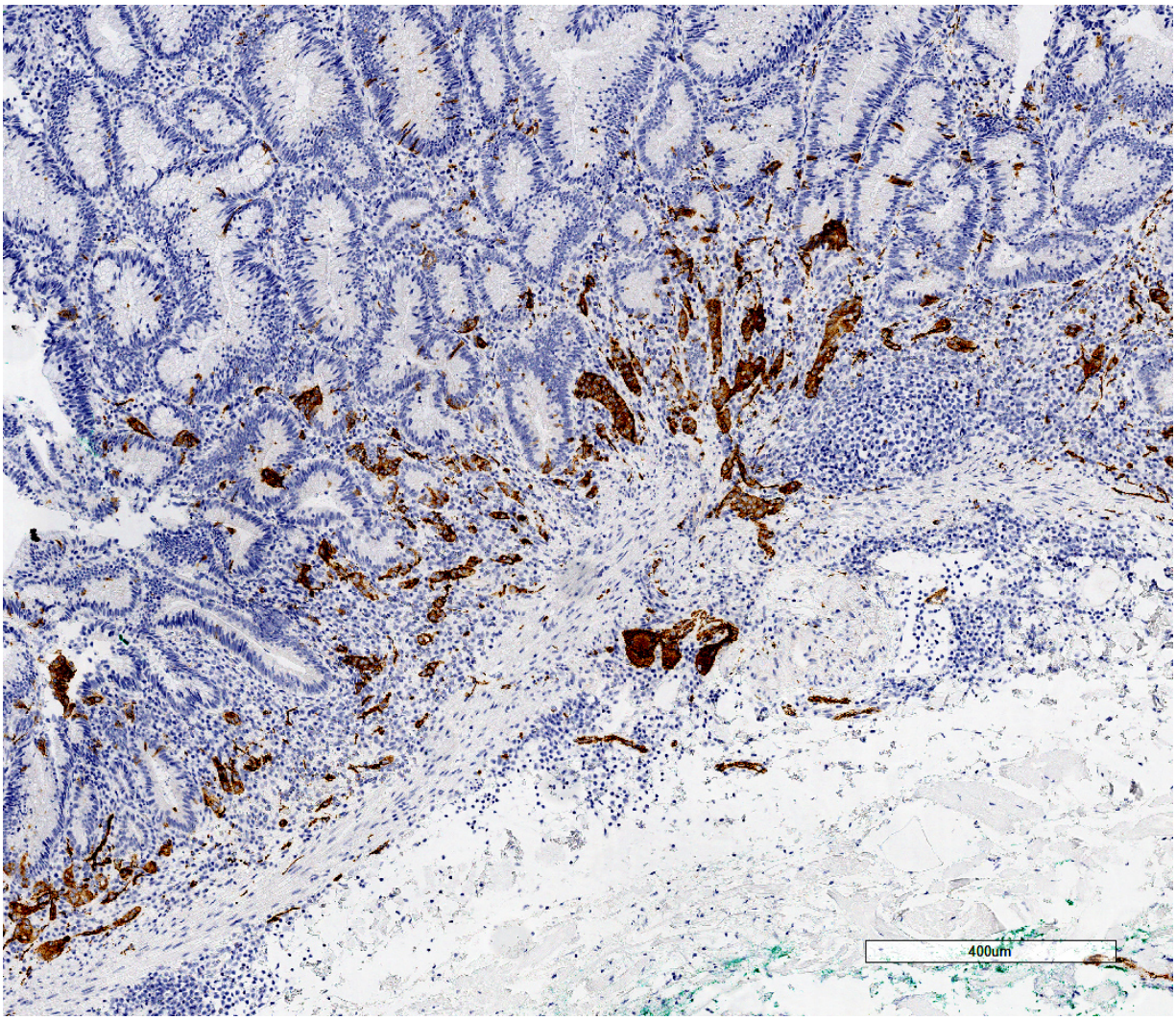


**Figure 3**. Synaptophysin immunohistochemistry

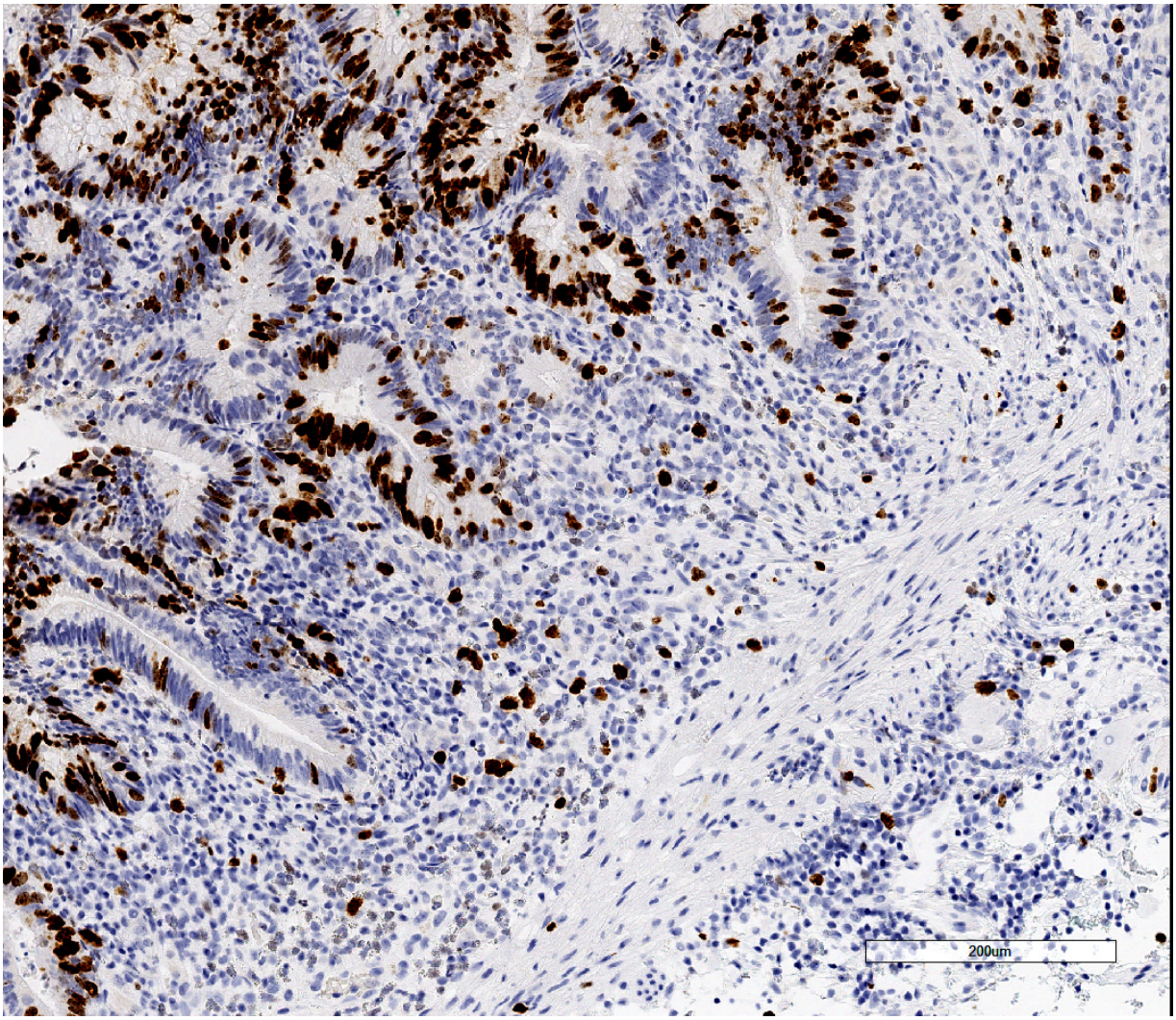


**Figure 4**. Ki-67 immunohistochemistry.

## What is your diagnosis?

A.) Tubulovillous adenoma (TVA)
B.) Tubular adenoma with squamous morules
C.) Neuroendocrine tumor
D.) Adenocarcinoma
E.) Composite intestinal adenoma-microcarcinoid (CIAM)

## Correct answer is: E.

## Discussion:

**What is Composite Intestinal Adenoma-Microcarcinoid**?
In contrast to grossly evident neuroendocrine tumors of the colon, the Composite Intestinal Adenoma-Microcarcinoid (CIAM) is an uncommon colorectal lesion predominantly consisting of a classic adenoma interwoven with microscopic foci of neuroendocrine-type cells (1-4).

**Histologic features of CIAM**
The adenomatous component of the CIAM is typically a tubular or tubulovillous adenoma of variable size, with some demonstrating mucosal prolapse or desmoplastic-like fibrosis (2). The "microcarcinoid" component represents a small proportion of the polyp. No sharp demarcation between the glandular component and the microcarcinoid component is seen. Architecturally, the microcarcinoid component is arranged in multifocal nests or cords near the base of the adenomatous crypts in the basal lamina propria (1-3). "Drop-off" of neuroendocrine cells from the base of the adenomatous glands may be seen, and the surrounding stroma may mimic desmoplasia (3). In polyps with mucosal prolapse, the clusters of microcarcinoid cells may be enveloped by a fibromuscular proliferation worrisome for an infiltrating adenocarcinoma. Rarely, the microcarcinoid cells breach the muscularis mucosae, which can also raise concerns for invasion. Cytologically, the neuroendocrine cells are small and bland with pale, granular cytoplasm. The nuclei are monotonous and round with finely stippled chromatin and inconspicuous nucleoli. Concerning features such as pleomorphism, hyperchromasia, mitotic figures, and necrosis are usually absent.

The histological origin of the CIAM is not clear. Proposed origins include a common precursor cell with divergent differentiation along adenomatous and neuroendocrine lines (6); a collision of two distinct, separately arising entities; or metaplasia secondary to chronic injury of the adjoining adenoma.

**Immunohistochemical Profile of the Microcarcinoid Component of CIAM**
The microcarcinoid component is immunoreactive for synaptophysin, with variable reactivity to chromogranin A and CD56 (1-4). The microcarcinoid component also tends to display strong and diffuse nuclear β-catenin reactivity (1). Some microcarcinoids may demonstrate squamoid differentiation with variable reactivity to p63 and/or CK5/6 (1). The low mitotic rate observed in the H&E stain is confirmed by Ki-67 nuclear proliferative index staining <2%. The microcarcinoid should demonstrate wild-type p53 immunostaining (1).

**Clinical Outcome**
Gastric microcarcinoids are well-recognized in the setting of type A gastritis (5). CIAMs, in contrast, are relatively rare. Although their clinicopathologic characteristics are less well understood, CIAMs appear to have a favorable clinical outcome. Thus, surgical resection is not routinely considered if the lesion has been completely excised endoscopically. However, resection is still the treatment of choice in cases of submucosal invasion and increased proliferative activity.

**References**:

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