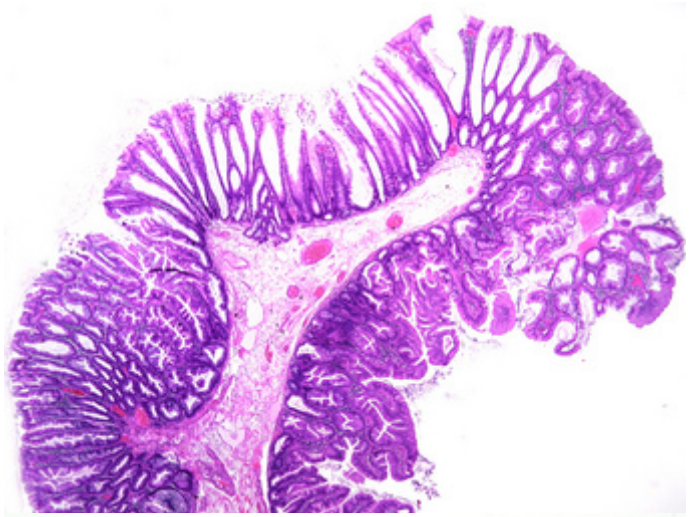
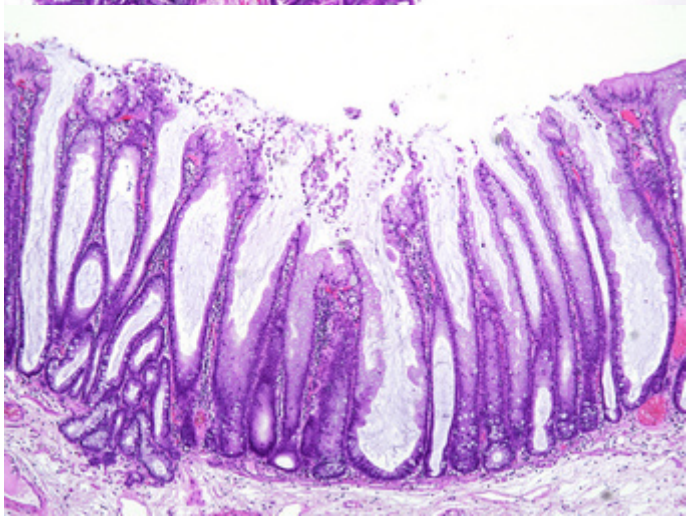
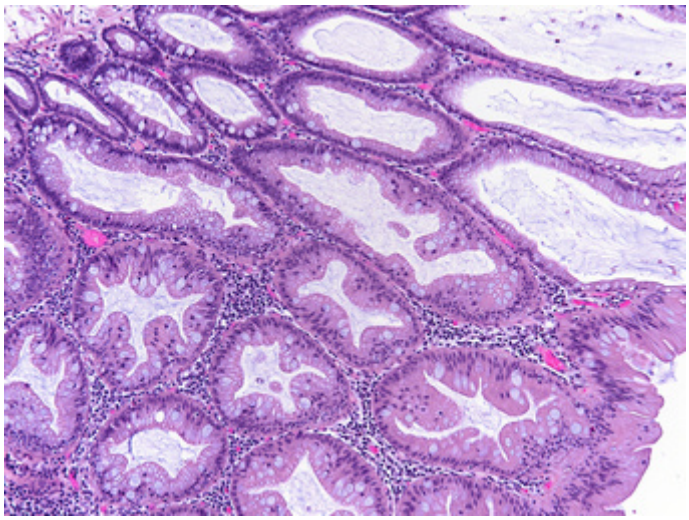
November 2021

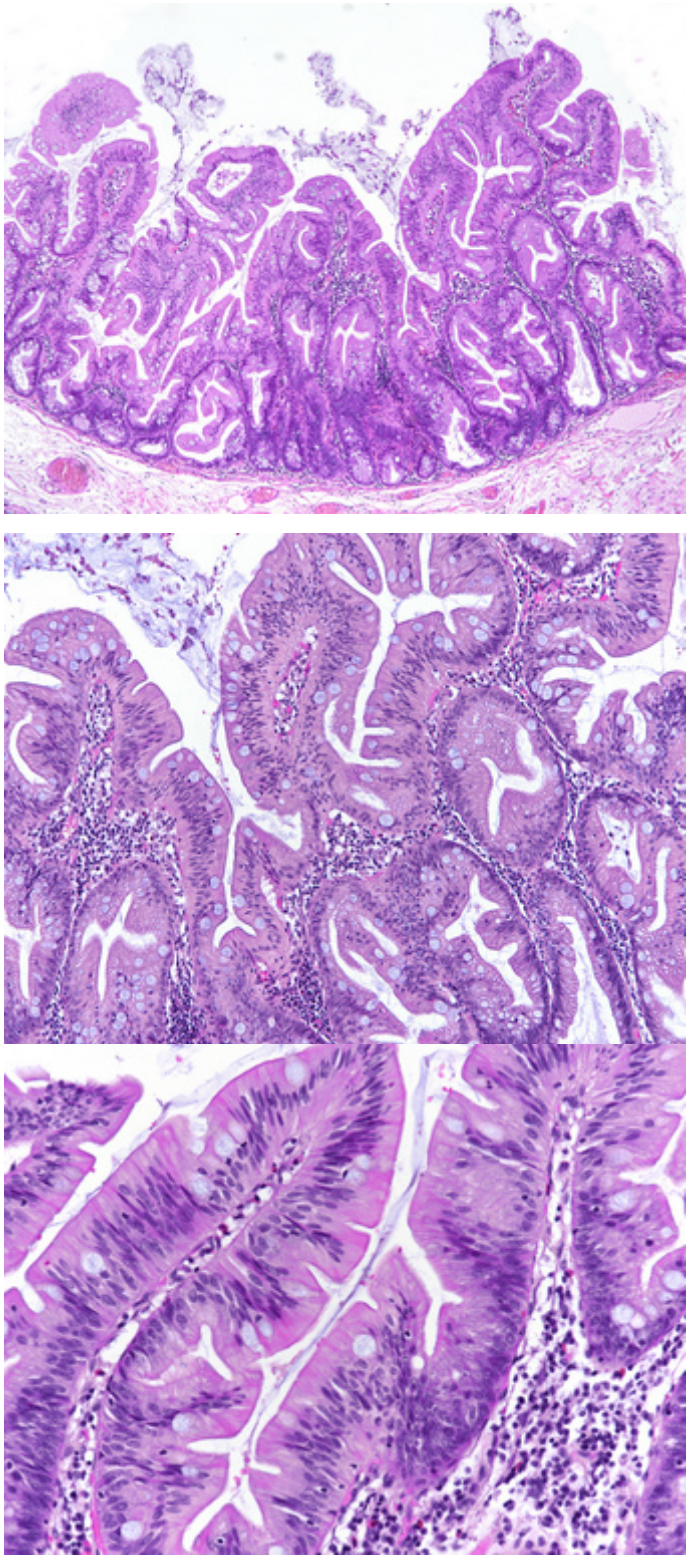
Caecal polyp in a 50- year- old male.

What is your diagnosis?









Diagnosis:

Flat-type traditional serrated adenoma (TSA) arising from a precursor lesion.

Comment:

The caecal polyp is formed by architecturally distorted serrated crypts (Panel A). The crypts show deep serrations and basal dilatation with lateral growth along the muscularis mucosae. Focal mucosal herniation is observed (Panel B). The crypts also show areas of transition into a distinctive morphology where the crypts have slit-like serrations, lined by tall columnar cells with intensely eosinophilic cytoplasm and pencillate nuclei (Panel C-E). Occasional abortive ectopic crypts are seen (Panel F). No overt dysplasia or malignancy observed.

Serrated lesions of the colorectum are characterized histologically by a serrated (or saw-toothed) appearance of the crypt epithelium and are the precursors of one-third of colorectal cancers. They are currently classified by the WHO into three general categories: hyperplastic polyp (HP), sessile serrated lesion (SSL) and traditional serrated adenoma (TSA). Traditional serrated adenomas (TSAs) are the least common of the three serrated colonic polyps, accounting for only about 5% of serrated polyps.

SSL and TSA are premaligant lesions, but the former is the principle serrated precursor of colorectal cancers. TSA has a protuberant exophytic configuration with a complex villous growth pattern, found predominantly in the distal colon (70%). Some TSA demonstrate a flat growth pattern (flat TSA), defined as polyps being elevated less than twice the height of the normal mucosa and lack prominent villiform projections. They are typically found in the proximal colon. The other two morphological variants of TSA are filiform and mucin-rich type. The morphological criteria for diagnosing a TSA include typical cytology (ie. elongated, narrow pencillate nuclei with delicate dispersed chromatin and cytoplasmic eosinophilia), ectopic crypt foci (ECF), and typical slit-like clefted serration. At least two of these three features are required (with at least one of these features being present in 50% of the polyp) to render a diagnosis of TSA. However, it is important to remember that ECF is rarely seen and is not necessary for the diagnosis of flat TSA.

TSA arises via three molecular pathways. The first mechanism is via BRAF mutation and CpG island methylation (CIMP) resulting in the CIMP-high (CIMP-H) phenotype. These TSA tend to be right sided, associated with a precursor microvesicular HP or SSL. The second pathway is mediated through KRAS mutations and these are CIMP-low (CIMP-L) TSA. These TSA are usually located in the left colon and are not associated with another precursor serrated polyp. Both these pathways result in microsatellite stable colorectal carcinoma with retention of MLH1 staining. The third pathway consist of both BRAF and KRAS wild type and arise by an unknown molecular events.

An adjacent precursor polyp (hyperplastic polyp or sessile serrated lesion) is found in as many as 50% of TSA. These precursor components are usually seen as a discrete area with clear morphological distinction from the TSA component, either at the edge of, or underlying the TSA. Bettington et al noted that 38% of the 200 TSAs in their series were accompanied by HP/SSL, with the vast majority being SSL. Interestingly, this paper also highlights the fact that flat TSA are BRAF mutant and arises in sessile serrated lesion.

It is important to distinguish between traditional serrated adenoma arising in a sessile serrated lesion from a sessile serrated lesion with dysplasia. This is because the later has a significantly greater degree of malignant risk than the former. Four types of dysplasia have been described to occur in sessile serrated lesions. Among these, the serrated dysplasia is by definition high grade and characterized by closely packed small glands with abundant eosinophilic cytoplasm that occupy the full thickness of the mucosa. Notably, serration is less prominent. In contrast, ordinary traditional serrated adenomas arising in a sessile serrated lesion do not have these high grade features.

Like in SSL, areas of overt dysplasia can also be observed in TSA, which are the intestinal and serrated type dysplasia. These features are different from the senescent changes of typical TSA cell (which was also highlighted by Bettington et al). These polyps probably represent a more advanced lesion and should be reported separately when high- grade dysplasia is present. At the moment, assigning a grade or dividing dysplasia into serrated versus conventional types has no clinical utility.

For further reading:

- Mark L Bettington, Neal I Walker, Christophe Rosty, Ian S Brown, Andrew D Clouston, Diane M McKeone, Sally-Ann Pearson, Kerenaftali Klein, Barbara A Leggett and Vicki LJ Whitehall, A clinicopathological and molecular analysis of 200 traditional serrated adenomas. Modern Pathology 2015; 28: 414–427
- Runjan Chetty, Traditional serrated adenoma (TSA): morphological questions, queries and quandaries. J Clin Pathol 2015; 69: 6-11

- Cheng Liu, Neal I Walker, Barbara A Leggett, Vicki LJ Whitehall, Mark L Bettington, Christophe Rosty. Sessile serrated adenomas with dysplasia: morphological patterns and correlations with MLH1 immunohistochemistry. Mod Pathol. 2017; 30: 1728-1738
- Aoife J McCarthy, Stefano Serra, Runjan Chetty, Traditional serrated adenoma: an overview of pathology and emphasis on molecular pathogenesis. BMJ Open Gastro 2019; 6: e000317. doi: 10.1136/ bmjgast-2019-000317
- Rish K. Pai, Mark Bettington, Amitabh Srivastava, Christophe Rosty, An update on the morphology and molecular pathology of serrated colorectal polyps and associated carcinomas. Modern Pathology 2019; 32: 1390–1415

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