The cutting edge of serrated polyps: a practical guide to approaching and managing serrated colon polyps CME

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The most common colonic polyps include the conventional adenomas (tubular, tubulovillous, and villous adenomas) and serrated polyps. Serrated polyps account for as many as 36% of colonic polyps, and, until 1996, the hyperplastic polyp was the only recognized serrated polyp.[1] Today, we recognize the term *serrated polyp* as a general term describing a heterogeneous family of polyps with distinct molecular underpinnings, clinicopathologic features, and a varied capacity for malignant potential (Tables 1 and 2). In this review, the salient clinicopathologic features of serrated polyps and practical management recommendations are discussed.

CLINICOPATHOLOGIC PRESENTATION

Hyperplastic polyp

The hyperplastic polyp is the original founding member of the serrated polyp category. Hyperplastic polyps are the most common serrated polyp, comprising more than 75% of serrated polyps and 28% to 42% of all colonic polyps detected on endoscopy.[2-5] In autopsy studies, estimates of hyperplastic polyp prevalence are widely variable, ranging from 13.4% to 68% of all colonic polyps.[6-8] The median age of patients found to have hyperplastic polyps is 59 years, and these polyps are more commonly found in men.[3-5,9,10]

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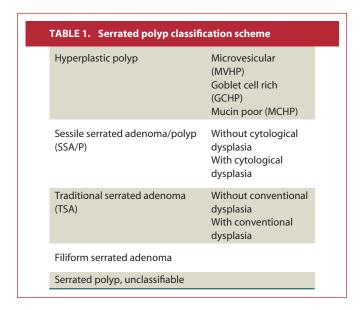
Endoscopically, these polyps appear smooth, pale, and smaller than 5 mm with a regional preference for the distal colon (Fig. 1). Hyperplastic polyps tend to flatten or depress when the colon is fully distended by air insufflation, adding to the difficulty in detection.[11] The diminutive size (<5 mm) and color of the hyperplastic polyp has endoscopic overlap with an inverted diverticulum and a collapsed mucosal fold. A distinguishing endoscopic feature favoring the hyperplastic polyp is a papillary or stellate (type II) pit pattern on magnification endoscopy, although this tool is not routinely used in clinical care.[12,13]

Importantly, the hyperplastic polyp's characteristic diminutive size and left-side predilection provide important points of contrasts from the remaining serrated family members. Therefore, the location and size of the polyp are extremely helpful for the clinician and pathologist, and both should be documented on the pathology requisition. To illustrate the importance of polyp location and size descriptors, recent expert consensus opinions indicate that all proximal serrated polyps should be completely removed, and all proximal serrated polyps larger than 10 mm diagnosed as hyperplastic polyps should be clinically managed as sessile serrated adenomas/polyps (SSA/Ps) to ensure proper clinical management (see also the clinical management subsection).[14] Similarly, the polyp location and size can provide important information for the pathologist because, unfortunately, histologic overlap can exist between the hyperplastic polyp and the other serrated family members, particularly the SSA/P. Moreover, limited assessable biopsy material, tangential embedding, histologic staining artifact, and/or cautery artifact can further complicate the diagnostic process. In these challenging cases, the polyp location and size serve as essential elements of the diagnostic process: a diagnosis of an SSA/P would be favored in a proximal large serrated polyp, and a diagnosis of a hyperplastic polyp would be favored in a distal, diminutive polyp, for example.

In 2003, the hyperplastic polyps were subclassified into 3 categories: microvesicular hyperplastic polyps (MVHPs), goblet cell–rich hyperplastic polyps (GCHPs), and mucin-poor hyperplastic polyps (MPHPs) (Fig. 2).[15] The majority of hyperplastic polyps, especially those in the right side of the colon, are MVHPs. Key histologic features include a "saw-tooth" or serrated surface, stellate-shaped crypt lu-

TABLE 1. Serrated polyp classification scheme	
Hyperplastic polyp	Microvesicular (MVHP)
	Goblet cell rich (GCHP)
	Mucin poor (MCHP)
Sessile serrated adenoma/polyp (SSA/P)	Without cytological dysplasia
	With cytological dysplasia
Traditional serrated adenoma (TSA)	Without conventional dysplasia
	With conventional dysplasia
Filiform serrated adenoma	
Serrated polyp, unclassifiable	

mens, vesicular or "frothy" eosinophilic cytoplasm, and narrow and uniform crypt bases. A thickened subepithelial collagen table and increased neuroendocrine cells can be additional helpful diagnostic clues.[14] In contrast, GCHPs are found almost exclusively in the left side of the colon, exhibit surface serrations less prominently than in MVHPs, and contain cells with large, distended goblet cells with essentially no intervening enterocytes. The GCHPs may be underrecognized because of the more subtle nature of the histologic findings. Last, MPHPs are thought to account for less than 1% of hyperplastic polyps. MPHPs show reactive and regenerative features such as mucin loss, nuclear hyperchromasia, and goblet-cell loss. The MPHP is a controversial entity that some consider simply a reparative form of the MVHP rather than its own true diagnostic entity. At this point, the subclassification of hyperplastic polyps is for academic purposes only because no clear clinical significance has been established. Most pathologists use hyperplastic polyp as a general term without specific subclassification of MVHP, GCHP, and MPHP.

Traditional serrated adenoma and filiform serrated adenoma

The traditional serrated adenoma (TSA) was introduced in 1990 and comprises less than 1% of all colonic polyps.[9,16] This polyp was initially termed "serrated adenoma," but this nomenclature is now strongly discouraged because it lacks clarity and is too easily confused with the SSA/P. In a large case series of 709 patients with TSAs, the median patient age was 63 years and there was no difference in the rates of TSAs found in men or women.[4] Endoscopically, the TSA is usually left-side predominant, pedunculated, and larger than 5 mm (Fig. 1). As such, the polyp location, configuration, and size are also important clues to the diagnosis. The endoscopic appearance of the TSA can resemble the conventional adenoma based on the

granulonodular and lobular appearance.[17] On high-definition endoscopy, however, the TSA often exhibits combined papillary or stellate (type II) and/or tubular (short, type IIIS; long, type IIIL) pit patterns, patterns not commonly seen in combination in the conventional adenoma.[18,19] Histologically, key features of a TSA include a serrated architecture, cytoplasmic eosinophilia, ectopic crypt foci (small, superficial invaginations of the surface epithelium that form cryptlike structures lacking a connection to the muscularis mucosae), and uniform pencillate nuclei with pseudostratification.[16,20]

The precise classification of dysplasia in the TSA is somewhat controversial. Some argue that the TSA's low mitotic count and Ki-67 proliferation index are evidence of a senescent state with a low proliferation capacity.[20,21] However, in the initial report, 37% of TSAs were associated with significant histologic dysplasia and 11% were associated with intramucosal carcinoma, underscoring the malignant potential of these lesions.[16] As such, the World Health Organization (WHO) classification regards the TSA without conventional dysplasia as having malignant potential similar to other low-grade dysplastic lesions, a viewpoint that is in parallel with the SSA/P without cytologic dysplasia (see discussion below). In both cases of the TSA without conventional dysplasia and the SSA/P without cytological dysplasia, the term adenoma has evolved to become synonymous with malignant potential rather than histologic dysplasia. This differs from most other "adenomas" in the GI tract that are synonymous with histologic low-grade dysplasia (ie, the conventional tubular adenoma, tubulovillous adenoma, and villous adenoma all demonstrate histologic low-grade dysplasia by definition). Morphologically, conventional dysplasia refers to elongated cells with basophilic cytoplasm, nuclear pseudostratification, and coarse chromatin. When conventional dysplasia is seen in the TSA, the terminology "TSA with conventional (low- or high-grade) dysplasia" is advised. The dysplasia can also be of the serrated dysplasia variety, which generally refers to smaller cells with eosinophilic cytoplasm, enlarged rounded nuclei, open chromatin, and prominent nucleoli. At this point, there is no clinically important distinction between conventional versus serrated dysplasia.

In 2007, the filiform serrated adenoma was described, and this lesion is thought to be a variant of the TSA.[22] Although too few reports are available for meaningful prevalence data, these lesions seem to share similar gross and morphologic features with the TSA: serrated architecture, cytoplasmic eosinophilia, ectopic crypt foci, and uniform pencillate nuclei with pseudostratification (Fig. 1).[22,23] However, features distinguishing the filiform serrated adenoma from the TSA include more prominent elongated projections, a larger size, and a higher incidence of high-grade dysplasia and invasive adenocarcinoma. Interestingly, a case of so-called filiform serrated polyposis was recently reported in a pa-