Serrated colorectal polyps and polyposis

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Abstract

Serrated polyps represent a heterogeneous group of lesions, some of which have well-documented malignant potential. The histological classification of serrated polyps has evolved over the last two decades to recognize three major subtypes: hyperplastic polyp, sessile serrated adenoma/polyp and traditional serrated adenoma. Sessile serrated adenoma/polyp remains under-diagnosed while it represents up to 25% of all serrated polyps and is the precursor lesion to colorectal carcinoma evolving though the serrated neoplasia pathway with *BRAF* mutation and CpG island methylator phenotype. Pathologists need to be aware of the World Health Organisation criteria to correctly diagnose each entity as patient management guidelines are based upon the use of this classification. Serrated polyposis is an under-recognized syndrome with unknown genetic cause conferring an increased risk of colorectal carcinoma. Pathologists have a pivotal role in identifying these patients who should undergo yearly surveillance colonoscopy.

Keywords hyperplastic polyp; serrated neoplasia pathway; serrated polyp; serrated polyposis; sessile serrated adenoma; traditional serrated adenoma

Introduction

The vast majority of colorectal carcinomas (CRC) develop from benign precursor polyps, which can be detected and removed by appropriate screening colonoscopy programs. Colorectal polyps comprise a wide range of neoplastic and non-neoplastic lesions with various risks of malignant transformation. The majority of neoplastic colorectal polyps fall into one the two following categories: conventional adenomas (tubular, tubulo-villous and villous adenomas) and serrated polyps. Over the last 20 years, new subtypes of serrated polyps associated with malignant potential have been recognized from what was collectively known as hyperplastic polyps in the past. As often occurs when new entities are described, this led to confusion, misdiagnosis and under-recognition among pathologists. In an attempt to solve these issues, the 4th edition (2010) of the World Health Organisation (WHO) classification defined new histological criteria for all currently recognized subtypes of serrated polyps: hyperplastic polyp (HP), sessile serrated adenoma/polyp (SSA/P) and traditional serrated adenoma (TSA). These criteria should be universally applied to ensure standardized diagnosis and thus the reliable application of surveillance colonoscopy protocols.

This review outlines the current knowledge on the histological diagnosis of serrated polyps of the large intestine and addresses the impact of these diagnoses on patient management. We also address the main features of molecular pathways involved in the malignant transformation of serrated polyps. Serrated polyposis is also be discussed with an emphasis on the role of pathologists in the diagnosis of this under-recognized syndrome.

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Histological diagnosis of serrated polyps

The common morphological feature of serrated polyps is the 'saw-tooth' appearance of the crypts, which occurs due to decreased apoptosis and increased senescence of the epithelial cells. The 4th edition of the WHO classification book published in 2010[1] subcategorized serrated polyps into three groups: HP, SSA/P and TSA. The morphological aspects that characterizes each group are the result of differences in the location of the proliferation zones within the colonic crypts.[2,3] The main characteristics of each serrated polyp subtype are summarized in Table 1.

Hyperplastic polyps

HP is the most common subtype, representing 70–80% of serrated polyps. Forsberg et al. reported that 21% of asymptomatic individuals aged 19–70 years had at least one HP in a Swedish population-based prospective colonoscopy study.[4] In HP, the proliferation zone is normally located at the base of the crypts with preserved maturation of epithelial cells symmetrically along the crypts towards the luminal surface. Approximately 75% of HPs are located in the distal colon or rectum as small (<10 mm; usually 1–5 mm) sessile lesions with insignificant malignant potential.[5] However, HPs can also be detected in the proximal colon, possibly with increased frequency now that some gastroenterologists use enhanced endoscopic procedures that allow better detection of small sessile polyps compared with white light endoscopy. The possibility that some of these proximal lesions may progress to SSA/P and to malignancy is still unknown and cannot be excluded. The common underlying feature of HP is the normal architecture of elongated and straight crypts with serration restricted to the upper compartment.[6] Cytological dysplasia is absent. One caveat to this definition is that the crypt architecture can sometimes appear abnormal displaying dilatation of the bases when mucosal prolapse changes are superimposed (Figure 1). Often, there is a mild thickening of the subepithelial basement membrane compared to the adjacent normal mucosa. Further subdivision of HP into microvesicular HP and goblet cell HP is mostly of academic interest and does not need be included in pathology reports. More importantly, one should consider goblet cell HP when a biopsy of a lesion described as a polyp by endoscopists looks close to normal mucosa on multiple levels. Changes in goblet cell HPs are very mild, characterized by slight crypt elongation with numerous

Summary of pathological and molecular characteristics of serrated polyps

	Microvesicular HP	Goblet cell HP	TSA	SSA/P	SSA/P with cytological dysplasia
Proportion	40–50%	20–30%	2–5%	15–25%	2–5%
Predominant colonic location	Distal	Distal	Distal	Proximal	Proximal
Pathological features	Normal architecture with elongated straight crypts and upper serration Microvesicular mucin, no dysplasia	Normal crypt architecture with subtle surface serration Goblet cell mucin, no dysplasia	Exophytic (distal) or sessile (proximal) Villiform configuration with ectopic crypt formations Eosinophilic cells with pencillate nuclei Conventional dysplasia can arise	Abnormal architecture with dilated crypt base and basal serration Dystrophic goblet cells in crypt base, no dysplasia	SSA/P features with sharp demarcation to dysplasia Conventional intestinal type or serrated type dysplasia
Most common molecular alteration	*BRAF*^{V600E} mutation (70–80%)	*KRAS* mutation (50%)	*BRAF*^{V600E} mutation (50%) *KRAS* mutation (30%)	*BRAF*^{V600E} mutation (70–80%) CIMP-high	*BRAF*^{V600E} mutation (80–100%); CIMP-high; MSI or *TP53* alteration

HP: Hyperplastic polyp; SSA/P: Sessile serrated adenoma/polyp; TSA: Traditional serrated adenoma; CIMP: CpG island methylator phenotype; MSI: Microsatellite instability.

Table 1

goblet cells and subtle serration at the surface that can be easily overlooked (Figure 2). The significance of goblet cell HP is unclear; some authors have suggested that it may represent the precursor lesion of TSA.[7] On the other hand, the upper serration in microvesicular HP is more obvious and the presence of epithelial cells with microvesicular mucin contrasts with the normal adjacent mucosa. A mucin-poor subtype of HP with reactive cytological atypia has also been described but the significance of this rare lesion is unknown and is likely to represent an injured microvesicular HP.[2]

Sessile serrated adenoma/polyp

The prevalence of SSA/P seems to have increased over the last years as gastroenterologists and pathologists alike became more aware of this entity. In a recent study reviewing the histology of 6340 colorectal polyps from a single pathology practice, SSA/P represented 12.1% of all polyps and 25.3% of serrated polyps.[8] However, SSA/P remains under-diagnosed in some pathologist communities due to a lack of awareness of the lesion, when it will be misdiagnosed as HP.[9] In contrast to HP, SSA/P displays crypt architectural alteration following the shift of the proliferation zone from its normal location at the base to the side of the crypts. This results in asymmetrical maturation of epithelial cells towards both the crypt surface and base.[2] The crypts then develop abnormal shapes with dilatation at the bases often in an L-shaped or inverted T-shaped configuration (Figure 3). An expanded proliferation zone is commonly found in the upper part of the crypts and superficial mitoses may sometimes be seen. If cross-sectioned at the level of an active proliferation zone, the appearance may cause misdiagnosis as dysplasia. SSA/P is more frequently found in the proximal colon and tend to be >10 mm in size (Figure 4). However, small SSA/Ps are increasingly recognized and SSA/Ps distal to the transverse colon can also occur.

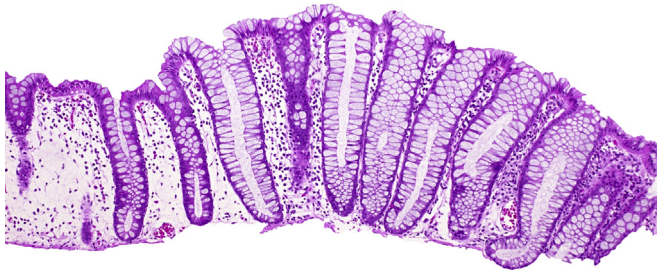

Figure 1 Goblet cell hyperplastic polyp with elongated crypts and increased number of goblet cells compared with the normal mucosa on the left part of the image.

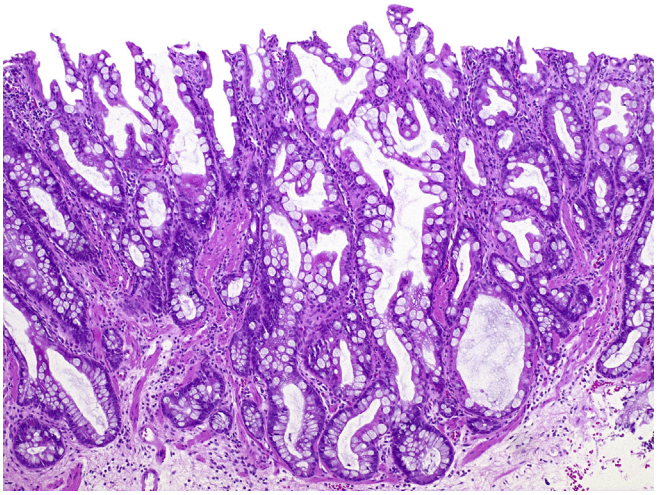

Figure 2 Microvesicular hyperplastic polyp with mucosal prolapse changes showing more complex crypt serration and distortion than the usual hyperplastic polyp, and smooth muscle in the lamina propria.