Serrated polyps

Colorectal carcinogenesis and clinical implications

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CHAPTER 11

Serrated Polyposis Syndrome; a silent killer when undetected

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CHAPTER 11

This report describes the clinical course of a 59-year-old woman who was diagnosed with metachronous colorectal cancer (CRC). She was diagnosed with a T3 N0M0 sigmoid carcinoma in 2002 (at the age of 46) for which she underwent a sigmoid resection and received follow-up at another hospital. Follow-up colonoscopies in 2003 and 2004 did not show any colonic abnormalities, while colonoscopy in 2006 showed a flat polyp in the cecum, which was biopsied. Histopathologic examination revealed a sessile serrated polyp with a focus of dysplasia and surveillance colonoscopy was advised in 3 years. At a subsequent ileocolonoscopy in 2009, no abnormalities were detected in the cecum or elsewhere in the colon and a 5-year surveillance interval was recommended. During colonoscopy 5 years later (2014), a cecal tumor was detected. Further inspection of the colon did not reveal any other lesions. The patient underwent a right-sided hemicolectomy; histopathologic examination of the resection specimen showed a T2 N0 Mx adenocarcinoma. Furthermore, seven serrated polyps were identified, of which at least five were larger than 10mm.

The patient was referred to a clinical genetics outpatient clinic elsewhere for analysis of an underlying hereditary cancer syndrome. The clinical geneticist accurately analyzed the family history, which was negative, and requested molecular analysis on the tumor tissue of both CRCs. The tumor resected in 2002 was microsatellite stable and showed normal expression of the mismatch repair proteins (MLH1, MSH2, MSH6, and PMS2). The tumor resected in 2014 was microsatellite instable and showed loss of function of both MLH1 and PMS2 due to promoter hypermethylation of the MLH1 gene, indicating that this carcinoma had developed via the serrated neoplasia pathway. On the basis of these findings, the patient was diagnosed with serrated polyposis syndrome. Subsequent DNA analysis showed no germline mutation in the MutYH gene. The patient was referred for a second-look colonoscopy, which was performed at our center and demonstrated 14 sessile serrated polyps and 2 hyperplastic polyps up to 15mm in size, which were confirmed by histopathology (Figure 1). Surveillance colonoscopy within 1 year was advised.

Serrated polyposis syndrome (SPS), clinically characterized by multiple serrated polyps throughout the colorectum, is accompanied by an increased lifetime risk of CRC. A recent large retrospective study demonstrated that, once cleared from all polyps and under close surveillance, CRC risk in these patients is only moderately increased. However, most cases of SPS remain unrecognized and as a consequence patients do not receive proper surveillance intervals, significantly increasing their risk of developing CRC. For this reason it is important that endoscopists become acquainted with the diagnosis, risk, and optimal treatment strategies for SPS.
Figure 1 | Representative images of sessile serrated polyps that were missed during the initial colonoscopy. A) High resolution white-light endoscopy (HR-WLE) image of the transverse colon showing sessile serrated polyps in the left and right upper quadrants; B) Narrow-band imaging (NBI) of the polyp situated in the left upper quadrant showing the characteristic appearance with a covering mucus cap; C) HR-WLE image of a large sessile serrated polyp located on a fold (often erroneously described as a thickened fold); D) The corresponding NBI image showing typical features of a sessile serrated polyp including clouded surface, indistinct borders, irregular shape, and dark spots inside the crypts.
REFERENCES


