Improving the Accuracy of Serrated Colon Polyp Designation

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I. ABSTRACT

Background: Serrated polyps are among the common polyps of the large bowel. In the past decade, the focus on sessile serrated polyp (SSP) has been increased as it has proved that untreated SSP is associated with substantial increased risk of developing colon cancer. The microscopic diagnosis can be challenging due to overlapping features with hyperplastic polyps, which can cause misdiagnosis and inappropriate follow up of the patients.

Methods: The purpose of this study is to assess the effect of educational sessions on appropriate designation of sessile serrated polyps. We re-evaluated hyperplastic polyps for two years and repeated the re-evaluation after few educational sessions.

Results: During the first phase, we evaluated 365 hyperplastic polyps and reclassified 60 (16%) of them as SSP. We also found 11 tubular adenoma, 2 traditional sessile serrated adenoma and 8 mucosal tags. After the education, in phase 2, we reviewed another 191 hyperplastic polyps and reclassified 16 (8%) of them as SSP. We found 3 tubular adenoma, but no other polyps. Most of these polyps (67%) were 0.5 cm in diameter or larger.

Conclusion: Our study shows that the educational intervention was successful in increasing the accurate designation of SSP and improved that significantly.

Key words: Sessile serrated polyp, hyperplastic polyp, MLH1
II. INTRODUCTION

The serrated neoplasia pathway accounts for up to 30% of all sporadic colorectal cancers\(^1\), the third common cancer after breast/prostate and lung.\(^2\) Sessile serrated polyp/adenoma (SSP) is the leading precursor lesion for the development of the colorectal carcinoma through the serrated pathway.\(^3\)\(^-\)\(^4\) In SSP, the proliferation zone is to the side of the crypts, unlike the base in hyperplastic polyps, resulting in maturation of epithelial cells laterally, towards the surface and the base, leading to crypt base dilatation.\(^5\) Figure 1 shows a hyperplastic polyp with serration in top half and narrow crypts in the lower third. The crypt in the lower part may also have elongated hyperchromatic nuclei. Figure 2 shows a SSP with branching of crypts, dilatation of base of crypts and peculiar growth pattern of the deeper crypts adjacent to muscularis mucosa.

The morphologic distinction between serrated polyps can be challenging and some authors suggest using ancillary studies, such as Ki67, to make this distinction. Studies show that a substantial portion of these lesions harbor inactivation of the mismatch repair gene MLH1 by promoter hypermethylation to become dysplastic.\(^6\)\(^,\)\(^7\)

Recently, a retrospective study has shown that prevalence of detecting SSP in a screening population is increased to 8.1% if a colonoscopist with a high lesion detection rate and an experienced pathologist collaborate.\(^8\) In this study, we assessed the effect of education on the accurate classification of the SSP.

III. MATERIAL AND METHOD

A gastrointestinal pathologist re-evaluates the hyperplastic polyps of the colon that were diagnosed at our tertiary hospital over a two-year period (between 2/1/2013 and 2/1/2015) by 8 pathologists to determine if any of these polyps should be reclassified as SSP. Our practice is a mixed general/subspecialty model. Subsequently, several slide review sessions were performed for our practicing pathologists on the pitfalls of the SSP histologic assessment with the emphasis on the broader superficial part of a hyperplastic polyp compare to presence of dilated/boot-shaped glands superficial to the muscularis mucosa of a SSP to reach the correct diagnosis. During the second phase of our study (from 2/1/2016 to 2/1/2017), we looked at the cases that were diagnosed as hyperplastic polyps over one year after the educational sessions. We compared the re-evaluation rates before and after the education.

During both phases, the H&E stained glass slides were re-evaluated and pathology reports were reviewed to document age and sex of the patient, location and size of the polyps. We used the data to perform statistical analysis.
IV. RESULTS

During phase 1, we reviewed 365 hyperplastic polyps from 302 patients [160 (53%) women, 142 (47%) men]. Forty-five patients had more than one polyp. The patients were between 26 and 91 years old with a mean of 57 years old. The polyp size was from 0.1 to 1.3 cm. We re-evaluated 365 hyperplastic polyps and reclassified 60 of them (18%) as SSP. We also found 11 tubular adenoma, 2 traditional serrated adenoma and 8 mucosal tags.

During phase 2, we reviewed 191 hyperplastic polyps from 157 patients (102 women and 89 men). Twenty-one patients had more than one polyp. The patients were between 25 to 91 years old with an average age of 57 years. The polyp size was from 0.1 to 1.3 cm. The majority of hyperplastic polyps were resected from rectosigmoid (67%) followed by transverse (14%) and descending colon (10%).

After careful re-evaluation of H&E stained glass slides, 16 (8%) polyps were reclassified as SSP (figure 3). We also found 3 tubular adenomas. Ten (62%) of the SSP were in the distal colon (descending, and sigmoid colon, and rectum). Seven were smaller than 0.4 cm in diameter, while 9 polyps (56%) were 0.5 cm in diameter or larger. The largest polyp was 1 cm in the largest dimension (table 1). In both phases, the gastroenterologists were informed about the change in diagnoses, so the patients’ surveillance would be modified.

The statistical analysis was done using Cox & Snell R2 or Nagelkerke R2 methods. Women were 3.75 times (p=0.04) more likely to have sessile serrated polyp than men. Increasing size was associated with an increased likelihood of sessile serrated polyp (p=0.01), and descending colon was associated with a decrease in the likelihood of exhibiting SSP, but it was not satisfactory significant (p=0.07).

V. DISCUSSION

Hyperplastic polyp is one of the common polyps of the large bowel. Sessile serrated polyp (SSP) was introduced in 1996 as a subset of serrated polyps. Although SSP had premalignant risk, it was not widely accepted. As more information became available, the rate of diagnosis was increased. An initiating molecular event in this pathway is BRAF activation, which is seen in 80% of SSP. SSPs also have frequent hypermethylation of CpG islands in the promoter region of cancer-associated genes (CIMP: CpG island methylator phenotype). At the same time, a group of sporadic colon cancers with deficient DNA mismatch repair (dMMR) have MLH1 hypermethylation and high BRAF V600E mutations, suggesting that SSPs may be precursor of dMMR cancers and possibly proficient MMR and BRAF mutated tumors.
The most recent edition (2010) of WHO classification of gastrointestinal tumors indicates that untreated SSP is associated with substantial (although undetermined) increased risk of developing colon cancer and suggests colonoscopy and polypectomy every 1-3 year for management.\textsuperscript{13-14}

Multiple endoscopy techniques, like chromoendoscopy, split-dose bowel preparation, high definition endoscopy, and a withdrawal of longer than 6 minutes, have shown to improve detection of serrated polyps. Sessile serrated polyps \(\leq 1\) cm and those with dysplasia increase the chance of malignancy in future, therefore it is becoming more reasonable to perform surveillance in 3 years. At the same time, patients with serrated polyposis syndrome should be survey every 1 to 2 years and their first-degree relatives should undergo screening every 5 years starting at age of 40.\textsuperscript{15}

Therefore, accurate diagnosis of SSP is critical for appropriate clinical management of the patient.\textsuperscript{6} Continued Medical Education (CME) is in place to help those in the medical field maintain competence and learn new developments in the field. Our study shows that the educational intervention was successful in increasing the accurate designation of SSP and improved that significantly. The only similar study available in PubMed was conducted in Netherlands and showed that an e-learning module improved consistency of histopathological diagnosis of sessile serrated lesion.\textsuperscript{16} Continued medical education in designation of the SSP is recommended to keep its prevalence in the vicinity of 8\%.\textsuperscript{6}

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**Declaration**
This study has our institutional IRB approval (H-36559). The authors have no conflict of interest and the article is not under consideration for publication elsewhere.
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