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Serrated lesions in patients with inflammatory bowel disease

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ABSTRACT
A new serrated histologic finding has recently been discovered in patients with inflammatory bowel disease (IBD), known as serrated epithelial change (SEC). Recent studies suggest that SEC is strongly associated with dysplasia. The case was a 62-year-old male in a dysplasia-colorectal cancer screening program with periodic chromoendoscopies, with CES findings in the previous chromoendoscopy studies. A prophylactic colectomy seems a reasonable option for patients with several serrated lesions identified via chromoendoscopy screening. Particularly, if they are extensive and poorly defined, due to the possibility of developing high-grade dysplasia or colorectal cancer (CRC) during surveillance.

Key words: Serrated epithelial change. Dysplasia. Inflammatory bowel disease.

INTRODUCTION
Patients with inflammatory bowel disease (IBD) have a risk of developing dysplasia and colorectal cancer (CRC). The main risk factors include duration, extent, age and the presence of primary sclerosing cholangitis (PSC) (1,2). Recently, the serrated neoplastic
pathway has been linked to CRC in patients with IBD (2,3). Most studies have found serrated lesions to be less frequent in patients with IBD compared to the general population. However, it is not clear whether they are actually less common or if they are misdiagnosed. Classic serrated lesions of the colon include hyperplastic polyps, traditional serrated adenomas (TSA) and sessile serrated adenomas (SSA) (1,3). A new serrated histopathologic finding has recently been discovered in patients with IBD, known as serrated epithelial change (SEC). This is a different entity to the classic serrated lesions of patients without IBD (2) and recent studies suggest that the presence of SEC is strongly associated with dysplasia (2,3).

CASE REPORT
A 62-year-old male was diagnosed with steroid-dependent left ulcerative colitis 15 years previously, which was E2 according to the Montreal classification. The patient is currently under maintenance treatment with 2 g of oral mesalamine, azathioprine (AZA) of 2.5 mg/kg (200 mg) and infliximab with dose intensification to 10 mg/kg (800 mg) every eight weeks due to a secondary loss of response seven years previously. The drug levels are around 4.6-6 ug/ml and anti-infliximab antibodies (ATIS) are negative. The case was in clinical and analytical remission for four years with mucosal healing and pseudopolyps. He had also been included in a dysplasia-colorectal cancer screening program with periodic chromoendoscopies. SEC was identified in the last chromoendoscopy images. In December 2017, a flat lesion (0-IIb) of around 20 mm in diameter was identified on the 1st rectal valve, which was well-delineated with well-defined edges and a type II pit pattern according to Kudo’s classification. Biopsies were taken and the histopathological analysis identified a serrated lesion, which was different to classic serrated lesions of patients without IBD. According to a histopathological review by two different pathologists, the lesion was compatible with SEC with the absence of dysplasia (Fig. 1). An endoscopic resection of the lesion was performed during a second procedure. In January 2018, a chromoendoscopy was performed to visualize the resection of the lesion in figure 1. An endoscopic mucosal en block resection (EMR) was attempted over the rectal lesion discovered in the previous endoscopy. However, a block
resection was not achieved due to its large size and was finally resected by the piecemeal technique. A 10 mm polypectomy snare was used after submucosal injection of glycerol. A complete histopathological analysis confirmed that the lesion was a new histological entity of a serrated lesion known as SEC. In addition, low-grade dysplasia (LGD) foci were identified in the lesion, which had not been seen in previous biopsies. Furthermore, another previously unidentified lesion was identified during the colonoscopy in the distal sigmoid colon. A large flat (0-IIb) un-delineated lesion that extended by several haustinations was seen. Biopsies confirmed that it was similar to the previous lesion and was compatible with SEC with absence of dysplasia (Fig. 2).

The best management of this new lesion was discussed in a clinical session and the possibility of resection using endoscopic submucosal dissection (ESD) technique was considered. However, this option was rejected as the sigmoid colon lesion was extensive, large, encompassed several haustations and the margins of the lesion were not clearly identified. This prevented the lesion from being optimally delineated and was considered as endoscopically unresectable by ESD techniques according to the latest SCENIC consensus. Therefore, the multidisciplinary committee of digestive diseases and general surgery decided to perform a prophylactic colectomy. This was due to the risk of malignant transformation of these lesions and also avoided new serrated lesions during the surveillance. The long-term risks and benefits of the surgical procedure were discussed with the patient. A total laparoscopic proctocolectomy with ileal pouch-anal anastomosis was chosen as the best available prophylaxis measure in order to prevent a high-grade dysplasia (HGD) lesion or CRC development. Histopathological analysis of the surgical specimen identified a SEC type lesion that measured 6.3 x 3.8 cm, with LGD in some areas. No other lesions were identified in the rest of the colon.

**DISCUSSION**

There is an activation of the signal of mitogen-activated protein kinase pathway (MAPK) in the serrated pathway. This is characterized by BRAF or KRAS mutations and microsatellite instability that results in an uncontrolled cell proliferation and cell invasion, which often occurs in the right side of the colon. The latter is considered as
the main mechanism of activation of the serrated neoplastic pathway (1,4).

Even though histopathology of serrated lesions does not show dysplasia, these are preneoplastic lesions which quickly lead to CRC (2). Recently, SEC has been discovered in patients with IBD. This is thought to be a new serrated histopathologic entity that presents the same molecular alterations found in the serrated pathway of carcinogenesis, but differs in some morphological features. SEC is characterized histologically by a serrated architecture of the crypts as well as the classic serrated lesions and differs due to a greater number of goblet cells and nucleolus. SSA are often flat, visible lesions, whereas SEC is a histological diagnosis often found on flat or nodular mucosa, which are indistinguishable via white light endoscopy, therefore chromoendoscopy is essential for characterization (5). In addition, SEC lesions tend to be more extensive and are usually found in the left colon, unlike classic serrated lesions in patients without IBD. Recent studies have shown a strong association between SEC and dysplasia. IBD patients with SEC have a higher risk of developing HGD and CRC during surveillance in a shorter time compared to patients without SEC (2,3,5).

In conclusion, CES is an entity which is infrequently recognized and reported by pathologists, which is likely due to its unknown significance until a few years ago. More studies are required to assess the extent of SEC involvement in the development of dysplasia in IBD patients. Furthermore, the genetic and molecular markers of serrated lesions should be studied in order to better identify higher risk cases. This would result in an improved stratification of the surveillance recommendations (2,3). Prophylactic colectomy seems a reasonable option in patients with several serrated lesions identified via the screening chromoendoscopies, due to the possibility of developing HGD or CRC during surveillance. Particularly, if they are extensive and poorly defined.

REFERENCES


Fig. 1. A flat lesion (0-IIb) of around 20 mm in diameter on the 1st rectal valve, which is well-delineated with well-defined edges and a type II pit pattern according to Kudo’s classification. Histopathological analysis of biopsies identified a serrated lesion compatible with SEC with the absence of dysplasia.
Fig. 2. A large flat lesion (0-IIb) in the sigmoid colon that encompasses several haustrations. The lesion is non-ulcerated, the margins are not clearly identified and it has a type II pit pattern according to Kudo’s classification. Histopathological analysis of biopsies identified a serrated lesion compatible with SEC with the absence of dysplasia.