

Case and Review

Hereditary Nonpolyposis Colorectal Cancer in Association with Crohn's Disease and Lynch Syndrome: The Importance of a Strict Endoscopic Surveillance

Gustavo Drügg Hahn^{a, b} Panu Wetwittayakhleng^{a, c} Waqqas Afif^a
Talat Bessissow^a Peter L. Lakatos^{a, d}

^aDivision of Gastroenterology, McGill University Health Center, Montreal, QC, Canada;

^bUniversidade Federal do Rio Grande do Sul, School of Medicine, Graduate Course Sciences in Gastroenterology and Hepatology, Porto Alegre, Brazil; ^cGastroenterology and Hepatology unit, Division of Internal Medicine, Faculty of Medicine, Prince of Songkla University, Songkhla, Thailand; ^dDivision of Gastroenterology, Semmelweis University, Budapest, Hungary

Keywords

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Abstract

Crohn's disease (CD) and Lynch syndrome (LS) are two different entities, yet both are associated with increased risk of colorectal cancer (CRC). We present the case of a young female patient in long-standing remission of her ileocolonic luminal CD, and a family history of LS on a regular short interval (every 2 years) colonoscopy surveillance. Despite normal blood tests, fecal calprotectin, and ileocolonoscopy, her last colonoscopy showed an approximately 1.3–1.5 cm polyp in the cecum and mild UC-like colitis in the ascending colon. Histology confirmed the presence of a moderately differentiated adenocarcinoma (T2N0M0) with loss of PSM2 expression at immunohistochemistry, in line with a hereditary nonpolypoid CRC associated origin. Laparoscopic subtotal colectomy with ileorectal anastomosis was offered as the treatment of choice, which revealed a 2.4 cm exophytic ulcerated lesion and pathology confirmed invasive moderately differentiated adenocarcinoma (pT2N0M0). Patient will remain on close endoscopic surveillance for the rectum. Our case highlights the importance of a strict endoscopic surveillance in patients with long-standing CD colitis, especially in patients with additional risk factors. The aim of this article was to highlight the importance of a

strict endoscopic surveillance in CD in association with LS regarding a higher risk of CRC, which mandates the adaptation of the endoscopic surveillance intervals as well as the surgical approach and postoperative management/surveillance.

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Introduction

Crohn's disease (CD) is a chronic immune-mediated disorder of the gastrointestinal tract, primarily inflammatory; however, depending on its natural history, it could evolve to a stricturing and/or penetrating presentation [1]. On the other hand, Lynch syndrome (LS) comprehends a genetic disorder, which can lead to specific types of cancer development, predominantly colorectal cancer (CRC) [2].

LS and CD are both known to confer an increased risk for developing CRC. LS is the most common cause of inherited CRC, accounting for approximately 3 percent of newly diagnosed cases and 8 percent of the cases in patients under the age of 50 [2]. As to CD, the overall combined risk of CRC is over 2.5 times that of general population; 4.5 times in case of extensive colonic disease [3]. Additionally, after 10 years of the onset of the disease the risk of CRC is 2 percent, 8–12 percent at 20 years, and 18 percent at 30 years [4]. The aim of this article was to present a clinical case of hereditary nonpolyposis CRC (HNPCC) in a young female patient with ileocolonic CD and LS with a brief review of the literature.

Case Report

We present the case of a 29-year-old, female patient, nonsmoker, with history of luminal, ileocolonic CD (Montreal classification L3B1) diagnosed in 2006 and in clinical and endoscopic remission with no therapy since 2007. She had a family history of CRC, her father, and known LS in the family. She was treated with prednisone 2.5 mg for 1 year for nasal polyps and montelukast and she is allergic only to NSAIDs. Since October 2019, she has been experiencing mild abdominal cramps with normal bowel movement per day, without blood or urgency. Fecal calprotectin and blood tests at that time were normal. One month later, the abdominal cramps stopped, but there was a slight change in her bowel movements (2–3 per day) with formed stools, without blood or urgency. Fecal calprotectin and blood tests were normal. In December 2019, she underwent a surveillance ileocolonoscopy, with normal findings and no dysplasia in the histology. She also had a consultation at the Medical Genetics Department for LS and a new surveillance colonoscopy scheduled. She underwent the current surveillance colonoscopy in May 2021, which showed mild colitis in transverse and ascending colon (shown in Fig. 1) and, in the cecum, a 1.3–1.5 cm, round, flat depressed polyp with nonlifting sign, suggestive of early CRC (shown in Fig. 2). Pathology report confirmed focally active colitis with minimal chronicity, negative for dysplasia, consistent with CD in the ascending colon and for the cecum polyp it confirmed the presence of a moderately differentiated adenocarcinoma with immunohistochemistry showing PMS2 loss (high probability of LS). Laparoscopic subtotal colectomy with ileorectal anastomosis was offered as the treatment of choice. Surgery revealed a 2.4 cm exophytic ulcerated lesion at the junction of the cecum with ascending colon. Pathology confirmed invasive moderately differentiated adenocarcinoma, stage pT2N0M0. Patient will remain on close endoscopic surveillance for the rectum.



Fig. 1. Mild colitis in the ascending colon.



Fig. 2. Cecum adenocarcinoma.

Discussion

This is a unique case of the association of ileocolonic CD and HNPCC in a young female patient with CD. Our case confirms the high risk of CRC in these patients and suggests that a special attention with tight endoscopic surveillance should be offered to patients presenting both conditions.

CD is a chronic immune-mediated disease of the gastrointestinal tract that affects mainly the small intestine and the colon, characterized by periods of remission alternating with periods of relapse. The inflammatory pattern represents an initial form of the disease; however, approximately 50 percent of all CD patients develop stricturing or penetrating intestinal complications after 10 years of disease [5].

The development of CRC, in this case, is due to inflammation and follows a sequence of genetic alterations (inflammation-dysplasia-carcinoma sequence), instead of an adenoma-sequence as it happens in sporadic CRC [5–7]. The presence of an excessive inflammatory cell infiltration and expression of several inflammatory genes that IBD patients usually have promotes cellular proliferation and ultimately CRC development [4].

Of note, endoscopic surveillance is of utmost importance, once the risk of CRC in CD patients increases with longer duration and extent of severe colitis, family history of CRC, young age at disease onset, personal history of primary sclerosing cholangitis, and personal history of dysplasia. Recent ECCO and ASGE guidelines suggest that endoscopic surveillance begins in all patients at 8 years of disease, who are at endoscopic remission, regarding an interval of every 1–3 years. If one of these factors is present: active inflammation, anatomic abnormality (stricture, multiple pseudopolyps), history of dysplasia, family history of CRC in first-degree relative, or primary sclerosing cholangitis, endoscopic surveillance should be done annually [7, 8].

In IBD patients who underwent either subtotal colectomy end-ileostomy or diversion for medically refractory, the risk of rectal cancer is still increased, and surveillance endoscopy was associated with a further decrease in the rate of rectal cancer in these patients [9]. Thus, endoscopic surveillance is also indicated in these patients [10].

LS is an autosomal dominant disorder that is caused by a germline mutation in one of several DNA MMR genes or loss of expression of MSH2 due to deletion in the EPCAM gene [11, 12]. The most common MMR gene involved is PMS2; however, MLH1 and MSH2 are associated with the higher risk of developing CRC [11–13]. About 20 percent of patients with CRC have a family history of CRC in at least one first-degree relative [11].

CRCs in LS develop predominantly in the right colon (60–80 percent), proximal to splenic flexure, differing from sporadic CRCs, which develop mostly in the left colon [13]. Although most LS-associated CRCs are thought to evolve from adenomas, the adenomas tend to be larger, flatter, often proximal, and are more likely to have high-grade dysplasia and/or villous histology. The adenoma-carcinoma sequence may also progress faster in LS [13].

Surgical management of CRC in HNPCC is still considered to be controversial. The most chosen techniques range between a segmental colectomy and total colectomy. So far, there is lack of evidence that suggest one technique rather than the other. In this setting, total colectomy eliminates patients' future risk of metachronous high-risk colonic adenomas or cancers; however, it is associated with a higher morbidity and with poorer functional outcomes and lower quality of life compared with segmental colectomy [14]. Regarding segmental colectomy usually is the choice for sporadic CRC, with less morbidity, yet with the need of regular endoscopic surveillance for metachronous colonic lesions in the remaining colon. Heneghan et al. [15] reported that, despite morbidity for both procedures in the HNPCC is not well delineated, segmental resection of HNPCC is considered the gold standard, except if the patient's preference is prophylactic extended resection.

Conclusion

In summary, despite the rarity, it is important to be aware of the potential association between CD and LS, which mandates the adaptation of the endoscopic surveillance intervals as well as the surgical approach and postoperative management/surveillance, in patients diagnosed with dysplasia and/or CRC due to the increased risk for metachronous CRCs, subtotal colectomy is probably the best treatment option for patients with CD/HNPCC diagnosed with dysplasia and/or cancer.

Statement of Ethics

This study protocol was reviewed, and the need for approval was waived by the McGill University Health Centre – Research Ethics Board. Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

G. Hahn and P. Wetwittayakhlang reviewed the literature, wrote, and edited the manuscript. G. Hahn, P. Lakatos, W. Afif, and T. Bessissow revised the final manuscript. P. Lakatos is the article guarantor.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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