Considerations and management of a patient with three metachronous cancers in association with Lynch syndrome and ileal Crohn's disease: A case report

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A B S T R A C T

INTRODUCTION: Lynch syndrome and Crohn's disease are two entirely separate conditions but each have major gastrointestinal characteristics and carry a substantial increase in the risk of intestinal malignancy. Their co-existence in the patient who is the subject of this report dictated the need for an individualised treatment plan to deal with both conditions adequately.

PRESENTATION OF CASE: We report a case of a 51 year old female with a past medical history that includes Lynch syndrome and small bowel Crohn's disease. Over a period of fifteen months, she developed three separate primary metachronous tumors in her endometrium, colon and duodenum.

DISCUSSION: A patient with a combination of Lynch syndrome and ileal Crohn's disease presents significant therapeutic implications that are not usually present when these conditions are treated in isolation.

CONCLUSION: The surgical treatment of patients with Lynch syndrome requires a sound knowledge of the possible neoplastic conditions that can arise in the syndrome. Early detection is paramount, either by implementation of evidence based surveillance programs or at least by a heightened clinical awareness of the features of this disease. Ideally this will result in both reduced surgical morbidity and improved oncologic outcome. Furthermore, the medical treatment of Crohn's disease in a patient with tumors arising from Lynch syndrome must be undertaken with at least a consideration of the possibility that the use of immunosuppressive medication might increase the risk of cancer recurrence.

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1. Introduction

Lynch syndrome, described as a family cancer syndrome by Henry Lynch in 1966, is an autosomal dominant genetic disorder that carries a high risk for the development of colon cancer and several other types of cancer including endometrial, ovarian and small bowel cancer [1]. The syndrome arises from a mutation in the genes (MSH2, MLH1, MSH6 or PMS2) responsible for the repair of DNA mismatch errors that arise during DNA replication [2].

Lynch later named the syndrome hereditary non polyposis colon cancer (HNPPC). However, as other cancers were later seen to be part of the syndrome, the term Lynch syndrome has been restored to avoid the misleading use of HNPPC, which refers only to colorectal cancer [3].

Cancers of the stomach, small bowel, endometrium, ovaries and urothelium have all been found in Lynch syndrome. However, the commonest malignancy is colon cancer with a lifetime risk of greater than 50% for its development and accounting for more than 2% of all newly diagnosed colorectal cancers [4–6].

Crohn's disease is an inflammatory disease of unknown etiology, primarily affecting the gastrointestinal tract. Presenting symptoms include abdominal pain, diarrhoea, bowel obstruction and intra-abdominal sepsis [7]. Complications can include intestinal perforation, intra-abdominal abscess, internal fistulas, strictures and complex perianal disease. Crohn's disease also carries an increased risk of small bowel and colorectal cancer, and its incidence and prevalence are rising [7,8]. Medical management includes the use of immunomodulators and corticosteroids, which can cause immunosuppression [7]. Surgical intervention is required for patients with failed medical therapy or surgical complications.

There is no known association between Crohn's disease and Lynch syndrome. The occurrence of the two conditions creates unique challenges as treatment options for one disease might impact on the management of the other. These challenges are discussed in the reported case below.

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2. Presentation of case

A 51 year old female with a 24 year history of Crohn’s disease involving the terminal ileum presented with postmenopausal bleeding. She also had a family history of Lynch syndrome and previous genetic testing had confirmed that she carried an MLH1 mutation. A hysteroscopy confirmed the presence of endometrial cancer. She underwent a laparoscopic assisted hysterectomy, bilateral salpingo-oophorectomy and pelvic lymph node dissection. Histopathology revealed a grade one endometrial cancer. Immunohistochemistry confirmed a loss of staining for MLH1. She made an uneventful postoperative recovery.

Three months after hysterectomy she was referred by her general practitioner for a colorectal surgery opinion regarding worsening symptoms of Crohn’s disease and known Lynch syndrome. A colonoscopy was performed and revealed an ulcerated lesion in the caecum. Biopsies demonstrated inflammatory tissue with associated moderate dysplasia. Colonoscopy also revealed multiple pseudopolyps at the rectosigmoid junction along with features of a sigmoid fistula. A CT scan demonstrated a mass involving thickened ileal loops and sigmoid colon representing an ileosigmoid fistula. A serum carcinoembryonic antigen (CEA) level was elevated at 52.6 μg/L (normal level <5 μg/L).

Despite the negative biopsy, clinical suspicion of a carcinoma remained high. Given the combination of Crohn’s disease with a likely carcinoma of the caecum related to the Lynch syndrome, surgical management required careful consideration.

For patients with Lynch syndrome and colon cancer, a total colectomy and ileorectal anastomosis is usually recommended, because of the high risk of metachronous colon tumors and a relatively low risk of rectal tumors [9–11]. However total colectomy has an adverse impact on bowel function, which would likely be substantially worse in this patient given the need for a significant ileal resection, required for her Crohn’s disease.

Under these circumstances, the surgery recommended was a right hemicolectomy with associated terminal ileal resection along with resection of the sigmoid colon due to the presence of the ileosigmoid fistula. This would deal with the two separate conditions of likely caecal cancer and ileal Crohn’s disease. Although the fistula to the sigmoid colon might have been managed by simple closure, resection was recommended to prevent tumor “seeding” along the fistula track.

Surgery proceeded as described and the postoperative recovery was uneventful. Histopathology demonstrated a moderately differentiated adenocarcinoma of the caecum with no lymphovascular involvement and no metastases in regional lymph nodes. Crohn’s disease was confirmed in the ileum and sigmoid colon, and resection margins for both cancer and Crohn’s disease were negative. Immunohistochemistry revealed a loss of staining of the MLH1 protein as expected. Given the absence of unfavourable histologic features and the known better prognosis for patients with colon cancer in Lynch syndrome, adjuvant chemotherapy was not recommended [12].

Given the circumstances, regular follow up was undertaken. Nine months following the bowel resections, the patient was well and without signs of metastases but was found to have iron deficiency anemia with a hemoglobin of 106 g/L. Iron studies recorded a serum iron of 5 μmol/L and ferritin of 8 ng/ml. A gastroscopy and colonoscopy were performed. Colonoscopy demonstrated a normal colorectal remnant but gastroscopy revealed a 2.0 × 1.5 cm flat lesion with central ulceration in the third part of the duodenum. Biopsies revealed a poorly differentiated adenocarcinoma. Capsule endoscopy of the small bowel confirmed the duodenal lesion and excluded other lesions in the small bowel.

Duodenal resection was undertaken and again the patient made an uneventful recovery. Histologic examination of this third tumor indicated this was a new primary tumor confined to the duodenal wall.

After a further twelve months of follow up, the patient remains well with no evidence of new primary tumors or of metastatic disease. In the absence of any recurrence of her Crohn’s disease, no medical treatment for Crohn’s disease has been instituted.

3. Discussion

This case is noteworthy because of the presentation of three metachronous tumors in the context of Lynch syndrome combined with ileal Crohn’s disease and an ileosigmoid fistula. This combination of diseases had significant therapeutic implications that are not usually relevant when the conditions are treated in isolation.

In a patient with Lynch syndrome, the risk of a second colon tumour after treatment for a primary colon tumor by segmental colectomy is 16% after ten years [13]. Not surprisingly, many of the guidelines published on the management of Lynch syndrome recommend that a total colectomy should be considered, particularly for younger patients with Lynch syndrome presenting with colon cancer [14].

However, the surgical management for Crohn’s disease in this patient required an ileal resection, the extent of which would be dictated by the amount of ileum involved.

To treat both conditions in the same way as when they appear in isolation would combine a possibly extensive ileal resection with a total colectomy that would very likely result in extremely poor bowel function. In view of that, an alternative surgical approach was considered and it was determined after discussion with the patient, that total colectomy should be avoided and an ileal resection with a right hemicolectomy along with a segmental sigmoid colon resection be performed in an effort to preserve a significant colonic remnant and thereby reduce the impact of surgery on bowel function and quality of life. Furthermore, as at least 30% of patients who have had one resection for Crohn’s disease will require a further resection within five years, this added another reason to avoid total colectomy [15].

As the surgery undertaken in this case has left the patient with a substantial colonic remnant, regular colonoscopic surveillance was seen as particularly important.

There is debate about how frequently this surveillance should be undertaken in Lynch syndrome, with recommendations generally being for a period of between one and three years [16]. The Australian National Health and Medical Research Council (NHMRC) guidelines recommend yearly colonoscopy and this is the program that was suggested to our patient [17]. Given her subsequent development of duodenal cancer, there may also be a place for regular gastroduodenoscopy and capsule endoscopy of the small bowel although the evidence base for these recommendations is limited [14,18].

Of further note in the management of this patient, it is recognised that some immunosuppressive drugs used in the treatment of Crohn’s disease are associated with an increased risk of certain types of cancer, including skin cancers and lymphomas [19,20]. There is little evidence to suggest an increase in the incidence of metastatic cancer of any nature in patients taking these medications, but the potential for these drugs to induce cancer should at least be considered before they are prescribed for patients who have suffered multiple episodes of other forms of malignancy.

4. Conclusion

This case highlights the necessity for an individualised treatment plan in a patient who presented with two serious gas-
trointestinal conditions associated with Lynch syndrome (caecal cancer) and Crohn’s disease (a symptomatic ileo-sigmoid fistula).

Of further note in this case is the presence of three separate primary cancers arising over a less than two year period in the context of Lynch syndrome. Whilst clearly a possibility, this situation has not previously been encountered by the senior author despite him having treated a large number of patients with Lynch syndrome referred from a comprehensive familial cancer registry over more than 25 years.

Conflict of interest

None declared.

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Ethical Approval

N/A.

Consent

Written and signed consent has been obtained from the patient for the publication of this case.

Author contribution

Kaleb Lourensz: study design, literature review, writing the paper.

Ian Jones: study concept and design, writing the paper.

Guarantor

Kaleb Lourensz; Ian Jones.

References

[1] H.T. Lynch, M.W. Shaw, C.W. Magnuson, A.L. Larsen, A.J. Krush, Hereditary factors in cancer: study of two large midwestern kindreds, Arch. Intern. Med. 117 (2) (1966) 206–212.
[2] S.B. Gruber, New developments in Lynch syndrome (hereditary nonpolyposis colorectal cancer) and mismatch repair gene testing, Gastroenterology 130 (2) (2006) 577–587.
[3] C.R. Boland, H.T. Lynch, The history of Lynch syndrome, Fam. Cancer 12 (2) (2013) 145–157.
[4] H. Hampel, J.A. Stephens, F. Pukkala, R. Sankila, L.A. Aaltonen, J.-P. Mecklin, et al., Cancer risk in hereditary nonpolyposis colorectal cancer syndrome: later age of onset, Gastroenterology 129 (2) (2005) 415–421.
[5] L.A. Aaltonen, R. Salovaara, P. Kristo, F. Czanizan, A. Hemminki, P. Peltomaki, et al., Incidence of hereditary nonpolyposis colorectal cancer and the feasibility of molecular screening for the disease, N. Engl. J. Med. 338 (21) (1998) 1481–1487.
[6] P. Watson, B. Riley, The tumor spectrum in the Lynch syndrome, Fam. Cancer 4 (3) (2005) 245–248.
[7] B.C. Baumgart, W.J. Sandborn, Crohn’s disease, Lancet 380 (9853) (2012) 1590–1605.
[8] T. Jess, M. Gamburg, P. Matzen, P. Munkholm, T.J. Sorenson, Increased risk of intestinal cancer in Crohn’s disease: a meta-analysis of population-based cohort studies, Am. J. Gastroenterol. 100 (12) (2005) 2724–2729.
[9] J.P. Mecklin, H.J. Jarvinen, Clinical features of colorectal carcinoma in cancer family syndrome, Dis. Colon Rectum 29 (3) (1986) 160–164.
[10] M.A. Rodríguez-Bigas, H.F. Vasen, J. Pekka-Mecklin, T. Myrhej, P. Rozen, L. Bertario, et al., Rectal cancer risk in hereditary nonpolyposis colorectal cancer after abdominal colectomy: International Collaborative Group on HNPCC, Am. Surg. 225 (2) (1997) 202–207.
[11] J.C. Saurin, F. Pilleul, E.B. Soussan, T. Maniere, P.N. D’Halluin, M. Gaudric, et al., Revised guidelines for the clinical management of Lynch syndrome (HNPCC): recommendations by a group of European experts, Gut 62 (6) (2013) 812–823.
[12] V. Stigliano, D. Assisi, M. Cosimelli, R. Palmirotta, D. Giannarelli, M. Monteleone, et al., Survival of hereditary non-polyposis colorectal cancer patients compared with sporadic colorectal cancer patients, J. Exp. Clin. Cancer Res.: 27 (1) (2008) 39.
[13] H.F. Vasen, I. Blanco, K. Aktan-Collan, J.P. Gopie, A. Alonso, S. Arze, et al., One to 2-year surveillance intervals reduce risk of colorectal cancer in families with Lynch syndrome, Gastroenterology 138 (7) (2010) 1594–1600.
[14] J.G. Williams, W.D. Wong, D.A. Rothenberger, S.M. Goldberg, Recurrence of colorectal cancer in families with Lynch syndrome, Gastroenterology 120 (12) (2001) 1588–1594.
[15] F. Canzian, A. Hemminki, K. Lourensz; Ian Jones.

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