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Review of Small Bowel Carcinomas in Patients with Hereditary Colorectal Cancer: Case Report of Multiple Adenocarcinomas of the Ileal Anal Pouch

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1. Abstract

1.1. Background

The patient with known hereditary colorectal carcinoma presenting with multiple small bowel carcinomas occurring in an ileal anal pouch prompted the search for similar small bowel carcinomas occurring in patients with hereditary colorectal carcinoma in the medical literature.

1.2. Purpose

The purpose of the paper is to increase the awareness of the possibility of occurrence of small bowel carcinomas in patients with hereditary colorectal carcinomas, which have been widely reported in the medical literature.

1.3. Method

We are reporting a case with multiple adenocarcinomas of the small bowel occurring in an ileal anal pouch in a patient with known history of hereditary colorectal carcinoma. The patient had three separate carcinomas of the ileal pouch.The patient underwent successful pouch excision and end ileostomy.The patient received chemotherapy and has no clinical or radiographic evidence of recurrent disease at 3 years post treatment.

1.4. Results

At three years post-treatment, having received chemotherapy immediately after the surgical procedure with dedicated follow up clinically and radiographic evaluations, the patient has not had any evidence of recurrent disease.

1.5. Conclusion

A vast review of medical literature indicated a lack of recommended surveillance protocols for evaluation of small bowel carcinomas in patients with hereditary colorectal carcinoma. Our experience highlights a need for a surveillance protocol for small bowel carcinoma occurring in patients with hereditary colorectal carcinoma who have undergone total proctocolectomy with ileal pouch anal anastomosis or other related surgical interventions.

2. Material and Methods

This case report was given cite approval by our institutional human research review committee at TriCity Colorectal Surgery Institute. The authors have also obtained a full informed consent from the patient described in this case report.

3. Case Report

3.1. History of Past Surgical Treatments

The patient was originally seen in our office in March 2006. The patient had undergone two prior colon resections, one in 1988 and one in 1989, at a different institution. The patient had colon carcinoma without evidence of any metastatic disease or nodal involvement in 1988. The patient was found to have a recurring tumor in 1989. The patient had resection of the right colon and half of his transverse colon in sum from these two prior surgical resections with an ileal transverse colon anastomosis. In both of these surgical procedures, the respective pathology reports did not indicate nodal involvement. The patient was also found to have a few tubular adenomas, which were resected along with the colon cancer at the time of bowel resection.

3.2. History of Initial Treatment at our Institution

The patient was seen in our institution in March 2006 and underwent endoscopic evaluation of the colon for cancer surveillance. During this examination, the patient was found to have two lesions, one in the transverse colon (adenocarcinoma) and other in the descending colon (tubular adenoma with high grade dysplasia).Because of the two prior colon carcinomas, the two prior resections, a family history of colon carcinoma occurring in his cousin, and the newly discovered adenocarcinoma and dysplastic lesion of the transverse and descending colon respectively, the patient was recommended a total proctocolectomy with either end ileostomy or ileal pouch anal anastomosis. The patient chose the latter option and underwent ileal pouch anal anastomosis with resection of the remaining colon and rectum in March 2006. His protective loop ileostomy, performed simultaneously, was reversed in November 2006. The pathology of the proctocolectomy specimen was designated T3N1, with one node positive for carcinoma. The tumor penetration was to the subserosa. The patient underwent FOLFOX therapy in the adjuvant setting. The patient experienced intermittent episodes of diarrhea due to pouchitis following the surgical resection that were successfully treated with a combination of Ciprofloxacin and Metronidazole and anti-diarrheal agents. Pouchitis was confirmed by clinical examination as well as endoscopic evaluation of the pouch.

3.3. Review of Genetic Mutation

In 2007, the patient required surgical excision of multiple skin cancers, pathologically confirmed as sebaceous adenocarcinomas. Because of the combination of multiple colon cancers and sebaceous adenocarcinoma, the patient was sent for genetic counseling. In 2008, a complete mapping of family genetic tree was constructed. The patient's cousin, who had previously undergone a resection for colon carcinoma, was found to have a mutation of MSH 2. The patient's two daughters were also found to have a mutation of MSH 2. Given the patient's aforementioned personal and family histories, he was diagnosed with Muir-Torre Syndrome, a condition that combines hereditary non-polyposis colon cancer with sebaceous carcinoma.

3.4. Postoperative Follow up with Serial Pouchoscopies

Postoperatively, the patient was periodically evaluated with pouchoscopy, CT and PET scan. Pouchoscopies were performed in 2008, 2009, and 2010. These endoscopic examinations were negative for any lesions in the pouch, rectal cuff, or the terminal ileum. Because of these three consecutive negative pouchoscopies, the surveillance interval was increased to every two years. In 2012, the patient was found to have a rectal cuff adenoma that was ultimately removed by transanal excision. Pathologically, the polyp was a tubular adenoma without evidence of dysplasia. However, because of the identification of adenoma, the endoscopic surveillance interval was decreased back to a yearly basis. In 2013 and 2014, these examinations were again negative for any lesions of the pouch, rectal cuff, or terminal ileum. In 2016, the patient had an additional pouchoscopy demonstrating a small granuloma/inflammatory polyp. Because of the consecutive negative examinations, the patient was once again advised to come back every two years for follow up examination. In 2018, pouchoscopy revealed a 2 cm polyp at the rectal cuff. Complete endoscopic snare excision was performed yielding a tubular adenoma without high grade dysplasia or carcinoma. Because of the presence of this larger polyp in the rectal cuff, the patient underwent repeat endoscopic evaluation at three months and then six months from the time of excision. Both these evaluations were negative.The patient was not seen again until December 2021 partly because of the COVID pandemic. At that time, the patient was found to have anemia and did undergo a complete evaluation that included CT scan, PET scan and pouchoscopy. The CT scan revealed thickening of the pouch with presence of subcentimeter lymph nodes in the pelvis but with no distinct lesions in the pouch. Endoscopically, two lesions were then identified. One was near the ileal anal anastomosis, but in the ileal pouch. The other one was near the proximal end of the ileal pouch. The biopsy of the proximal lesion was consistent with carcinoma. The pathology of the distal pouch polyp showed high grade dysplasia without invasive carcinoma. The PET incidentally demonstrated increased activity in both lesions.

3.5. History of Most Recent Surgical Procedure/Pouch Excision

Because of the identification of carcinoma in the ileal pouch, the patient did undergo pouch excision as well as excision of 15 cm of terminal ileum proximal to the pouch and creation of an end ileostomy. The patient tolerated the surgical procedure very well without any complications. The histopathological evaluation interestingly did indicate three carcinomas of the ileal pouch. The most proximal one was 1.5 cm from the proximal margin of the ileal pouch. The second carcinoma was approximately 7-8 cm from the proximal end of the ileal pouch. The distal most lesion was approximately 1.5-2 cm from the ileal anal anastomosis. Pathologically, these lesions were classified as T3N0 lesion with microscopic lymphovascular invasion. The depth of penetration was to the subserosa, and all resected lymph nodes were negative for cancer. The PET CT scan did not indicate any metastatic disease.

3.6. Follow up Since the Last Surgical Procedure

Since the surgical resection, the patient has undergone chemotherapy as well as multiple surveillance evaluations with CT, PET scan and CT enterography on a yearly basis. Thus far, the patient has not had any local or distant recurrence of tumor. The patient's two daughters, who were also found to be positive for mutation of MSH 2, have also undergone regular screening colonoscopies without any evidence of polypoid lesions or tumors. The patient's associated clinical conditions include hypertension,

skin cancer, sebaceous adenocarcinoma, nephrolithiasis, and non-obstructing gallstones. The patient was also found to have a small cyst in the pancreatic neck measuring 1.6 cm. After multiple thorough evaluations with endoscopic ultrasound, this was found to be a benign lesion and has not changed appreciably on repeat evaluations.

4. Discussion

Our patient with hereditary non-polyposis colon cancer syndrome/ Muir-Torre Syndrome was found to have three cancers of the ileal pouch. Upon review of the literature, we were unable to identify a prior case wherein three cancers of the ileal pouch had been reported previously. The literature indicates that the overall incidence of small bowel cancer is very low even though the small bowel accounts for 75% of the length of the gastrointestinal tract and 90% of the mucosal surface of the gastrointestinal tract [1]. Small bowel carcinomas are more common in the duodenum and jejunum. The neuroendocrine tumors are more common in the ileum. Roughly 5300 new cases of small bowel carcinoma are reported per year with approximately 1100 deaths [2]. In Europe, the estimated case numbers are 3595 annually [3]. The small bowel is the site of less than 25% of all gastrointestinal neoplasms and less than 2% of all malignant neoplasms [1]. Age adjusted incidence of 1:100,000 population with a prevalence rate of 0.6% has been reported for the occurrence of small bowel carcinoma [4]. There is a higher incidence of small bowel neoplasms in males and colon cancer is roughly 50-60 times more common than small intestinal cancer [5]. Lifetime risk of developing small bowel cancer in patients with hereditary non-polyposis colorectal syndrome increases with age [6,7]. It is estimated to range between 0.4-12% [6-14]. This is more than 100 times the occurrence of small bowel cancer when compared to the general population. The median age of diagnosis of small bowel cancer in patients with Lynch syndrome is usually between 39-53 years of age, which is about 10 to 20 years earlier than the general population [15]. It is also higher in men than women [16].The small bowel carcinoma risk is increased in individuals with hereditary colorectal cancer syndrome, such as inherited polyposis syndrome, familial adenomatous polyposis coli, Peutz-Jeghers, Lynch syndrome, and Constitutional Mismatch Repair Deficiency (CMMR-D) [17]. The small bowel carcinoma in Lynch syndrome, also referred to as hereditary non-polyposis colorectal cancer (HNPCC) syndrome, is an inherited autosomal dominant disease and is caused by germ line mutation of mismatch repair (MMR) genes MLH 1, MSH 2, MSH 6, or PMS 2 [18]. The affected individuals are at risk of developing both colorectal as well as extracolonic cancers. The extracolonic malignancies include endometrial, ovarian, breast cancer in subsets of families, gastric cancer, laryngeal cancer, pancreatic cancer, brain tumors and urological tumors [19-24]. A germ line mutation in one of the mismatch protein repair gene proteins responsible for Lynch syndrome can predispose to developing small bowel carcinoma [25]. Inactivation of the DNA mismatch repair genes is characterized by tumor microsatellite instability [26]. As indicated earlier, four MMR genes have been described: MLH 1, MSH 2, MSH 6, and PMS 2. Mutation of these genes can be assessed by immunohistochemistry [27]. The loss of MLH 1 protein function could also be due to hypermethylation of MLH promoter, which accounts for less than 20% of all cases of colorectal carcinoma, primarily in the elderly population [28]. BRAF V600E mutation is frequently associated with MLH 1 promoter methylation and sporadic colorectal cancer [26]. Regarding the genotype of the small bowel cancer, the incidence appears to be very similar between MLH 1 and MSH 2, wherein MSH 6 and PMS 2 mutation carriers are significantly low [29,30]. MLH 1 and MSH 2 mutation account for 70-90% of the small bowel carcinoma occurring in families with HNPCC or Lynch syndrome [15].The majority of the small bowel carcinomas occurring in HNPCC are adenocarcinomas [30,31]. The adenocarcinoma usually develops in the duodenum (43%) and jejunum (37%), and less frequently in the ileum (20%) [15,16,20,31,32,33]. Approximately 50% of the small bowel cancers will be within the reach of upper endoscopy [16]. The small bowel adenocarcinoma carries a poor prognosis for all stages with five year overall survival rate of 50-60% for stage 1, 39-55% for stage 2, 10-50% for stage 3, and 3-5% for stage 4 [34-36]. The mortality of small bowel cancer appears to be intermediary between colon cancer and gastric cancers [34,35]. Even though the incidence of small bowel and extracolonic cancers is higher in patients with Lynch syndrome compared to the general population, the international guidelines have not recommended small bowel surveillance on a routine basis [36-38]. There is no consensus among the international guidelines on small bowel surveillance in Lynch syndrome affected individuals as compared to the strict guidelines published for patients with familial adenomatous polyposis coli and patients with Peutz-Jeghers syndrome.The European guidelines of the Mallorca Group suggest performing inspection of the distal duodenum during upper endoscopy and ileal intubation during lower endoscopy, as well as performing pouchoscopy or colonoscopy in all individuals, but do not consider post-duodenal small bowel surveillance [39]. The National Comprehensive Cancer Network and American College of Gastroenterology suggest considering small bowel surveillance only in selected individuals with upper endoscopy every three to five years. The National Comprehensive Cancer Network also recommends in patients of Asian descent extended duodenoscopy of the duodenum and jejunum every three to five years beginning at age 30-35 [40]. The published European Society of Gastrointestinal Endoscopy Guidelines do not recommend any surveillance of the small bowel in patients with Lynch syndrome [41].

5. Conclusion

There is a definite need for a surveillance protocol for small bowel

carcinoma in patients with hereditary non-polyposis colon cancer syndrome, i.e. Lynch syndrome. There are no definitive accepted/followed international or American guidelines for surveillance of small bowel carcinoma in patients with hereditary non-polyposis colon cancer syndrome, either in patients who have the genetic mutation or patients who have had prior surgical resections for either colonic or extra-colonic cancers related to the hereditary non-polyposis colon cancer syndrome. Hopefully, with better guidelines and better surveillance, the discovery of small bowel carcinoma can be made earlier with resultant better prognosis and survival.

References

1. Herbsman H. Western L., Rosen Y. et al: Tumors of the small intestine. Curr Probl Surg. 1980; 17:121-182.
2. Jemal A, Siegel R, Ward E, Hao Y, Xu. Cancer statistics, 2009. CA Cancer J Clin. 2009; 59:225-249.
3. Faivre J, Trama A, De Angelis R, et al. Incidence, prevalence and survival of patients with rare epithelial digestive cancers diagnosed in Europe in 1995-2002. Eur J Cancer. 2012; 48: 1417-1424
4. DiSario JA. Small bowel tumors. PractGastoenterol. 1992;16:24E-24N.
5. Darling RC, Welch CE. Tumors of the small intestine. N Engl J Med. 1959; 260: 397-408.
6. Lynch HT, Smyrk TC, Lynch PM. Adenocarcinoma of the small bowel in Lynch Syndrome II. Cancer. 1989; 64: 2178-2183.
7. Aarnio M, Mecklin JP, Aaltonen LA. Life-time risk of different cancer in hereditary non polyposis colorectal cancer (HNPCC syndrome). Int J Cancer. 1995; 64: 430-433.
8. Barrow E. robinson L, Alduaji W. Cumulative life-time incidence of extracolonic cancers in Lynch syndrome: a report of 121 families wi proven mutation. Clin Genet. 2009; 75: 141-149.
9. Koornstra JJ, Mourits MJE, Sijmons RH. Management of extracolonic tumours in patients with Lynch syndrome. Lancet Oncol. 2009; 10: 400-408.
10. Park JG, Kim DW, Hong CW. Germline mutations of mismatch repair genes in hereditary non polyposis colorectal cancer with small bowel cancer: International Society for Gastrointestinal Hereditary Tumours Collaborative Study. Clin Cancer Res. 2006; 12: 3389-3393.
11. Watson P, Vasen HF, MecklinJPThe risk of extra-colonic, extra-endometrial cancer in the Lynch syndrome. Int J Cancer. 2008; 123:444-449.
12. Engel C, Loeffler M, Steinke V. Risks of less common cancers in proven mutation carriers with Lynch syndrome. J Clin Oncol. 2012; 30: 4409-4415.
13. Rodriguez-Bigas MA, Vasen HF, Lynch HT. Characteristics of small bowel carcinoma in hereditary non-polyposis colorectal carcinoma: International Collaborative Group on HNPCC. Cancer. 1998; 83: 240-244.
14. Win AK, Lindor NM, Young JP. Risks of primary extracolonic cancers following colorectal cancer in Lynch syndrome. J Natl Cancer Inst. 2012; 104: 1363-1372.
15. Ten Kate GL, Kleibeuker JH, Nagengast FM. Is surveillance of the small bowel indicated for Lynch syndrome families: Gut. 2007; 56: 1198-1201.
16. Koornstra JJ, Kleibeuker JH, and Vasen HF. Small bowel cancer in Lynch syndrome: Is it time for surveillance: Lancet Oncol. 2008; 9: 901-905.
17. Galiatsatos P and Foulkes WD. Familial adenomatous polyposis. Am J Gastroenterol. 2006; 101: 385-398.
18. Vasen HFA, Watson P, Mecklin JP. New clinical criteria for hereditary non polyposis colorectal cancer (HNPCC, Lynch syndrome) proposed by the International Collaborative Group on HNPCC. Gastroenterology. 1999; 166: 1453-1456.
19. Kohlmann W and Gruber SB. Lynch Syndrome: GeneReviews [Internet]: 2004 Feb 5 [updated 2014 May 22]. Seattle: University of Washington. 1993-2016.
20. Vasen HFA, Blanco I, Aktan-Collan K. Revised guidelines for the clinical management of Lynch syndrome (HNPCC): recommendations by a group of European experts. Gut. 2013; 62: 812-823.
21. Cristofaro G, Lynch HT, Caruso ML. New phenotypic aspects in a family with Lynch syndrome II. Cancer. 1987; 60: 51-58.
22. Lynch HT, Kriegler M, Christiansen TA. Laryngeal carcinoma in a Lynch syndrome II kindred. Cancer. 1988; 62: 1007-1013.
23. Lynch HT, Voorhees GJ, Lanspa SJ. Pancreatic carcinoma and hereditary non-polyposis colorectal cancer: A family study. Br J Cancer. 1985; 52: 271-273.
24. Lynch HT, Ens J, Lynch JF, Watson P. Tumor variation in three extended Lynch syndrome II kindreds. Am J Gastroenterol. 1988; 83: 741-747.
25. Bonadona V, Bonati B, Olschwang S, Grandjouan S, Hulart L. Longy M. Cancer risks associated with germline mutations in MLH1, MSH2, and MSH6 genes in Lynch syndrome. JAMA. 2011; 305: 2304-2310.
26. Zaanan A, Meunier K, Sangar F, Flejou JF, Praz F(2011b). Microsatellite instability in colorectal cancer: from molecular oncogenic mechanisms to clinical implications. Cell Oncol (Dordr). 2011; 34: 155-176.
27. Hampel H, Frankel WL, Martin E, Arnold M, Khanduja K, Kuebler P. Screening for the Lynch syndrome (hereditary nonpolyposis colorectal cancer). N Engl J Med. 2005; 352: 1851-1860.
28. Aparicio T, Manfredi S, Tougeron D, Bouche O, Pezet D, Mariette C.NADEGE prospective cohort: demographic date of 335 small bowel adenocarcinomas. Eur Cancer Congress. Abstract no 2466. 2013.
29. Koinuma K, Shitoh K, Miyakura Y, Furukawa T, Yamashita Y, Ota J. Mutations of BRAF are associated with extensive hMLH1 promoter methylation in sporadic colorectal carcinomas. Int J Cancer. 2004; 108: 237-242.

30. Schulmann K, Brasch FE, Kunstmann E. HNPCC-Associated small bowel cancer: clinical and molecular characteristics. Gastroenterology. 2005; 128: 590-599.

31. Haanstra JF, Al-Toma A, Dekker E. Prevalence of small bowel neoplasia in Lynch syndrome assessed by videocapsule endoscopy. Gut. 2015; 64: 1578-1583

32. Saurin JC, Pilleul F, Soussan EB. Small bowel capsule endoscopy diagnoses early and advanced neoplasms in asymptomatic patients with Lynch syndrome. Endoscopy. 2010; 42: 1057-1062.

33. Koornstra JJ. Small bowel endoscopy in familial adenomatous polyposis and Lynch syndrome. Best Pract Res Clin Gastroenterol 2012; 26: 359-368.

34. Talamonti MS, Goets LH, Rao S, Joehl RJ. Primary cancers of the small bowel: analysis of prognostic factors and results of surgical management. Arch Surg. 2002; 137: 564-570.

35. Dabaja BS, Suki D, Pro B, Bonnen M, Ajani J. Adenocarcinoma of the small bowel: presentation, prognostic factors and outcome of 217 patients. Cancer. 2004; 101: 518-526.

36. Overman MJ, Hu CY, Kopetz S, Abbruzzese JL, Wolff RA, Chang GJ. A population based comparison of adenocarcinoma of the large and small intestine: insights into a rare disease. Ann Surg Oncol. 2012; 19: 1439-1445.

37. Caspari R, von Falkenhasuen M, Krautmacher C, Schild H, Heller J, and Sauerbruch T. Comparison of capsule endoscopy and magnetic resonance imaging for the detection of polyps of the small intestine in patients with familial adenomatous polyposis or with Peutz-Jeghers syndrome. Endoscopy. 2004; 36: 1054-1059.

38. Parsi MA and Burke CA. Utility of capsule endoscopy in Peutz-Jeghers syndrome. GastrointestEndosc Clin N Am. 2004; 14: 159-167.

39. Vasen HFA, Moslein G, Alonso A. Guidelines for the clinical management of adenomatous polyposis (FAP). Gut. 2008; 57: 704-713.

40. Tumori Journal. Fondazione IRCCS Instituto. Nazionale Dei Tumori 2018. Article reuse guidelines: sagepub.com/journals-permissions. 2019.

41. Pennazio M, Spada C, Eliakim R. Small-bowel capsule endoscopy and device-assisted enteroscopy for diagnosis and treatment of small bowel disorders: European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline. Endoscopy. 2015; 47: 352-376.