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Case Report

Intussusception secondary to signet ring cell adenocarcinoma in adolescent ☆

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ABSTRACT

Despite the overall decrease in incidence and mortality rates for older adults, colorectal cancer in young adults is increasing. We present a case of a 15-year-old male who presented with 1.5 weeks of intermittent, sharp, severe right-sided abdominal pain. Abdominal radiograph demonstrated an air-fluid level within the right hemiabdomen. Computed tomography demonstrated marked wall thickening and a mass at the junction of the ascending colon and hepatic flexure causing obliteration of the lumen with a fluid-filled, dilated ascending colon. Follow-up ultrasonography demonstrated a 5.9 × 3.9 cm targetoid lesion in the right upper quadrant concerning for intussusception. Contrast enema revealed failure of contrast filling beyond the hepatic flexure due to a lobulated central filling defect surrounded by a claw-like contrast extension. Pathology of the polypoid lesion revealed poorly differentiated signet ring cell adenocarcinoma of the colon at the hepatic flexure. Despite its rarity, this case elucidates the need to consider colorectal carcinoma in adolescent and young adult patients who present with recurrent abdominal signs and symptoms.

Introduction

Colorectal cancer is the fourth most incident cancer among adult men and women [1]. Although the overall incidence and mortality rates for older adults are decreasing due to cancer screening, there has been a rise in incidence of colorectal cancer in younger adults in the United States [2]. However, colorectal cancer remains a rare malignancy in individuals <19 years of age with an approximate incidence of 1:1,000,000 [3]. Due to its rarity, other diagnoses are often considered prior to investigating a malignant etiology. We present an adolescent that developed intermittent, severe right-sided abdominal pain who was later found to have signet ring cell adenocarcinoma of the colon as initially evidenced by marked wall thickening and a mass on computed

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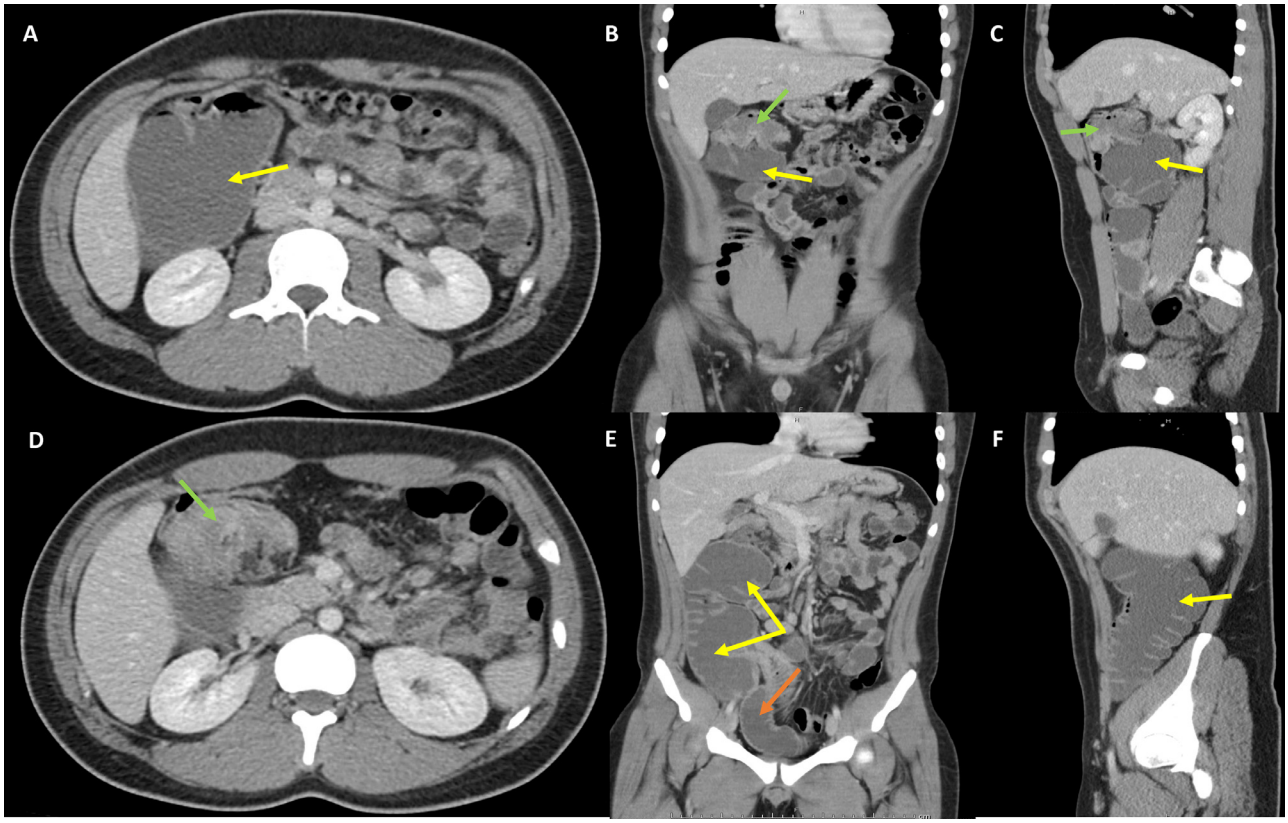

Fig. 1 – CT of the abdomen pelvis on the day of admission demonstrating severe distension and obstruction of a fluid-filled ascending colon measuring 7.4 cm diameter (yellow arrows; A-C, E, F). An obstructed and fluid-filled distal ileum is seen measuring 3.7 cm in diameter (orange arrow; E) with circumferential wall thickening of the terminal ileum. A mass at the level of the distal ascending colon/hepatic flexure of the large bowel is consistent with neoplasm/intussusception secondary to neoplasm (green arrows; B-D). The transverse colon and descending colon are nonobstructed and partially collapsed. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

tomography (CT) with filling defects seen on the contrast enema.

Case presentation

A 15-year-old male patient with no past medical history presented to an urgent care for approximately 1.5 weeks of intermittent, sharp, severe, right-sided abdominal pain. He had associated nausea without vomiting, constipation, and had not passed gas for past 2 days. An abdominal radiograph at that time revealed moderate stool burden with an air-fluid level in the right hemiabdomen. The patient was sent to an outside emergency department for further evaluation. A CT of the abdomen showed marked wall thickening and a mass at the junction of the ascending colon and hepatic flexure causing obliteration of the lumen and retrograde obstruction of the ascending colon and terminal ileum (Fig. 1). This was interpreted as intussusception or intussusception secondary to a colonic mass at the outside facility. He was then sent to our institution for exploratory laparotomy and definitive treatment.

On arrival to our hospital, the Pediatric Radiology Department was consulted for reduction of the intussusception with a contrast enema under ultrasound. Ultrasound showed a 5.9 × 3.9 cm targetoid lesion/mass in the right upper quadrant, which was suspicious for intussusception (Fig. 2). There was normal retrograde filling of contrast through the rectosigmoid and descending colon. In the proximal transverse colon/hepatic flexure, there was failure of contrast filling beyond the hepatic flexure due to a lobulated central filling defect surrounded by a claw-like contrast extension (Fig. 3). This lesion was better defined on post-evacuation images which again revealed a lobulated, frond-like mass or intussusception secondary to a colonic mass at the hepatic flexure marginated by residual contrast. However, attempts of reduction were unsuccessful.

The pediatric surgery team was consulted for surgical intervention for the colo-colonic intussusception secondary to a colonic mass as the lead point. The pediatric surgery team discussed the case in conjunction with the pediatric gastroenterology team and adult colorectal surgeons, should the mass turn out to be malignant. The decision to first pursue a colonoscopy with manual reduction was made. If unsuccessful, the contingency plan would be to perform a colotomy with polypectomy or potential hemicolectomy with or without stoma formation. During the colonoscopy, there was a partially obstructing, noncircumferential large mass found at the

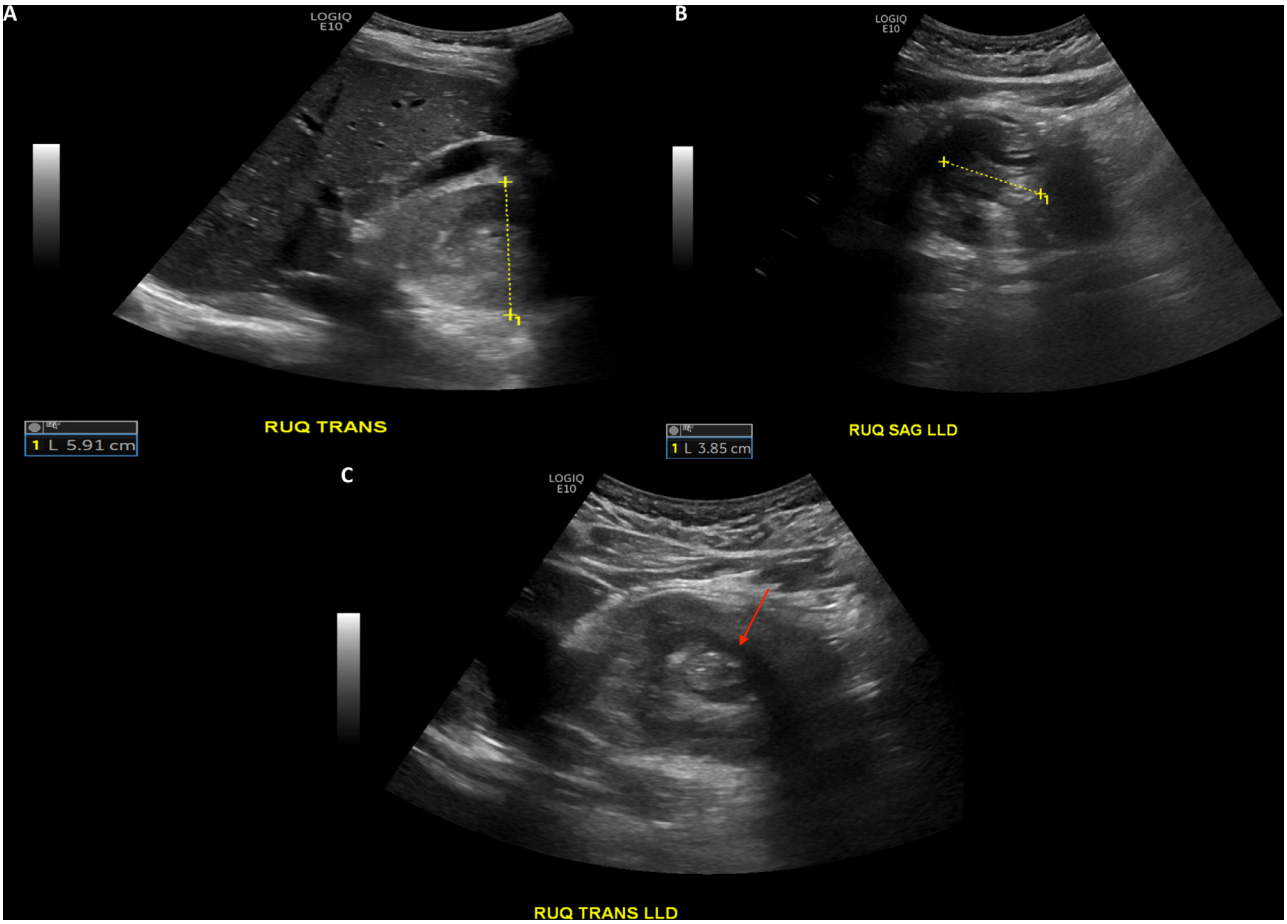

Fig. 2 – Abdominal ultrasound on the day of admission showing a 5.9 x 3.9 cm mass in the right upper quadrant, with what was originally thought to represent the classic "target-sign" (red arrow; C), consistent with intussusception. No free fluid is seen in the intraperitoneal space. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

hepatic flexure (Fig. 4). Blood was seen oozing from the mass. Biopsies were taken with cold forceps for histology. Given the very suspicious nature of the lesion for malignancy, the decision for an exploratory laparotomy and right hemicolectomy was made. The surgery was performed as planned and the patient had an open right hemicolectomy with a 10 cm distal margin and an ileocolic anastomosis to re-establish gastrointestinal continuity. Following the surgery, the patient had a postoperative recovery that was mostly unremarkable, with the exception of postprocedural pain.

Pathology of the 5.9 × 4.5 × 3.3 cm polypoid lesion returned as grade 3 poorly differentiated signet ring cell adenocarcinoma (Figs. 5 and 6). The tumor was seen invading through the muscularis propria into the pericolonic tissue. Immunohistochemistry testing for mismatch repair proteins did not reveal a loss of nuclear expression of mismatch repair proteins so the pathologists felt there was a low probability for microsatellite instability. However, it was recommended to confirm this finding with genetic sequencing. Examination of the lymph nodes revealed partial involvement. Pathologic stage classification was pT3N2a (American Joint Committee on Cancer 8th edition).

Several days after being discharged from the hospital, the patient was seen in an outpatient hematology-oncology office to initiate chemotherapy. Prior to the visit, carcinoembryonic antigen (CEA) and CT of the thorax to assess for metastatic disease was completed. CEA was 1.1 ng/mL (reference range: <3.4 ng/mL) and the CT of the thorax was found to be normal. A geneticist met with the patient to discuss hereditary forms of colon cancer and the increased familial risk for cancer. A CancerNext-Expanded test (Ambry Genetics, Aliso Viejo, CA) was sent to assess for mutations in the aryl hydrocarbon receptor-interacting protein. The patient was found to be heterozygous for the p.E24Q (c.70G>C) variant of unknown significance, which is a glycine to cysteine mutation at position 70 resulting in a missense amino acid substitution of glutamic acid for glutamine at position 24. No additional pathogenic mutations, variants of unknown significance, or gross deletions or duplications were detected. After the visit, the patient was subsequently scheduled for port placement to begin oxaliplatin, 5-fluorouracil, and leucovorin for a total of 12 cycles over the course of 6 months. To date, the patient has nearly completed his chemotherapy regimen without any evidence of metastatic, progressive, or recurrent disease.

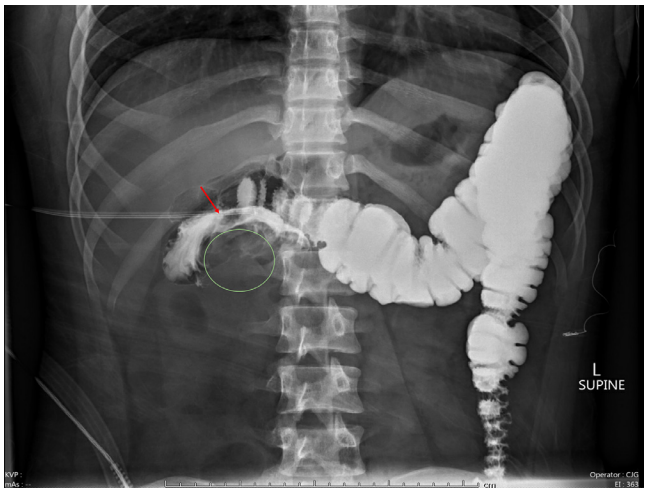

Fig. 3 – Radiograph of the abdomen after fluoroscopic administration of water-soluble contrast on day 1 of admission demonstrating failure of contrast filling beyond the hepatic flexure due to a lobulated central filling defect (green circle), surrounded by a claw-like contrast extension (red arrow) at the region of the hepatic flexure. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Discussion

Despite the rarity of pediatric colon cancer, the disease carries a poor prognosis compared to adult colorectal cancer patients due to the typically delayed diagnosis and thus, more advanced disease [4,5]. Pediatric colorectal cancer accounts for approximately 0.4% of all fatal malignancies in patients younger than 15 years old with some studies indicating that most cases occur in the second decade of life [6,7]. The transverse colon is the most common primary site for pediatric colorectal cancer [8]. As with adults, adolescent and young adults with inflammatory bowel disease and inherited disorders have an increased risk of developing colon cancer [9,10].

The majority of colorectal cancer are adenocarcinoma [11]. A rare primary subtype of mucinous adenocarcinoma is signet ring cell carcinoma, which is characterized by an abundance of intracellular mucin [7,12]. Children with these tumors have a poor prognosis (average 5-year survival is 18%) [12]. This may be explained due to the aggressiveness of the malignancy and advanced stage of the disease at presentation, often thought to be due to the disease rarity, more frequent presentation of right-sided colonic lesions, and workup of other more common causes prior to considering a malignant etiology [6-8].

Due to the young age of onset of colorectal cancer in our patient, heritable malignancies were considered. Our patient received next generation genetic sequencing to assess for mutations that are correlated with malignancies as one mechanism leading to the development of colorectal cancer is through genetic mutations. Destabilization of chromosomal structures may arise from amplification, deletion, or translocation of genetic material, or through microsatellites (short, tandemly repeated DNA sequences within genes) [13]. Patients with alter-

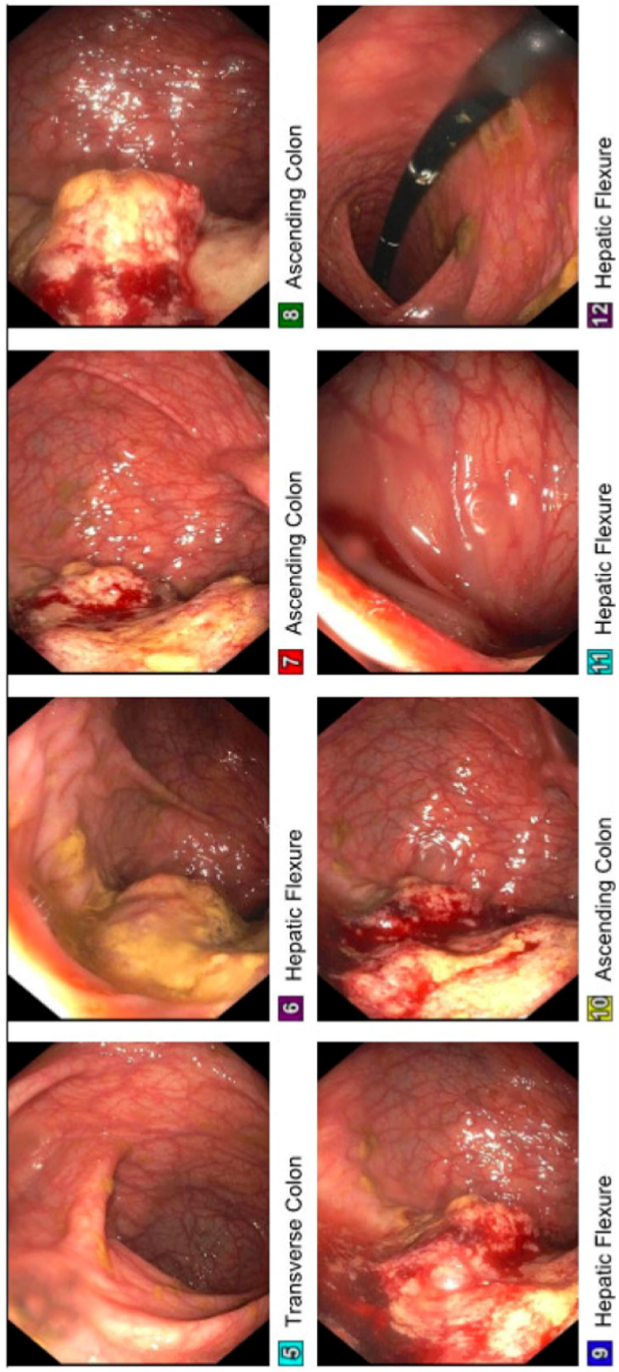

Fig. 4 – Images from a colonoscopy demonstrating a partially obstructing, noncircumferential large mass at the level of the hepatic flexure in the transverse colon extending into the ascending colon.

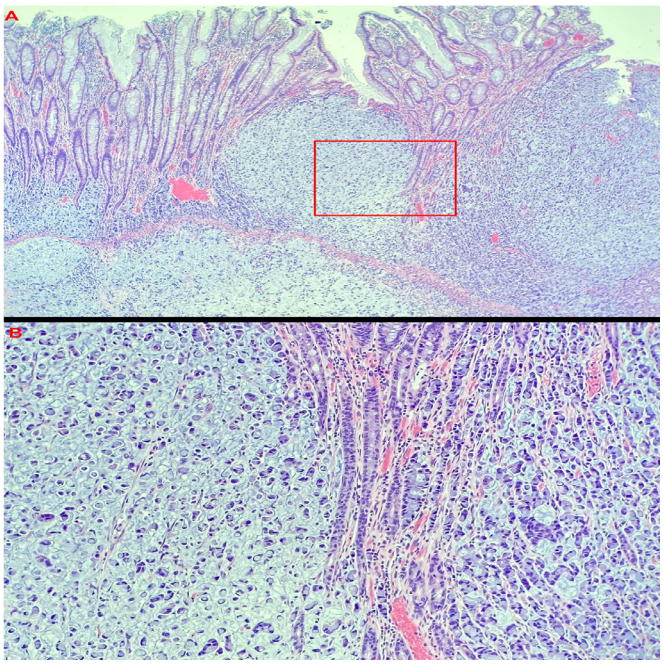

Fig. 5 – Microscopic pathology of the colonic mass stained with hematoxylin and eosin (A; ×5 magnification) revealed evidence of the grade 3, poorly differentiated tumor invading through the muscularis propria into the pericolonic tissue was present. Closer review with higher magnification (red box; A) reveals mucinous islands with occasional inflammatory cells and characteristic infiltrating cells with a signet ring nucleus (B; ×20 magnification). Immunohistochemistry testing of these specimens for mismatch repair proteins (not shown) revealed background nonneoplastic tissue with intact nuclear expression. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

ations in their mismatch-repair genes, which normally repair mismatched nucleotide bases, have a higher risk of developing colorectal carcinoma [14]. As many as 85%-90% of patients with hereditary nonpolyposis colorectal cancer (HNPCC) have high-frequency microsatellite instability (MSI-H) [14]. Furthermore, approximately 15% of sporadic cases of colorectal cancer have MSI-H and up to 80% of sporadic colorectal cancers may have hypermethylation of the hMLH1 gene promoter region, a gene that encodes for mismatch-repair proteins [15,16]. The presence of MSI-H has important implications on improved survival independent of age, tumor stage and grade, and primary site [17]. The characteristic colorectal tumor that arises from MSI-H typically occurs proximal to the splenic flexure, are poorly differentiated or of the mucinous cell type, less likely metastatic, and are more likely to occur in females [18]. Although our patient was young male, his primary tumor was in the distal ascending colon/hepatic flexure, was of the mucinous subtype (signet ring cell adenocarcinoma), and to date has not been found to be metastatic.

HNPCC accounts for approximately 1%-5% of all colorectal cancers as a result of a germline mutation in at least one of the DNA mismatch-repair genes (MSH2, MLH1, MSH6, PMS1, PMS2, MLH3, and EXO1) [19]. It is estimated that among the approximately 750 HNPCC kindreds worldwide, there are over 450 known pathogenic mutations in the DNA mismatch-repair genes that account for these observations [20]. Among the more common genes (MLH1 and MSH2), the majority of mutations arise from nonsense, missense, or frameshift mutations which creates an abnormal amino acid sequence subsequently causing alterations in splicing [19]. As a result, individuals with HNPCC have an increased risk for developing extracolonic malignancies, such as gastric cancer, endometrial

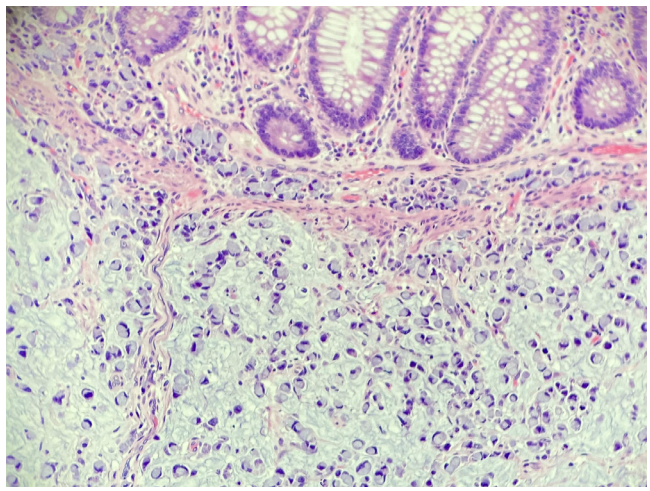

Fig. 6 – Microscopic pathology of area adjacent to colonic mass stained with hematoxylin and eosin (×40 magnification) revealed prominent extracellular mucinous islands with infiltrating signet ring cell adenocarcinoma and inflammatory cells.

carcinoma, ovarian carcinoma, urinary tract and hepatobiliary cancers [19].

Patients with predisposing factors for colorectal cancer and recurrent abdominal symptoms (such as intestinal obstruction or intussusception, intractable abdominal pain, alteration in bowel habits, and gastrointestinal bleeding), or otherwise suspected cases of HNPCC per family history should have a low threshold for diagnostic testing with a combination of genetic testing, CT, and/or colonoscopy. While unusual, colorectal cancer in an adolescent patient should not be excluded until properly evaluated. Prompt diagnosis and treatment is needed in patients with colorectal carcinoma as delayed diagnosis and treatment lend itself to an advanced stage of tumor at presentation, an important prognostication factor.

Conclusion

Despite its rarity, pediatric colorectal cancer remains an issue with significant implications on patients' morbidity and mortality. More common conditions, such as intussusception, are often considered prior to considering a malignant etiology. This delay in diagnosis may permit further advancement of the stage and grade of the tumor, which has a significant impact on patients' prognosis. During the initial workup for adolescent and young adults presenting with signs of weight loss or anorexia, intussusception, or bowel obstruction, colon cancer should be considered, especially if there is a family history of gastrointestinal, endometrial, or thyroid carcinoma as this may indicate an underlying hereditary cancer syndrome.

Patient consent

No consent obtained for this case report as this is a retrospective study with no patient identifiers.

Formal consents are not required for the use of entirely anonymized images from which the individual cannot be identified—for example, x-rays, ultrasound images, pathology slides, or laparoscopic images, provided that these do not contain any identifying marks and are not accompanied by text that might identify the individual concerned.

REFERENCES

[1] Siegel RL, Miller KD, Jemal A. Cancer statistics, 2020. CA Cancer J Clin 2020;70(1):7–30. doi:10.3322/caac.21590.

[2] Siegel RL, Fedewa SA, Anderson WF, Miller KD, Ma J, Rosenberg PS, et al. Colorectal cancer incidence patterns in the United States, 1974-2013. J Natl Cancer Inst 2017;109(8):djw322. doi:10.1093/jnci/djw322.

[3] Blumer SL, Anupindi SA, Adamson PC, Lin H, Price AP, Markowitz RI, et al. Sporadic adenocarcinoma of the colon in children: case series and review of the literature. J Pediatr Hematol Oncol 2012;34(4) e137-41. doi:10.1097/MPH.0b013e3182467f3e.

[4] Chantada GL, Perelli VB, Lombardi MG, Amaral D, Cascallar D, Scopinaro M, et al. Colorectal carcinoma in children, adolescents, and young adults. J Pediatr Hematol Oncol 2005;27(1):39–41. doi:10.1097/01.mph.0000149251.68562.8e.

[5] Kravarusic D, Feigin E, Dlugy E, Steinberg R, Baazov A, Erez I, et al. Colorectal carcinoma in childhood: a retrospective multicenter study. J Pediatr Gastroenterol Nutr 2007;44(2):209–11. doi:10.1097/01.mpg.0000252195.84084.52.

[6] Rao BN, Pratt CB, Fleming ID, Dilawari RA, Green AA, Austin BA. Colon carcinoma in children and adolescents. A review of 30 cases. Cancer 1985;55(6):1322–6. 10.1002/1097-0142(19850315)55:6<1322::aid-cncr2820550627>3.0.co;2-5.

[7] Angelini C, Crippa S, Uggeri F, Bonardi C, Sartori P, Uggeri F. Colorectal cancer with neuroendocrine differentiation in a child. Pediatr Surg Int 2005;21(10):839–40. doi:10.1007/s00383-005-1525-3.

[8] Karnak I, Ciftci AO, Senocak ME, Büyükpamukçu N. Colorectal carcinoma in children. J Pediatr Surg 1999;34(10):1499–504. doi:10.1016/s0022-3468(99)90112-4.

[9] Noh SY, Oh SY, Kim S-H, Kim H-Y, Jung S-E, Park K-W. Fifteen-year-old colon cancer patient with a 10-year history of ulcerative colitis. World J Gastroenterol 2013;19(15):2437–40. doi:10.3748/wjg.v19.i15.2437.

[10] Strate LL, Syngal S. Hereditary colorectal cancer syndromes. Cancer Causes Control 2005;16(3):201–13. doi:10.1007/s10552-004-3488-4.

[11] Washington MK, Berlin J, Branton P, Burgart LJ, Carter DK, Fitzgibbons PL, et al. Protocol for the examination of specimens from patients with primary carcinoma of the colon and rectum. Arch Pathol Lab Med 2009;133(10):1539–51. doi:10.1043/1543-2165-133.10.1539.

[12] Symonds DA, Vickery AL. Mucinous carcinoma of the colon and rectum. Cancer 1976;37(4):1891–900. 10.1002/1097-0142(197604)37:4<1891::aid-cncr2820370439>3.0.co;2-z.

[13] Lengauer C, Kinzler KW, Vogelstein B. Genetic instability in colorectal cancers. Nature 1997;386(6625):623–7. doi:10.1038/386623a0.

[14] Liu B, Parsons R, Papadopoulos N, Nicolaides NC, Lynch HT, Watson P, et al. Analysis of mismatch repair genes in hereditary non-polyposis colorectal cancer patients. Nat Med 1996;2(2):169–74. doi:10.1038/nm0296-169.

[15] Aaltonen LA, Salovaara R, Kristo P, Canzian F, Hemminki A, Peltomaki P, et al. Incidence of hereditary nonpolyposis colorectal cancer and the feasibility of molecular screening for the disease. N Engl J Med 1998;338(21):1481–7. doi:10.1056/NEJM199805213382101.

[16] Wheeler JM, Loukola A, Aaltonen LA, Mortensen NJ, Bodmer WF. The role of hypermethylation of the hMLH1 promoter region in HNPCC versus MSI+ sporadic colorectal cancers. J Med Genet 2000;37(8):588–92. doi:10.1136/jmg.37.8.588.

[17] Samowitz WS, Curtin K, Ma KN, Schaffer D, Coleman LW, Leppert M, et al. Microsatellite instability in sporadic colon cancer is associated with an improved prognosis at the population level. Cancer Epidemiol Biomark 2001;10(9):917–23.

[18] Kim H, Jen J, Vogelstein B, Hamilton SR. Clinical and pathological characteristics of sporadic colorectal carcinomas with DNA replication errors in microsatellite sequences. Am J Pathol 1994;145(1):148–56.

[19] Papp J, Kovacs ME, Olah E. Germline MLH1 and MSH2 mutational spectrum including frequent large genomic aberrations in Hungarian hereditary non-polyposis colorectal cancer families: implications for genetic testing. World J Gastroenterol 2007;13(19):2727–32. doi:10.3748/wjg.v13.i19.2727.

[20] Peltomäki P, Vasen H. Mutations associated with HNPCC predisposition – update of ICG-HNPCC/INSiGHT mutation database. Dis Markers 2004;20(4-5):269–76. doi:10.1155/2004/305058.