Case Report

# Colorectal Cancer on the Rise in Children and Young Adults: A Series of Three Cases and Its Implications for Early Detection

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**Introduction. Mucinous colorectal adenocarcinoma, a rare type of colorectal cancer (CRC), ranks as the second most common primary malignancy of the gastrointestinal system in children, accounting for 1% of pediatric neoplasms. Its extreme rarity and non-specific symptoms frequently result in delayed diagnosis and poor prognosis. We present three cases of this distinctive condition in adolescents. Case presentations. We present three adolescents with mucinous adenocarcinoma. The first patient complains of hematochezia, fluctuating abdominal pain, fatigue, and weight loss. The second patient complains of melena, left lower abdominal pain, weight loss, and an anal mass. The third patient complains of constipation, urinary retention, and weight loss. A digital rectal examination revealed a mass in the anorectal region, and the abdominal CT scan confirmed a malignant mass in that region. Discussion. The mucinous histopathological type is the most prevalent, demonstrating an increased capacity to invade surrounding stromal tissue. It is primarily found in the proximal colon and is the most common form of pediatric colorectal cancer (CRC). Most cases involve a less frequent type of CRC, which typically presents with non-specific signs and symptoms that often persist for three months before diagnosis. This biological behavior is reported to be associated with its aggressive nature. Furthermore, the delayed diagnosis of colorectal carcinoma in children contributes to the advanced stage of the disease at the time of diagnosis. Some reports estimate that 60% to 80% of children and adolescents present with stage 3 and 4 CRC, leading to a poor prognosis. Conclusion. Mucinous colorectal adenocarcinoma occurs in both children and adolescents despite its rarity. Since symptoms are nonspecific in children, it can lead to a delay in diagnosis, and a poor**

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**prognosis is linked with this delay. This underscores the urgent need for more pediatric prospective studies to guide treatment guidelines, which are currently extrapolated from adults.**

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## Introduction

Colorectal malignancies are rare malignancies in the pediatric population. Among 1 million people globally, 1-2 children or adolescents are diagnosed with colorectal cancer; however, the incidence has seen a rise.[1] Over 70% of colorectal cancers are sporadic.[2] After primary liver tumors, colorectal cancer is the second most common primary gastrointestinal system malignancy in children, comprising 1% of all pediatric neoplasms.[3] Low awareness of the disease plays a part in delayed diagnosis, causing a poor prognosis compared with adult cases. Non-specific presenting symptoms and symptoms mimicking many benign gastrointestinal conditions in children also cause delayed diagnosis in this population.[4] The youngest age at diagnosis for colorectal cancer is nine months old. However, the most common age range at diagnosis is within the second decade, averaging 15-19 years old.[5]

Mucinous adenocarcinoma is a histological subtype of colorectal cancer (CRC). It is defined as a tumor with >50% of its body showing a mucinous pattern upon histological examination, with a large amount of extracellular mucin produced by secreting acini.[6] It differs in clinical and histopathological features compared with other adenocarcinomas.[6] Mucinous CRC is more commonly located in the proximal colon and is the most frequent form of pediatric CRC. Most patients present with non-specific signs and symptoms.[7][8][9]

Symptoms of colorectal cancer in pediatric patients are not different from those seen in adults. In most cases, chronic abdominal pain, hematochezia or melena, weight loss, persistent iron deficiency, and anemia can be related to colorectal cancer. Typical symptoms of colorectal cancer include vomiting, severe abdominal pain, and bloody stools; however, in children, the symptoms might be restricted to only altered bowel habits. The location of the cancer can be a significant factor in the manifestation of specific symptoms.[3]

Due to its extreme rarity and non-specific symptoms, mucinous colorectal adenocarcinoma in adolescents tends to be diagnosed late and presents with a poor prognosis. This report describes three pediatric cases diagnosed with mucinous colorectal adenocarcinoma, each with a different disease

progression. With this case review, we highlight the significant impact of delayed diagnosis on patient outcomes, underscoring the need for early recognition and detection.

All patients in this series gave informed consent, and this report was written according to the Declaration of Helsinki.

## Case Presentation

### *Case 1*

A 16-year-old male presented with hematochezia for the past two months, accompanied by intermittent intense abdominal pain and a weight loss of 5 kg. The patient also reported weakness and extreme fatigue. During the physical examination, abdominal tenderness was noted, bowel sounds were normal, and no abdominal distension was observed. A digital rectal examination revealed a mass palpated 6 cm from the anocutaneous line, with no blood or feces present on the gloves. Vital signs were within normal limits. An abdominal CT scan confirmed the presence of a malignant mass in the high rectosigmoid wall, approximately 7 cm long, located 10 cm from the anocutaneous line. Minimal fat stranding was observed without any obstruction on the proximal side (Fig. 1). Multiple lymphadenopathies were found along the perirectal mesocolon, right para-obturator, bilateral internal para-iliac, and right external para-iliac regions. The CT scan also showed a fatty liver and hepatomegaly, with multiple liver nodules suggesting metastasis (Fig. 1). Following these findings, we performed a sigmoid colostomy and mass biopsy. Histological results confirmed mucinous adenocarcinoma. The patient was diagnosed with stage four mucinous rectal adenocarcinoma (cT3NxM1). A low anterior resection was performed four weeks after the colostomy and biopsy. The patient remained clinically stable following surgery and was discharged on postoperative day seven. Despite receiving adjuvant chemotherapy as planned, pulmonary metastatic lesions subsequently developed, resulting in progressive clinical deterioration characterized by respiratory distress, which ultimately led to the patient's demise.

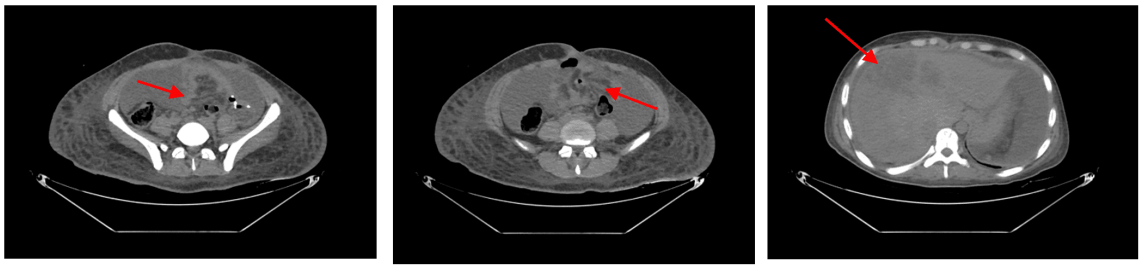

**Figure 1.** Abdominal non-contrast CT showing mass and hepatic nodule suggesting metastasis

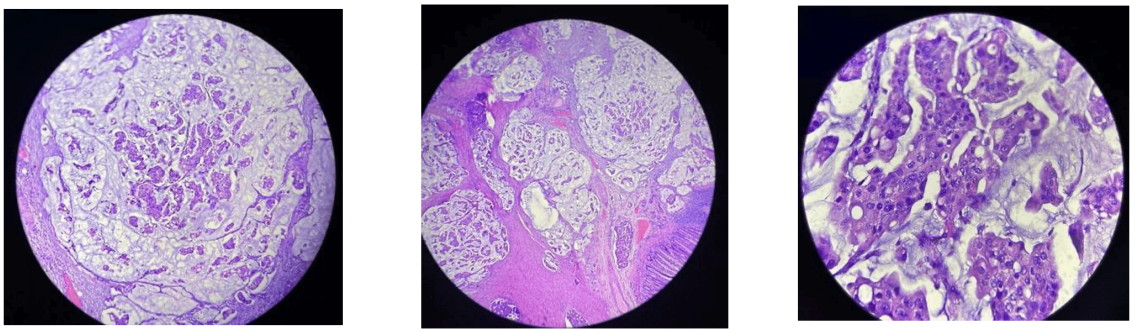


**Figure 2.** A (HE 40x), B (HE 100x), C (HE 400x): The mucinous adenocarcinoma tumor mass is arranged in glandular, cribriform, and infiltrative patterns, interspersed with pools of mucin.

## *Case 2*

A 16-year-old female presented with loose stools and blood lasting for the past 3 months. The patient also reports a mass in the anal region that tends to bleed. Additionally, she has experienced left lower quadrant abdominal pain and has lost approximately 12 kilograms over the last 5 months. Each time she passes gas, there are slimy secretions and fecal matter. Physical examinations showed typical vital signs. Colonoscopic findings revealed multiple nodular masses. Biopsy and sigmoid colostomy were performed to divert fecal matter. Abdominal CT indicated a malignant mass on the rectal wall that narrowed the lumen of the rectum (Fig. 3). Histological results confirmed mucinous carcinoma (Fig. 4). The patient was diagnosed with stage three mucinous rectal adenocarcinoma (cT4NxM0). Following the colostomy surgery, she was scheduled for neoadjuvant radiotherapy before definitive treatment. While under observation during radiotherapy, the tumor progressed to progressive disease, with infiltration into the

vagina observed. It was then decided to proceed with R1 resection surgery. The patient experienced a favorable postoperative recovery and was discharged on postoperative day ten. She returned for an initial follow-up and was scheduled to begin chemotherapy; however, she has not presented for subsequent appointments, and the medical team has been unable to establish further contact with her or her family.

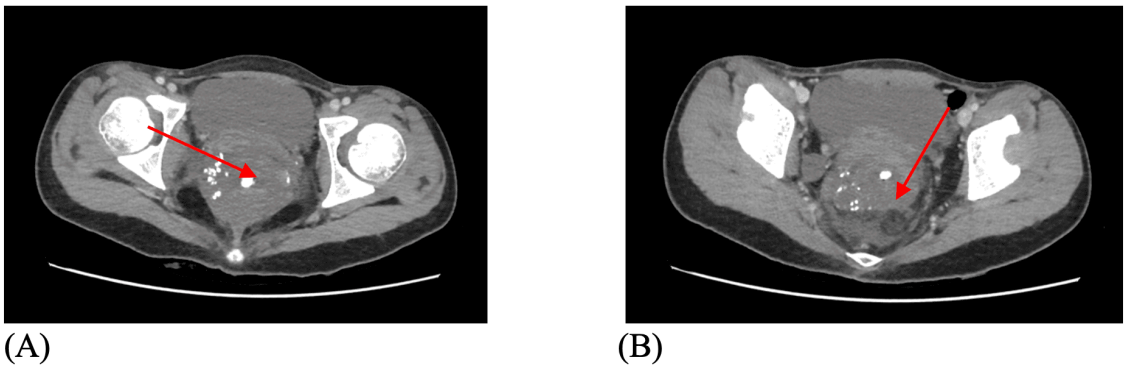


**Figure 3.** Abdominal contrast CT shows the mass. (A) Mass in the rectum with contrast enhancement. (B) Arrow pointing at the narrowed rectal lumen

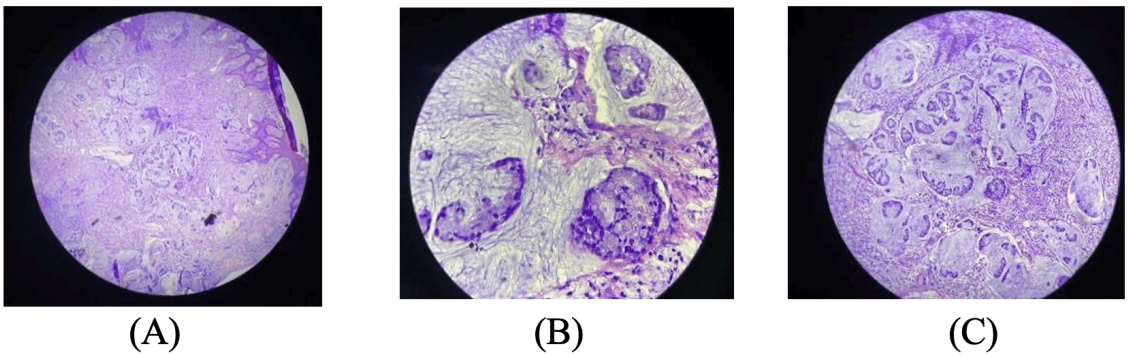


**Figure 4.** Histological finding: A (HE 40x), B (HE 100x), C (HE 400x): Mucinous adenocarcinoma is arranged in glandular, cribriform, and infiltrative patterns, interspersed with mucin pools

## *Case 3*

A 17-year-old female presented with one month of urinary retention and chronic constipation lasting four months. The patient reports significant weight loss during these four months. Additionally, there was a loss of appetite accompanied by nausea and vomiting. The patient also complains of hematuria and


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pain during urination. There is a family history of thyroid cancer on the patient's father's side, but genetic testing was not conducted for this patient; therefore, it remains unclear whether the disease has a genetic basis. An MRI examination revealed a contrast-enhancing mass in the sigmoid colon with papillary wall thickening (the image has since been lost). A sigmoidectomy showed a 13x12x7.5 cm mass (Fig. 5) with adhesions to the level of the pelvis. No metastases were found in the lungs, liver, lymph nodes, or intra-abdominal area. Histological results indicated mucinous adenocarcinoma with epithelial proliferation and mitosis (Fig. 6). Following the surgery, a 12-cycle chemotherapy regimen was initiated. The patient is currently on the $11^{th}$ cycle with 3,170 mg of 5-FU as adjuvant therapy, 170 mg of oxaliplatin, and 520 mg of leucovorin. The patient gained 19 kg, increasing from 29 to 48 kilograms after chemotherapy, and is clinically stable without significant complaints.

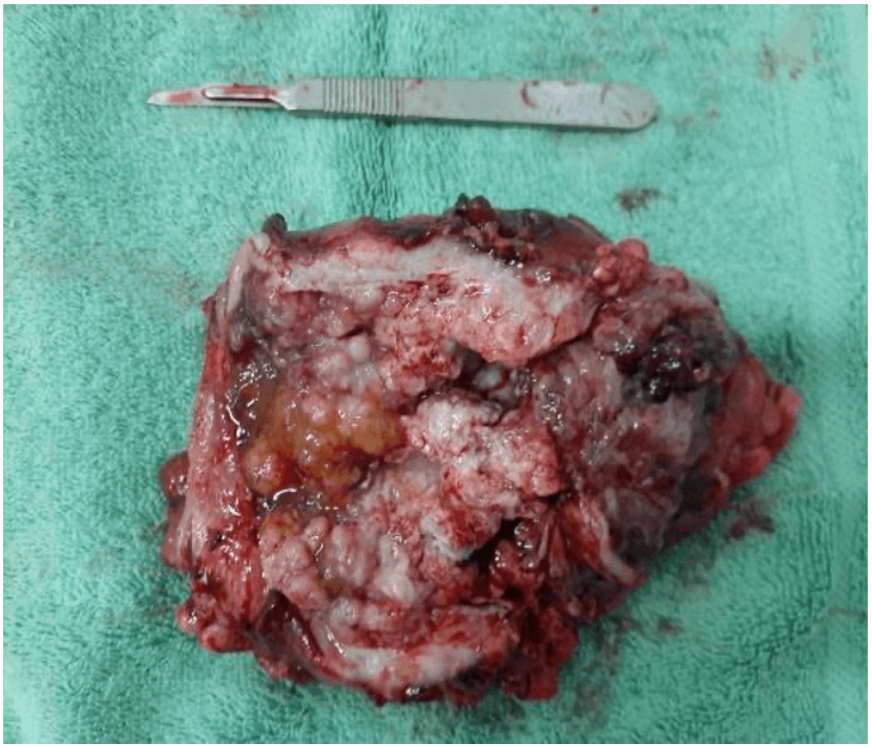

**Figure 5.** Gross pathology of the tumor


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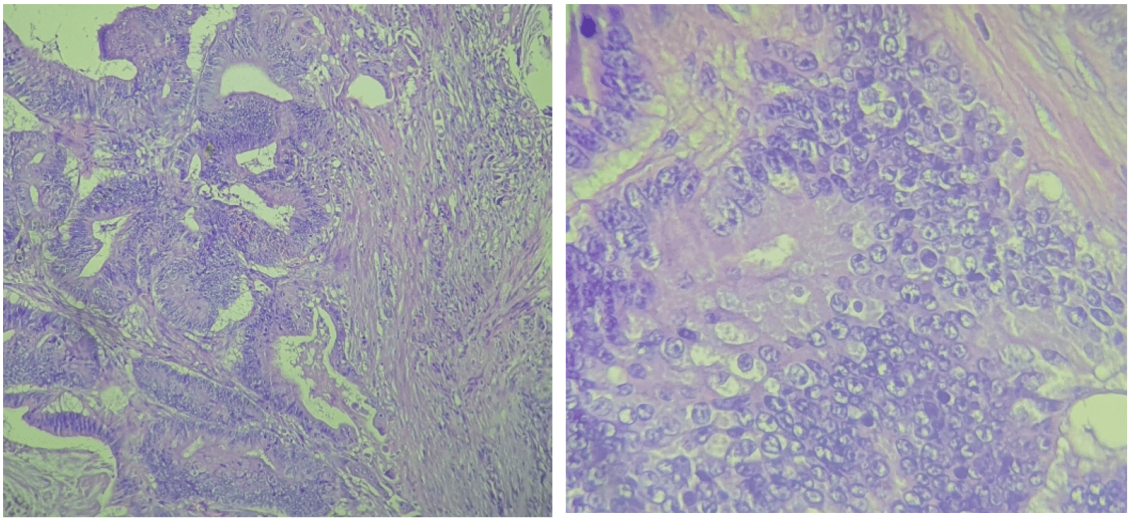

**Figure 6.** Histologic slide showing features of mucinous adenocarcinoma. Glands were arranged in a dense back-to-back pattern, and epithelial proliferation and mitosis were shown.

## Discussion

Despite its rarity, adenocarcinoma can occur in children and adolescents. A study on adenocarcinoma in the South Korean pediatric population revealed that nearly half of all patients experienced a delay of two months or more from the onset of initial symptoms to diagnosis. Regardless of family history, the diagnosis of pediatric adenocarcinoma was relatively delayed, often occurring at an advanced stage. [7] Most patients were also diagnosed with distant metastasis, which is further illustrated by the case we present here. For all the patients, colorectal carcinoma was not the initial diagnosis.

Colorectal carcinoma primarily affects older adults, with incidence peaking around age 65; it ranges between 5% and 6% in the general population. [5] Due to its rarity in children and adolescents, it is often overlooked when diagnosing abdominal pain, weight loss, and anemia. [10] According to data from Surveillance, Epidemiology, and End Results (SEER), colorectal cancer presents a similar natural history in patients aged 15 to 29 as it does in older adults. [11] Most reported cases involve older adolescents, while prepubertal cases are sporadic. [12] Although the disease is mainly sporadic, certain genetic disorders increase the risk of developing colorectal carcinoma[1]. Lynch Syndrome, also known as hereditary nonpolyposis colorectal cancer (HNPCC), can significantly elevate the risk of early-onset disease. Lynch Syndrome is an autosomal dominant disorder caused by mutations in DNA mismatch repair (MMR)

genes, which include MLH1, MSH2, MSH6, PMS2, or EPCAM.[13] There are documented instances of children with Lynch Syndrome developing colorectal cancer, and a definitive diagnosis depends on genetic testing for both the patient and their family members.[14] At our center, genetic testing has not been conducted regularly. This is due to its high costs and the lack of coverage by the government health care system that all our patients depend on. As a result, no genetic testing was carried out in any of the three cases mentioned above.

Decreased appetite, weight loss, bowel changes, and rectal bleeding can indicate colorectal cancer in children.[15] All our patients showed these symptoms. Children and adolescents may present with acute abdominal issues like obstruction, perforation, or pain resembling appendicitis.[16] Symptoms may occasionally be limited to altered bowel habits. The clinical presentation often varies depending on tumour location: right-sided colorectal cancer may grow to a considerable size before producing noticeable symptoms, and commonly presents as a palpable mass, anaemia, diarrhoea, or intussusception. In contrast, left-sided tumours are more likely to cause obstructive symptoms, including changes in stool calibre, rectal bleeding, altered bowel habits, and anaemia.[8][15][17] Studies indicate that adults more commonly have left-sided colorectal cancer, while in children, it is evenly distributed throughout the colon.[18] Nonspecific symptoms can lead to delayed diagnosis, with some reports suggesting 60-80% of affected youth are diagnosed at stages 3 and 4.[19] Colorectal cancer is more common in males than females in pediatrics, with a 2:1 ratio.[20]

Once a diagnosis is suspected, further investigation typically includes abdominal X-rays, a barium enema, colonoscopy, and an abdominal CT scan, which may reveal obstruction, narrowing of the colonic lumen, or an abdominal mass.[15] Depending on the circumstances, a colonoscopy with polyp excision or an initial biopsy followed by delayed excision of the mass would be the subsequent step.[17] A biopsy is essential for diagnosing colorectal cancer; it may be obtained during colonoscopy or laparotomy.[21] In our center, we confirm the diagnosis through biopsy before proceeding with resection, with or without neoadjuvant treatment prior to the resection.

Most colorectal cancers in adults are moderately differentiated or well differentiated. [7] In contrast, over half of the reported cases of colorectal cancer in children are poorly differentiated adenocarcinomas, many of which are of the signet ring cell type. [15] Mucinous histology is considerably more frequent in the pediatric population than in adults, likely reflecting a biological difference between pediatric and adult colorectal cancer. [10]

Mucinous colorectal cancer in children is a rare diagnosis. This adenocarcinoma subtype is marked by mucinous components making up at least 50% of the tumor volume and significant extracellular mucin from acini.[22] This differs from signet-ring adenocarcinoma, where mucin stays inside the cell. The latter is known for its aggressive nature,[23] differing clinically and histologically from other adenocarcinomas.[6] Signet-ring adenocarcinoma is primarily found in the proximal colon and is the most common pediatric colorectal cancer, mostly occurring sporadically.[24][25] These tumors are also more aggressive, showing poorer chemotherapy response and extensive intramural spread and peritoneal carcinomatosis.[10] The histological pattern of mucinous carcinoma has been debated since Parham's initial description.[26] Using mucinous histology as a prognostic indicator remains controversial.[6]

For staging, the American Joint Committee on Cancer (AJCC) Tumor Node Metastases (TNM) system, often used alongside the Dukes-MAC staging systems, remains the standard for colorectal cancer. In both systems, early-stage disease is typically curable.[27] However, most pediatric patients, including those presented in this report, are diagnosed at advanced stages, correlating with a poor prognosis. Histological features also significantly contribute to prognosis: whereas mucinous adenocarcinoma accounts for less than 5% of colorectal cancers in adults, over 50% of pediatric cases are mucinous, a factor associated with inferior outcomes.[12]

Managing pediatric colorectal cancer requires adjustments and enhancements of adult treatment protocols due to the lack of trials specific to children.[7][10][16] The primary approach continues to be complete surgical resection, which entails removing the main tumor along with at least a 5 cm margin, nearby lymphatic beds, and any affected organs. Performing retroperitoneal lymph node dissection is essential for tumors that can be resected and plays a vital role in improving patient survival; without en bloc resection, a cure is improbable.[28][16][29] Depending on the tumor's position, subtotal colectomy is suggested for left-sided tumors, while extended hemicolectomy is preferred for those on the right.[30] However, pediatric patients often present with unresectable or metastatic disease, which complicates surgical interventions. For these advanced cases (stages III and IV), initial chemotherapy and radiotherapy might be considered. The chemotherapy regimens typically include platinum-based agents and 5-fluorouracil, sometimes alongside bevacizumab. Adjuvant therapy usually features a fluorouracil backbone supported by folinic acid, oxaliplatin, irinotecan, and biological agents like cetuximab or bevacizumab, especially for those with high-risk or advanced disease.[3][7][10][24]

The disease prognosis depends on factors like aggressive histological subtypes (e.g., signet ring and mucinous adenocarcinoma), advanced tumor grade, and disease stage.[29][30] Long-term survival rates in pediatric colorectal cancer vary from 20-50% across studies.[12][19] Sultan et al.[31] analyzed pediatric colorectal patients using the Surveillance, Epidemiology, and End Results database from 1973 to 2005, revealing a poor prognosis for mucinous adenocarcinoma and signet ring cell carcinoma. The 5-year survival estimate was about 40%, attributed to poor differentiation.[7][31] Key predictors of worse outcomes, apart from stage, include incomplete resection, mucinous histology, >10% signet ring cells, and lack of an in situ component.[10] As seen in case 1 and 2, due to delay diagnosis and intervention, both patients presented with more severe conditions compared to the third case. From this, we conclude that delayed diagnosis negatively impacts patient prognosis.

## Conclusion

Mucinous colorectal adenocarcinoma occurs in both children and adolescents, despite its rarity. It is the most common histological type of colorectal cancer in the pediatric population and is known to have a poor prognosis. This poor prognosis is linked to delays in diagnosis, as symptoms may be nonspecific in children. Lynch syndrome is also associated with colorectal cancer in adolescents; however, a definitive diagnosis requires genetic testing. Treatment guidelines are still extrapolated from adults, as prospective studies in pediatrics are still lacking.

## References


1. ^a, ^b *Signoroni S, Di Bartolomeo M, Ferrari A. Tumors of the Small Intestine, Colon, and Rectum. In 2022. p. 223–44.*
2. ^ *Yahaya JJ, Msokwa EK, Mremi A. Mucinous Colorectal Carcinoma in a 17-Year-Old Male: A Diagnosis with Low Clinical Index of Suspicion. Case Rep Pediatr. 2019;2019:1–5.*
3. ^a, ^b, ^c *Salas-Valverde S, Lizano A, Gamboa Y, Vega S, Barrantes M, Santamaría S, et al. Colon carcinoma in children and adolescents: prognostic factors and outcome—a review of 11 cases. Pediatr Surg Int. 2009;25:1073–6.*
4. ^ *Koh K-J, Lin L-H, Huang S-H, Wong J-U. CARE—Pediatric Colon Adenocarcinoma. Medicine. 2015;94:e503.*
5. ^a, ^b *Dillon PA, Foglia RP. Gastrointestinal Tumors. In: Pediatric Surgery. Elsevier; 2006. p. 515–23.*

6. a, b, c, dLeopoldo S, Lorena B, Cinzia A, Gabriella DC, Angela Luciana B, Renato C, et al. Two Subtypes of Mucinous Adenocarcinoma of The Colorectum: Clinicopathological and Genetic Features. Ann Surg Oncol. 2008;15:1429–39.
7. a, b, c, d, e, fYang H-B, Namgoong J-M, Kim KH, Kim DY, Park J, Shin HB, et al. Pediatric Adenocarcinoma in Korea: A Multicenter Study. Cancer Res Treat. 2020;52:117–27.
8. a, bAhn C hoon, Kim SC. Two case reports. Medicine. 2017;96:e8074.
9. ^Mremi A, Yahaya JJ. Advanced mucinous colorectal carcinoma in a 14-year old male child: A case report and review of the literature. Int J Surg Case Rep. 2020;70:201–4.
10. a, b, c, d, e, fHill DA, Furman WL, Billups CA, Riedley SE, Cain AM, Rao BN, et al. Colorectal Carcinoma in Childhood and Adolescence: A Clinicopathologic Review. Journal of Clinical Oncology. 2007;25:5808–14.
11. ^Bleyer A, O'leary M, Barr R, Ries LAG. Cancer epidemiology in older adolescents and young adults 15 to 29 years of age, including SEER incidence and survival: 1975-2000. Cancer epidemiology in older adolescents and young adults 15 to 29 years of age, including SEER incidence and survival: 1975-2000. 2006;
12. a, b, cFerrari A, Rognone A, Casanova M, Zaffignani E, Piva L, Collini P, et al. Colorectal carcinoma in children and adolescents: The experience of the Istituto Nazionale Tumori of Milan, Italy. Pediatr Blood Cancer. 2008;50:588–93.
13. ^Huang SC, Durno CA, Erdman SH. Lynch Syndrome. Journal of Pediatric Gastroenterology and Nutrition. 2014;58(2):144-52.
14. ^MacArthur TA, Ongie LJ, Lanpher BC, Ishitani MB. Pediatric manifestations of Lynch Syndrome: A single center experience. Journal of Pediatric Surgery Case Reports. 2022;86:102431.
15. a, b, c, dAl-Tonbary Y, Darwish A, El-Hussein A, Fouda A. Adenocarcinoma of the colon in children: Case series and mini-review of the literature. Hematol Oncol Stem Cell Ther. 2013;6:29–33.
16. a, b, cSaab R, Furman WL. Epidemiology and Management Options for Colorectal Cancer in Children. Pediatric Drugs. 2008;10:177–92.
17. a, bPappo AS, Furman WL. Management of infrequent cancers of childhood. Principles and practice of pediatric oncology, 5th ed. Lippincott Williams & Wilkins, Philadelphia. 2006;1180–2.
18. ^Mremi A, Yahaya JJ. Advanced mucinous colorectal carcinoma in a 14-year old male child: A case report and review of the literature. Int J Surg Case Rep. 2020;70:201–4.
19. a, bChantada 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;27:39–41.

20. ^Pandey A, Gangopadhyay A, Sharma S, Kumar V, Gupta D, Gopal S, et al. Pediatric carcinoma of rectum - V aranasi experience. Indian J Cancer. 2008;45:119.

21. ^Skibber JM, Minsky BD, Hoff PM. Cancer of the colon. Cancer: principles and practice of oncology. 2001;6:12 16–318.

22. ^Symonds DA, Vickery AL. Mucinous carcinoma of the colon and rectum. Cancer. 1976;37:1891–900.

23. ^Nissan A, Guillem JG, Paty PB, Wong DW, Cohen AM. Signet-ring cell carcinoma of the colon and rectum. Di s Colon Rectum. 1999;42:1176–80.

24. a, bAhn C hoon, Kim SC. Two case reports: colorectal adenocarcinoma in children. Medicine. 2017;96:e8074.

25. ^Vastyan AM, Walker J, Pintér AB, Gerrard M, Kajtar P. Colorectal Carcinoma in Children and Adolescents - A Report of Seven Cases. European Journal of Pediatric Surgery. 2001;11:338–41.

26. ^Parham D. COLLOID CARCINOMA. Ann Surg. 1923;77:90–105.

27. ^Resch A. Lymph node staging in colorectal cancer: Old controversies and recent advances. World J Gastroe nterol. 2013;19:8515.

28. ^Yahaya JJ, Msokwa EK, Mremi A. Mucinous Colorectal Carcinoma in a 17-Year-Old Male: A Diagnosis with Low Clinical Index of Suspicion. Case Rep Pediatr. 2019;2019:1–5.

29. a, bJasperson KW, Tuohy TM, Neklason DW, Burt RW. Hereditary and familial colon cancer. Gastroenterolog y. 2010;138:2044–58.

30. a, bGeorge J, Rockall T. Surgery for colorectal cancer. Surgery (Oxford). 2020;38:32–7.

31. a, bSultan I, Rodriguez-Galindo C, El-Taani H, Pastore G, Casanova M, Gallino G, et al. Distinct features of col orectal cancer in children and adolescents. Cancer. 2010;116:758–65.

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