Adenosquamous Carcinoma of Sigmoid Colon: First Case Report in Pediatrics and Literature Review

Shuaibing Lu

Affiliated Tumor Hospital of Zhengzhou University: Henan Cancer Hospital

Fusheng Ge

Affiliated Tumor Hospital of Zhengzhou University: Henan Cancer Hospital

Chen Liu

Affiliated Tumor Hospital of Zhengzhou University: Henan Cancer Hospital

Liangqun Peng

Affiliated Tumor Hospital of Zhengzhou University: Henan Cancer Hospital

Fei Ma

Affiliated Tumor Hospital of Zhengzhou University: Henan Cancer Hospital

Wei Yang

Affiliated Tumor Hospital of Zhengzhou University: Henan Cancer Hospital

Zhandong Zhang

Affiliated Tumor Hospital of Zhengzhou University: Henan Cancer Hospital

Suxia Luo

Affiliated Tumor Hospital of Zhengzhou University: Henan Cancer Hospital

Yawei Hua (✉ huayawei1965@163.com)

Affiliated Tumor Hospital of Zhengzhou University: Henan Cancer Hospital

Research Article

Keywords: sigmoid colon, adenosquamous carcinoma, pediatrics, liver metastasis, case report

Posted Date: October 25th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-982723/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Background Colon adenosquamous carcinoma is an extremely rare cancer, especially in young people. No case of colon adenosquamous carcinoma in pediatric patient has been reported so far.

Case presentation Here we present the case of a 16-year-old Chinese girl diagnosed with adenosquamous carcinoma of sigmoid colon. We performed laparoscopic sigmoidectomy with lymphadenectomy on the patient. Unfortunately, she developed liver metastasis less than 1 month after surgery. Then we implemented percutaneous radiofrequency ablation of liver mass and 4 cycles of adjuvant chemotherapy on her. However, liver metastasis recurred less than 4 months after radiofrequency ablation. The girl eventually died in 8 months after surgical resection of sigmoid colon. As far as we know, this girl is the youngest patient with sigmoid colon adenosquamous carcinoma reported so far, and the first reported case of colon adenosquamous carcinoma in pediatrics.

Conclusion Only 8 months from detection to death, this case indicates the prognosis of colon adenosquamous carcinoma is poor, and adenosquamous carcinoma of colon may even have worse prognosis in pediatrics than in adults. In addition, cases with liver metastasis have a awfully unfavorable prognosis for colon adenosquamous carcinoma patients.

Background

According to the global cancer statistics for 2020 released by the International Agency for Research on Cancer of the World Health Organization, the incidence of colorectal cancer ranked third among all malignant tumors on a global scale(1). However, colorectal cancer is very rare among pediatric patients (< 21 years old) and the incidence is only about 1 per million(2).

Adenosquamous carcinoma(ASC) refers to malignancy that contains both glandular and squamous histologic components. ASC is most common in respiratory system (73.8%), but it is rare in digestive system(16.2%)(3). Studies have shown that ASC accounts for only 0.06%-0.09% of colorectal cancer(4, 5). What's more, this subtype of colorectal cancer is extremely rare in pediatric patients. There is only one case of pediatric ASC of rectum has been reported(6). To the best of our knowledge, no case of colon ASC in pediatric patient has been reported so far. The patient presented here is the youngest reported case of colon ASC, and the first reported case of colon ASC in pediatrics.

Since it is rare in clinical practice, the treatment for colonic ASC mainly refers to colon adenocarcinoma(ADC). Currently, surgical resection and adjuvant chemotherapy are the main treatment methods for this disease. But the results are generally unsatisfactory, especially for patients with distant metastases. In this report, the girl diagnosed with ASC of sigmoid colon, and developed liver metastasis after radical sigmoidectomy. Then she received 4 cycles of XELOX (consists of oxaliplatin and capecitabine) chemotherapy after radiofrequency ablation of liver mass. But, it is unfortunate that liver metastasis recurred soon after radiofrequency ablation. The timeline of the patient's diagnosis and

treatment course is shown in table1. We present the following case in accordance with the CARE reporting checklist.

Case Presentation

A 16-year-old Chinese girl was referred to our hospital with 1 month history of intermittent left lower abdominal pain. Laboratory tests showed the following values: hemoglobin, 104g/L; CA19-9, 49.55U/mL; CEA, 0.82ng/ml; AFP, 1.58ng/ml; CA125, 30.12U/mL; CA724, 5.61U/ml. The stool examination for occult blood was positive. Pelvic contrast-enhanced CT demonstrated unevenly thickened wall of the sigmoid colon(Figure1A). No significant lesions were observed on abdominal contrast-enhanced CT scan(Figure1B). Colonoscopy revealed a large circumferential mass at 25 cm from the anal verge(Figure2). The mass narrowed the lumen so that the body of colonoscope could not pass through. Pathologic analysis of biopsy specimen indicated adenocarcinoma of sigmoid colon. The patient had neither a significant past medical history nor a family history of colorectal cancer.

During laparoscopic exploration, we found the tumor was located in the sigmoid colon (approximately 7cmx6cmx5cm), invading the serosal membrane and closely adhering to part of the distal ileum. As a result, we performed laparoscopic radical resection of sigmoid colon plus partial ileectomy on the girl. Pathological examination of the sigmoid colon specimen revealed the tumor was adenosquamous carcinoma, including mucinous adenocarcinoma and poorly differentiated squamous cell carcinoma. Figure3 shows the hematoxylin-eosin staining of the sigmoid colon specimen.

Immunohistochemistry staining showed positive for CK5/6, P63, focal positive for CK20, CEA, CDX-2, negative for P16, Syn, CD56 and high Ki-67 expression(80%). Genetic testing showed wild type KRAS, microsatellite stable(MSS) and no mutation in BAP1 gene. The tumor invaded the adventitia, nerves and vessel. Three out of 39 lymph nodes contained metastatic tumor. According to the 7th edition of the UICC TNM classification system, the final pathological diagnosis of the sigmoid colon mass was stage IB (pT3N1bM0) adenosquamous carcinoma.

Less than 1 month after surgery, abdominal MRI showed a mass at the junction of liver S5 and S8(Figure4A), which was considered to be tumor metastasize to liver. After consultation with the girl and her parents, we implemented percutaneous radiofrequency ablation of liver mass and adjuvant chemotherapy on her. The regimen of chemotherapy wasXELOX, which includes oxaliplatin(200mg per day) and capecitabine(1.5g BID d1-14). This girl tolerated XELOX chemotherapy regimen well. After 2 cycles of adjuvant chemotherapy, re-examination of abdominal MRI showed stable condition(Figure4B), thus we continue to give the above chemotherapy regimen for 2 cycles.

After 4 cycles of adjuvant chemotherapy, abdominal MRI indicated recurrence of liver metastasis(Figure4C). The edge of the mass at the junction of liver S5 and S8 was enhanced and enlarged compared to the previous one. Nodules were found in the hilar area, which is considered to be lymph node metastasis. Genetic testing revealed no mutations in B-raf and N-ras gene. Then we invited doctors from the department of hepatobiliary surgery and medical oncology for consultation. After

discussion, reoperation and targeted therapy were recommended. The girl and her family members refused further treatment for financial reason and the girl eventually died in 2 months later.

Discussion And Conclusions

ASC is a malignant tumor that contains both glandular and squamous histologic components. According to the relationship between glandular and squamous ingredients, ASC can be classified into composite and collision types. Composite type refers to the mixed distribution of adenocarcinoma and squamous cell carcinoma, while collision type refers to the adenocarcinoma composition and squamous cancer composition has a clear boundary(7,8,9). There are four hypotheses about the histogenesis of squamous cell carcinoma in colonic ASC patients: 1) Ectopic squamous cells of the colonic mucosa directly transform into squamous cell carcinoma; 2) basal cells transform into squamous cells; 3) Squamous metaplasia of glandular cells; 4) Squamous metaplasia of adenocarcinoma cells. At present, the fourth hypothesis is most accepted by scholars.

The common clinical manifestations of colon ASC patients are similar to that of colon ADC, including abdominal pain, weight loss, altered bowel habits, bloody stool. Noteworthy, hypercalcemia is occasionally encountered in patients with colon ASC(10,11,12). The cause of hypercalcemia in colon ASC patients is mainly due to the release of parathyroid hormone by tumor, it means that hypercalcemia appears as a paraneoplastic syndrome of ASC(10). Secondly, for patients with advanced ASC, bone metastasis can also cause elevated serum calcium(11).

Colon ASC is rare in clinical practice and thus the understanding and treatment experience about this disease is very limited. Therefore, no consensus on effective treatment for colon ASC has been reached. At present, the treatment of colon ASC is mainly referred to colon ADC, that is surgery plus adjuvant chemotherapy. Regarding postoperative chemotherapy of colon ASC, FOLFOX (consists of fluorouracil, folinic acid and oxaliplatin) regimen is mostly used(13, 14, 15).

In recent years, postoperative chemotherapy combined with targeted therapy or immunotherapy has been proposed. For patients with suitable genetic test results, postoperative chemotherapy combined with targeted therapy or immunotherapy can be tried, although the effects of these treatments are not yet clear. A study showed that patients with BRAF V600E colorectal cancer have a poor clinical response to FOLFOX chemotherapy plus bevacizumab, leading to poor prognosis(16). In the future, more clinical trials are needed to optimize the postoperative treatment regimen of ASC and determine the exact extent of its clinical benefits.

Several studies have shown that the prognosis of colon ASC is worse than that of colon ADC(17, 18, 19, 20). In 2020, Nasser et al. conducted the largest retrospective cross-sectional examination of ASC from a national database for over 30 years. The mean age of patients in this study was approximately 64 years. The results showed the median overall survival for colon ASC patients was 13.9 months (95% CI: 10.98-16.83). For stage IV ASC and ADC of colon, the median overall survival was 14.1 months and 8.0 months($P=0.0001$), respectively(17). According to a study conducted by Frizelle et al, the prognosis of

colorectal ASC is worse than that of ADC in stage III or IV, but similar to ADC in stage I or II. The 5-year survival rate for patients with stage I-III colorectal ASC was about 65%, while the median survival rate for patients with stage IV disease was 8.5 months(18).

The prognosis of ASC is worse than that of ADC, which may be due to: 1) Both adenocarcinoma and squamous cell carcinoma can metastasise, but the later appears to spread more easily and more aggressively than the former(21-22). 2) At the time of diagnosis, the incidence of distant metastasis (stage IV) of colon ASC was significantly higher than that of ADC(5, 17). The most common metastasis sites of colon squamous cancer are liver, peritoneum and lung in order(18).

In this case, no distant metastasis was found on preoperative examinations. After radical resection, pathological diagnosis of the sigmoid colon mass was stage IIB (pT3N1bM0) adenosquamous carcinoma. When adjuvant chemotherapy is about to be performed 4 weeks after surgery, the imaging examination revealed a liver mass, which was considered to be tumor metastasis. It can be seen that colonic ASC is awfully aggressive in adolescents. Then we performed percutaneous radiofrequency ablation of liver mass on this patient. XELOX chemotherapy was started after radiofrequency ablation, and the patient was well tolerated. However, re-examination showed recurrence of liver metastasis after the completion of 4 cycles of chemotherapy. Eventually, the patient and her family decided to give up further treatment and the girl died 8 months postoperatively.

In Choi's report, a 43-year-old female underwent laparoscopic right colectomy. Pathological diagnosis of the colon specimen was stage IIIB (T3 N2a M0) adenosquamous carcinoma. The female patient received 6 cycles of FOLFOX4 (oxaliplatin, leucovorin, and fluorouracil) chemotherapy postoperative, and no tumor recurrence was found during the 10 months follow-up examinations since the completion of chemotherapy(13). Compared with the case reported by Choi, the outcomes of the girl in our report is quite frustrating. It's not difficult to draw the conclusion that cases with liver metastasis have an unfavorable prognosis for colon ASC patients. Besides, We speculate that the effect of FOLFOX chemotherapy regimen is superior or non-inferior to XELOX regimen in patients with colonic ASC.

Our medical team specially held a seminar on this case. The lessons we have learned from this case are as follows: 1) Colonic ASC can also occur in pediatrics. Therefore, do not ignore the possibility of colon ASC in adolescents with related symptoms. 2) For patients diagnosed with colon ASC, comprehensive examination must be performed to determine whether distant metastases have occurred. 3) After surgery, genetic testing of pathological tissue is required to determine if there is a suitable immunotherapy or targeted therapy. 4) During the treatment of colon ASC, the frequency of imaging examinations should be appropriately increased in order to detect changes in patients' condition in time. Then adjust to the most appropriate treatment in a timely manner.

Our team has two main expectations about future research on colon ASC. On one hand, lots of research on the etiology and tissue origin of colon adenosquamous carcinoma are needed. Only in this way can we understand this disease more clearly, and thus adopt more effective prevention and treatment

methods. On the other hand, studies on postoperative adjuvant treatment of colon ASC patients in different age groups are also needed, so as to obtain a better prognosis as much as possible.

In conclusion, colon adenosquamous carcinoma is an exceedingly rare malignancy. To our knowledge, this is the first reported case of colon ASC in pediatrics. This case demonstrates the prognosis of this disease is poor, and colon ASC may even have worse prognosis in adolescents than in adults. For colon ASC patients, cases with liver metastasis have an awfully unfavorable prognosis. In order to achieve better outcomes, more research are needed to find out the histogenesis of ASC, and determine the best postoperative adjuvant treatment for colon ASC patients.

Abbreviations

ASC

Adenosquamous carcinoma

ADC

Adenocarcinoma

Declarations

Ethics approval and consent to participate

All procedures performed in studies involving human participants were in accordance with the ethical standards of the ethics committee of our hospital (No. 2019156). Written informed consent was obtained from the patient's parent for publication of this case report and accompanying images. A copy of the written consent is available for review by the editor of this journal.

Consent for publication

The patient's parents has given their consents for the case report to be published. The written informed consent to publish this information was obtained from the patient's parent. A copy of the written consent is available for review by the editor office of this journal.

Availability of data and materials

All data during the study are included within the article.

Competing interests

The authors declare that they have no competing interests.

Funding

This work was supported by the National Cancer Climbing Fund (No.NCC201816B048); and Tackle Key Problems in Medicine of Henan Province (No.LHGJ20200188).

Authors' contributions

S Lu designed this report and write the manuscript. F Ge and C Liu helped to design this report and write the manuscript. L Peng, F Ma, W Yang, assisted in writing and editing the manuscript. Z Zhang, S Luo, Y Hua reviewed and revised the manuscript. All authors contributed to the article and approved the submitted version.

Acknowledgements

Here we extend our deep condolences to the family. Meanwhile, we want to thank the girl's parents for their permission to report this study.

Authors' information

1Department of General Surgery, the Affiliated Tumor Hospital of Zhengzhou University, No.127 Dongming Rd, Zhengzhou 450008, Henan, China; 2Department of Medical Oncology, the Affiliated Tumor Hospital of Zhengzhou University, No.127 Dongming Rd, Zhengzhou 450008, Henan, China.

References

1. Sung H, Ferlay J, Siegel LR, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA: Cancer J Clin.* 2021;0:1–41.
2. Poles GC, Clark DE, Mayo SW, et al. Colorectal carcinoma in pediatric patients: A comparison with adult tumors, treatment and outcomes from the National Cancer Database. *J Pediatr Surg.* 2016;51(7):1061–6.
3. Lan Y, Huang K, Liu C, et al. A nation-wide cancer registry-based study of adenosquamous carcinoma in Taiwan. *PLoS ONE.* 2015;10(10):e0139748.
4. Cagir B, Nagy MW, Topham A, et al. Adenosquamous carcinoma of the colon, rectum, and anus: epidemiology, distribution, and survival characteristics. *Dis Colon Rectum.* 1999;42:258–63.
5. Masoomi H, Ziogas A, Lin BS, et al. Population-based evaluation of adenosquamous carcinoma of the colon and rectum. *Dis Colon Rectum.* 2012;55(5):509–14.
6. García N, Cubero JH, Orduña VA, et al. Adenosquamous Cell Carcinoma of the Rectum in a Girl: First Case Reported and Review of the Literature. *J Pediatr Hematol Oncol.* 2015;37(6):e364–7.
7. Di Prete M, Bacciorri F, Franceschilli M, et al. Adenosquamous carcinoma of the right colon with diffuse signet-ring mucinous component. *Clin J Gastroenterol.* 2020;13(4):555–9.
8. Levendoglu H, Cox CA, Nadimpalli V. Composite (adenocarcinoid) tumors of the gastrointestinal tract. *Dig Dis Sci.* 1990;35:519–25.
9. Fukui H, Takada M, Chiba T, et al. Concurrent occurrence of gastric adenocarcinoma and duodenal neuroendocrine cell carcinoma: a composite tumour or collision tumours? *Gut.* 2001;48:853–6.

10. Chevinsky AH, Berelowitz M, Hoover HC. Adenosquamous carcinoma of the colon presenting with hypercalcemia. *Cancer*. 1987;01(5):1111–6. 60(.
11. Palvio DH, Sørensen FB, Kløve-Mogensen M. Stem cell carcinoma of the colon and rectum. Report of two cases and review of the literature. *Dis Colon Rectum*. 1985;28(6):440–5.
12. Thompson JT, Paschold EH, Levine EA. Paraneoplastic hypercalcemia in a patient with adenosquamous cancer of the colon. *Am Surg*. 2001;67(6):585–8.
13. Choi JW, Park HU. Adenosquamous Carcinoma of the Ascending Colon: A Case Report and Review of the Literature. *Annals of coloproctology*. 2013;29(2):83–6.
14. Toumi O, Hamida B, Njima M, et al. Adenosquamous carcinoma of the right colon: A case report and review of the literature. *International Journal of Surgery Case Reports International journal of surgery case reports*. 2018;50:119–21.
15. Kang DB, Oh JT, Jo HJ, et al. Primary adenosquamous carcinoma of the colon. *J Korean Surg Soc*. 2011;80(Suppl 1):31-5.
16. Ishida H, Yamaguchi T, Chiba K, et al. A case report of ascending colon adenosquamous carcinoma with BRAF V600E mutation. *Int Cancer Conf J*. 2017;6(3):93–7.
17. Nasser Y, Cox B, Shen W, et al. Adenosquamous carcinoma: An aggressive histologic sub-type of colon cancer with poor prognosis. *Am J Surg*. 2021;03(3):649–53. 221(.
18. Frizelle FA, Hobday KS, Batts KP, et al. Adenosquamous and squamous carcinoma of the colon and upper rectum: a clinical and histopathologic study. *Dis Colon Rectum*. 2001;44(3):341–6.
19. Nozoe T, Anai H. Adenosquamous carcinoma of the sigmoid colon: report of a case. *Surg Today*. 2001;31:830–2.
20. Dong Y, Wang J, Ma H, et al. Primary adenosquamous carcinoma of the colon: report of five cases. *Surg Today*. 2009;39:619–23.
21. Kontozoglou TE, Moyana TN. Adenosquamous carcinoma of the colon—an immunocytochemical and ultrastructural study. Report of two cases and review of the literature. *Dis Colon Rectum*. 1989;32(8):716–21.
22. Cerezo L, Alvarez M, Edwards O, et al. Adenosquamous carcinoma of the colon. *Dis Colon Rectum*. 1985;28:597–603.

Figures

Figure 1

A. Pelvic contrast-enhanced CT showed unevenly thickened wall of the sigmoid colon; B. No significant lesions were observed on abdominal contrast-enhanced CT scan.

Figure 2

Colonoscopy revealed a large circumferential mass at 25 cm from the anal verge.

Figure 3

Hematoxylin-eosin staining of the sigmoid colon specimen.

Figure 4

A. Abdominal MRI showed a mass at the junction of liver S5 and S8; B. Abdominal MRI showed stable condition after 2 cycles of adjuvant chemotherapy; C. Abdominal MRI indicated recurrence of liver

metastasis after 4 cycles of adjuvant chemotherapy.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [Table1.jpg](#)