Journal of Neonatal Surgery
ISSN(Online): 2226-0439
Vol. 14, Issue 19s (2025)
https://www.jneonatalsurg.com

OPEN ACCESS

Hepatoid Adenocarcinoma of the Sigmoid Colon: A Challenging Diagnosis and Management

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Cite this paper as: Dr. Anto Olivia J., Prof.Dr.K. Balaji Singh, Dr. Supriya P, (2025) Hepatoid Adenocarcinoma of the Sigmoid Colon: A Challenging Diagnosis and Management. *Journal of Neonatal Surgery*, 14 (19s), 900-905.

ABSTRACT

Hepatoid adenocarcinoma of the sigmoid colon exists as a rare cancer type which resembles both hepatocellular carcinoma in its histological appearance and immunohistochemical markers. The medical field has a limited understanding of this distinct malignancy because hepatoid adenocarcinoma of the sigmoid colon appears rarely throughout the medical literature. This study presents key information on the diagnostic methods and treatment procedures for this aggressive cancer including early recognition and proper healthcare delivery. The patient is a 76-year-old woman who experienced constipation together with rectal bleeding. The sigmoid colon examination through colonoscopy showed a wide extensive lesion that combined ulcerative changes with proliferative growth. A biopsy examination of the lesion proved the presence of adenocarcinoma inside the sigmoid colon. Subsequently, the patient underwent sigmoidectomy. The tissue examination following surgery demonstrated moderately differentiated adenocarcinoma containing hepatoid differentiation to establish a diagnosis of hepatoid adenocarcinoma. A second test modality named immunohistochemical analysis reinforced the diagnosis by displaying characteristics related to both adenocarcinoma and hepatocellular carcinoma. Hepatoid adenocarcinoma of the sigmoid colon demonstrates rapid progression because of its aggressive nature which generally results in unfavorable predictions for patient treatment. The limited nature of this cancer presents two essential requirements: prompt diagnosis by suitable tests and surgical removal along with chemotherapy. Chemotherapy can act as an adjunct therapy for achieving the best possible result of tumor free survival. Early intervention stands as the most essential factor to advance the survival chances of patients diagnosed with this unusual adenocarcinoma subtype.

Keywords: *Hepatoid adenocarcinoma, Sigmoid colon, Adenocarcinoma, Rare malignancy*.

1. INTRODUCTION

Hepatoid adenocarcinoma exists as a distinct and uncommon adenocarcinoma variant which medical experts have examined since the 1980s because of its special tissue characteristics and its link to elevated alpha-fetoprotein (AFP) levels in blood. (Wong et al.2015) The glycoprotein AFP functions as a marker for hepatocellular carcinoma (HCC) yet medical examinations have shown that it increases in gastric cancer along with colon cancer and other gastrointestinal tumors. Medical literature indicates the Bourreille et al. group from 1970 as the first to observe gastric adenocarcinoma that produced elevated levels of serum AFP. (Uefuji et al.1994) When they examined the particular tumor its characteristics showed AFP positivity together with hepatocellular differentiation along with hepatocellular-like differentiation patterns making the neoplasm an AFP synthesizing tumor. The discovery enabled researchers to focus their work on tumors with similar traits that eventually termed as hepatoid adenocarcinoma. (Zender et al.2010) Introduced the medical community to "hepatoid adenocarcinoma" as a term to describe tumors which combine AFP production with hepatocellular differentiation patterns following an analysis of their differences from standard adenocarcinomas. Hepatoid adenocarcinomas develop in stomach, colon and ovaries resulting in frequent aggressive clinical progression together with a poor treatment outcome. The microscopic appearance of such cancers features both hepatocellular carcinoma-like trabecular and pseudoglandular patterns alongside features of hepatic development which include bile production within the cellular structures.

(Wee, A. 2011) stressed that histopathological features outweigh AFP elevation for the proper identification of hepatoid adenocarcinoma even though AFP elevation remains significant for diagnosis. The distinctive hepatocellular-like characteristics of these tumors create a reliable diagnostic methodology since AFP detection might also occur in liver diseases leading to decreased specificity of this marker (Nagai et al., 1993). The diagnostic process should use both detailed histological assessment together with immunohistochemical testing as an alternative to serum AFP because it results in better diagnostic outcomes.

Research findings demonstrate that hepatoid adenocarcinoma exhibits demanding clinical behavior because it rapidly spreads through tissues while maintaining a negative treatment response. Frequent presence of AFP production serves as a diagnostic marker separating hepatoid adenocarcinomas from other adenocarcinomas especially when conventional markers fail to provide a clear diagnosis. (Tateishi et al.2008) The available treatment methods for hepatoid adenocarcinoma primarily consist of surgical resections but some patients may receive adjunct chemotherapy. Current understanding of this uncommon cancer subtype remains limited because of its scarcity since researchers have many unanswered questions about basic pathophysiology, ideal treatments and patient survival patterns. (Elmore et al.2021)

The expansion of hepatoid adenocarcinomas knowledge requires clinical and research focus on diagnostic refinement and molecular AFP-production studies while developing better therapeutic treatments for affected patients. Early diagnosis followed by prompt treatment plays a crucial role in improving survival chances because hepatoid adenocarcinomas carry such bad prognosis. (Attwa et al.2015)

2. AIM

A rare case of hepatoid adenocarcinoma in a 76-year-old female sigmoid colon is presented with a synthesis of literature focusing on diagnostic difficulties and therapeutic practices.

CASE DESCRIPTION

The patient being evaluated is a 76-year-old female who had experienced intermittent constipation over two years and she had noticed rectal bleeding while defecation for past one month. Unintentional weight loss combined with reduced appetite was present. There is no complaints of abdominal pain or vomiting. The patient has systemic hypertension for which she taking antihypertensive medications. During the general examination the patient appeared to have pallor but otherwise remained vitally stable.

Colonoscopy procedure was done which showed an ulceroproliferative lesion noted 25 cms from the anal verge causing severe luminal narrowing. Colonoscopic biopsy was performed and histopathology revealed moderately differentiated adenocarcinoma. Further evaluation with PET-CT demonstrated asymmetrical, heterogeneously enhancing wall thickening in the mid-sigmoid colon, measuring 2.5 cm, with periserosal infiltration and loss of fat planes involving the rectal wall and left ovary. FDG-avid pericolic lymphadenopathy suggested malignant involvement, and the clinical staging was determined as T4aN2aM0.

Following multidisciplinary tumor board review and consultation with medical oncology, the patient was scheduled for a definitive surgical management. She underwent laparoscopic-assisted sigmoid colectomy. The resected specimen was subjected to extensive histopathological analysis including immunohistochemistry with 14 markers. The final diagnosis was moderately differentiated adenocarcinoma of the sigmoid colon with hepatoid differentiation (pT3pN2b). Importantly, all surgical margins were free of invasive carcinoma.

The patient subsequently received adjuvant chemotherapy, consisting of six cycles of intravenous oxaliplatin (150 mg) and oral capecitabine administered over two weeks per cycle. Hepatoid adenocarcinoma, although most frequently reported in the stomach, has also been described in rare cases involving the colon and rectum, exhibiting aggressive behavior and poor prognosis. Its diagnosis relies on histological resemblance to hepatocellular carcinoma and AFP expression, although not all cases demonstrate elevated serum AFP levels (Ishikura et al., 1985; Nagai et al., 1999).

Given the aggressive nature of this subtype and its rarity, early identification through a combination of imaging, histopathology, and immunohistochemistry is critical for guiding appropriate treatment. The role of surgical resection followed by adjuvant chemotherapy remains the cornerstone of management, although long-term outcomes remain guarded due to the tumor's high metastatic potential and recurrence risk. (Mahvi et al.2018).

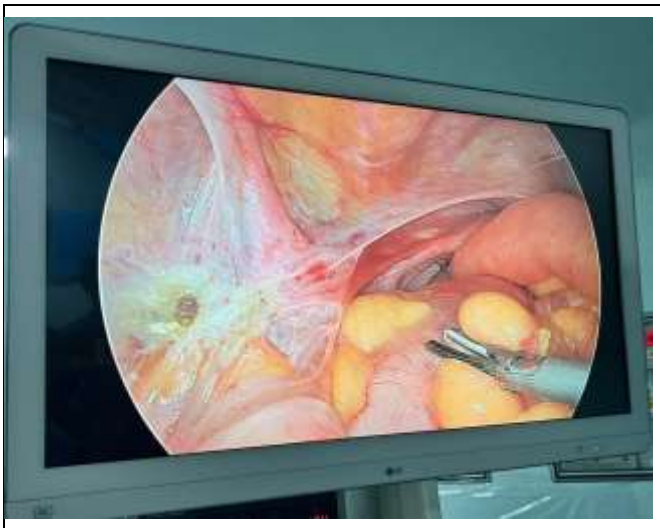

Fig 1: Intraoperative picture showing the lesion in the sigmoid colon pointed with the instrument.

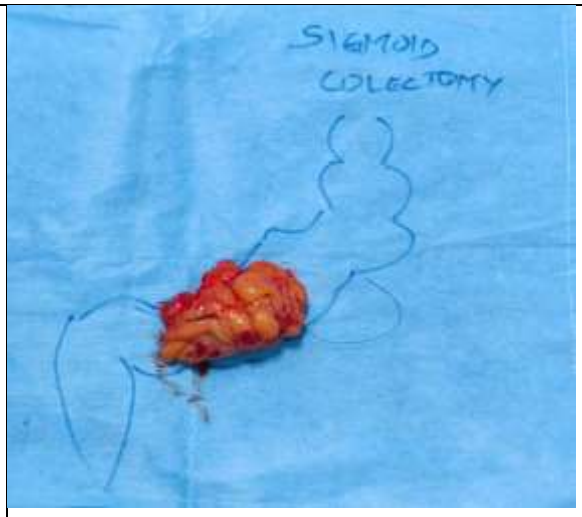

Fig 2: Picture showing the resected segment of the sigmoid colon with the sigmoid mesocolon.

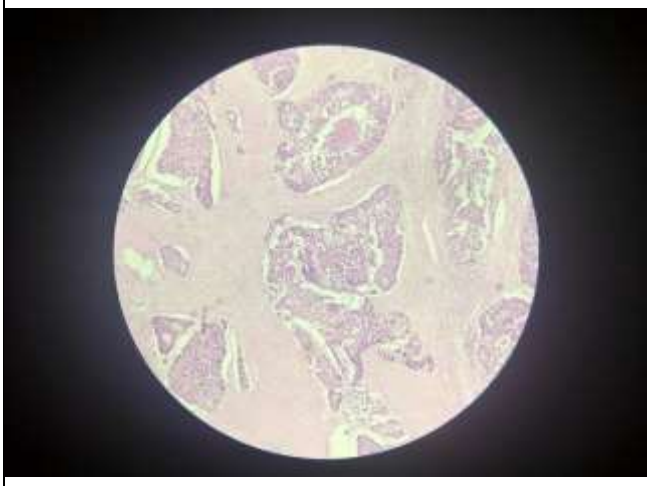

Fig 3: Picture showing the cross section of adenocarcinoma of sigmoid colon with desmoplastic stomal reaction.

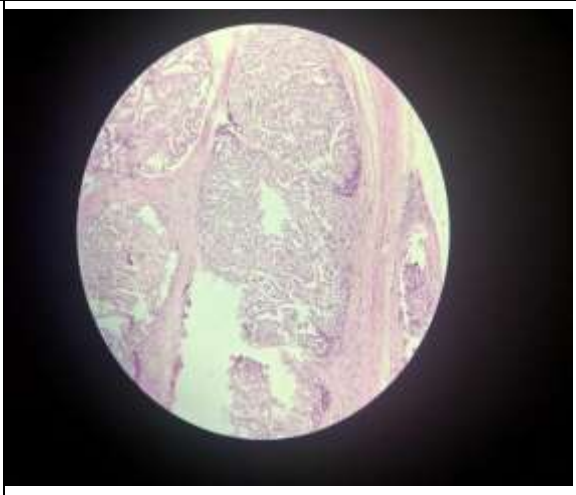

Fig 4: Picture showing the cross section of areas of hepatoid differentiation in the sigmoid colon.

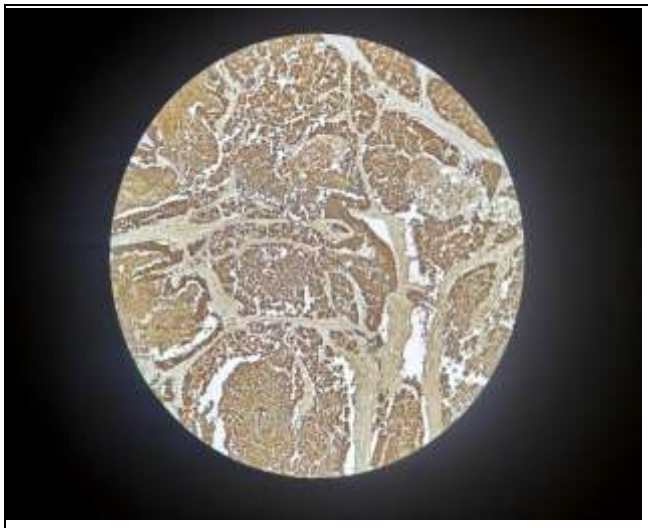

Fig 5: Picture showing cross section of sigmoid colon growth with Pan CK positivity.

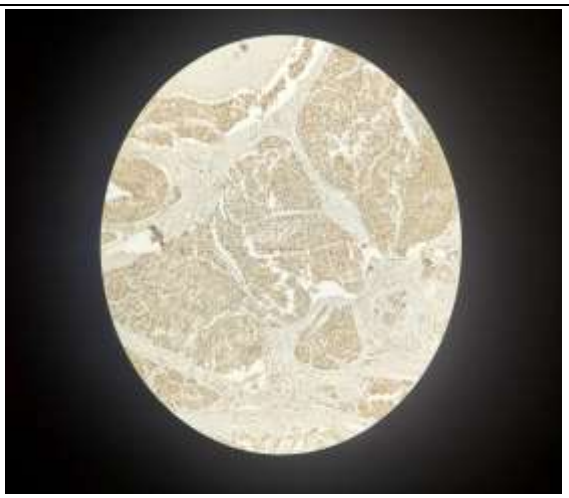

Fig 6: Picture showing the cross section of areas of hepatoid differentiation in the sigmoid colon demonstrating AFP positivity.

3. DISCUSSION

Hepatoid adenocarcinoma (HAC) of the colon is a rare and aggressive malignancy characterized by morphological and functional similarities to hepatocellular carcinoma (HCC), including the potential to produce alpha-fetoprotein (AFP) and exhibit hepatocellular differentiation. The tumor's high metastatic potential, particularly to lymph nodes and liver, contributes to its poor prognosis. Reported incidences of HAC in the gastrointestinal tract range between 0.38% and 0.743%, with colorectal HAC being particularly uncommon, accounting for only approximately 0.5% of all cases.

A retrospective analysis published in 2023 identified just 39 reported cases of colorectal HAC worldwide, highlighting the rarity of this entity (Kimura et al., 2023).

Most HAC cases arise in the stomach, representing about 83.9% of gastrointestinal cases. Less frequently, HAC has been reported in the gallbladder (3.7%), uterus (3.2%), lungs (2.3%), and urinary bladder (1.8%). (Zhang et al.2023)The strikingly low incidence of colorectal involvement may be attributed to the embryological differences: while hepatocytes originate from the foregut, the colon derives from the midgut and hindgut. Despite this, the presence of hepatoid differentiation in colonic adenocarcinoma is hypothesized to result from the pluripotent capacity oof the colorectal stem cells to undergo both glandular and hepatocellular transformation (Hwang et al., 2021).

Histologically, HAC in the colon often appears as a conventional adenocarcinoma interspersed with areas resembling hepatocellular carcinoma, featuring eosinophilic cytoplasm, trabecular growth patterns, and bile production. (Tabassum et al.2011) Difficulty exists in diagnosing HAC due to its double nature because hepatoid elements appear in scattered distributions throughout the tumor. Detection of the hepatoid component in postoperative histopathological and immunohistochemical evaluation becomes imperative because colonoscopic biopsy often fails to identify this particular tissue. HepPar-1 protein together with glypican-3 and AFP assists in diagnosing hepatoid differentiation patterns. (Wang et al.2020)

The research connection between HAC in the colorectum and inflammatory bowel disease stands unclear since no direct relationship has been proven. Further investigation becomes necessary to establish possible connections between inflammation-driven carcinogenesis in IBD because of its unclear relationship with HAC. HAC presents a distinct tendency towards metastasis which researchers can confirm without uncertainty. The liver together with regional lymph nodes represent the primary locations for metastasis in patients while advanced stage cases often develop distant metastases that result in diminished survival expectations (Lee et al., 2020).

There are currently no disease-specific treatment guidelines for HAC of the colon. Given its morphological overlap with conventional intestinal adenocarcinoma, standard treatment involves radical surgical resection followed by adjuvant chemotherapy, typically using regimens such as FOLFOX or CAPOX. Interestingly, due to the hepatocellular-like features of HAC, therapies traditionally used for hepatocellular carcinoma, such as sorafenib or lenvatinib, are being explored in select cases with variable success (Matsumoto et al., 2021). The role of AFP as a prognostic marker also remains debated,

as not all patients exhibit elevated serum AFP, and its levels do not necessarily correlate with tumor burden or treatment response. Complete tumor resection is associated with better outcomes, though long-term survival remains poor due to the disease's aggressive course. Multidisciplinary management involving oncologists, pathologists, and surgeons is essential for optimizing treatment strategies and improving prognosis.

4. CONCLUSION

Hepatoid adenocarcinoma of the colon is a rare but highly aggressive malignancy, with very few reported cases globally. Despite its morphological resemblance to hepatocellular carcinoma and AFP production in some cases, its origin in the colon remains a diagnostic challenge due to embryological differences and the tumor's deep-seated hepatoid components. Current treatment aligns with that of conventional colorectal cancers, but emerging evidence suggests that HCC-targeted therapies may offer additional benefit. The rarity of this tumor highlights the urgent need for more extensive studies, standardized diagnostic protocols, and tailored therapeutic guidelines to better manage and understand this distinctive subtype of colorectal carcinoma.

ACKNOWLEDGEMENT

Funding

There are no sources of funding for this study.

Author Contributions

Conceptualization, A.O.J., B.S.K., S.P.; Methodology, A.O.J., B.S.K., S.P.; Formal Analysis, A.O.J., B.S.K., S.P. ; Investigation, A.O.J., B.S.K., S.P.; Resources, A.O.J. and S.P.; Data Curation, A.O.J.; Writing – Original Draft Preparation, A.O.J.; Writing – Review & Editing, A.O.J and S.P.; Supervision, B.S.K.; Funding Acquisition, none.

Competing Interest

The authors declare that there is no competing interest.

Availability of data and materials

All supporting data related to this case report are included within the manuscript.

Ethical Approval

The authors reported that they acquired the necessary informed consent form from the patient, who consented to the publication of their photo, video materials, and other clinical information. The patient was informed that confidentiality would be ensured

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