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Case Report

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Hepatoid adenocarcinoma of the colon: a case report of a rare aggressive cancer

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Abstract

Hepatoid adenocarcinoma (HAC) is a rare and aggressive malignancy with histological and immunohistochemical features resembling hepatocellular carcinoma originating from non-hepatic organs. We report a case of HAC in a 34-year-old male, arising from the transverse colon, with metastases to the stomach, liver, lungs, and right femur. He presented with persistent anaemia and sub-acute intestinal obstructive symptoms. Laparotomy confirmed a transverse colon tumour infiltrating the stomach, accompanied by hepatic and peritoneal lesions. He underwent extended right hemicolectomy and en-bloc resection of the distal stomach, with a histopathological diagnosis of hepatoid adenocarcinoma. Subsequently, he suffered a pathological hip fracture and was treated with open reduction and internal fixation, followed by radiotherapy and palliative adjuvant chemotherapy. The disease progressed, leading to thoracic spine bone metastasis, necessitating further radiotherapy. He is alive, eight months post-surgery, despite a poor prognosis and disease progression.

Keywords: Hepatoid adenocarcinoma, pathological fracture, radiotherapy, extended right hemicolectomy, palliative adjuvant therapy

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INTRODUCTION

Hepatoid adenocarcinoma (HAC) is a rare and aggressive malignancy with histological and immunohistochemical features resembling hepatocellular carcinoma despite originating from non-hepatic organs [1]. It has been observed in various locations, such as the stomach, lung, ovary, pancreas, colon, and uterus, with just 24 global cases reported by 2015 [2,3]. Due to its rarity, there is a need to understand its epidemiology, clinical presentation, and pathology for specific treatment guidelines. The clinical presentation of HAC can vary depending on the primary site of the tumour and the extent of metastasis. HAC is often diagnosed at an advanced stage with early distant metastasis, contributing to its poor prognosis [4]. This report highlights a case of HAC in a young Ghanaian male with a transverse colon tumour infiltrating the stomach and multiple metastatic sites, emphasising its aggressive nature.

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Case

A 34-year-old male presented with persistent anaemia, sub-acute intestinal obstruction, rectal bleeding, and rapid weight loss of 13 kg in one month. He had no family history of colorectal malignancy, did not smoke, and worked in retail for office supplies. Physical examination revealed a pale, ill-looking man with tachycardia, a pulse rate of 108 beats per minute, a blood pressure of 123/69 mmHg, no haemic murmur, abdominal distension, and a palpable epigastric mass. Due to the bleeding per rectum and symptoms suggestive of sub-acute intestinal obstruction, a colonoscopy was done, which revealed an obstructing

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Figure 1. Exteriorized small bowel at laparotomy showing multiple 0.1-3cm lesions (black arrows) on the mesentery.

tumour in the distal transverse colon, histologically identified as undifferentiated carcinoma. An abdominopelvic computerised tomography (CT) scan confirmed a poorly delineated mass in the transverse colon with an exophytic component extending toward the stomach, multiple mesenteric and perirectal lymph nodes, mild ascites, and mildly enlarged liver and a sclerotic focus in the right acetabulum. A chest X-ray showed multiple canon-ball-like pulmonary lesions suggestive of lung metastasis. Abdominopelvic ultrasound showed intraluminal filling defects within the portal vein with no spontaneous flow suggestive of portal vein thrombosis.

The patient presented with severe anaemia (haemoglobin [Hb]: 6.9 g/dl), abnormal liver function tests, and a carcinoembryonic antigen (CEA) level of 1.3 µg/L. Due to active rectal bleeding, anticoagulation therapy for portal vein thrombosis was deferred until after the surgical intervention.

A multidisciplinary team, including surgeons and oncologists, recommended surgery followed by palliative chemotherapy due to impending obstruction and persistent anaemia. He was optimised by transfusing with three units of concentrated red cells, raising Hb to 8.7 g/dl. He was

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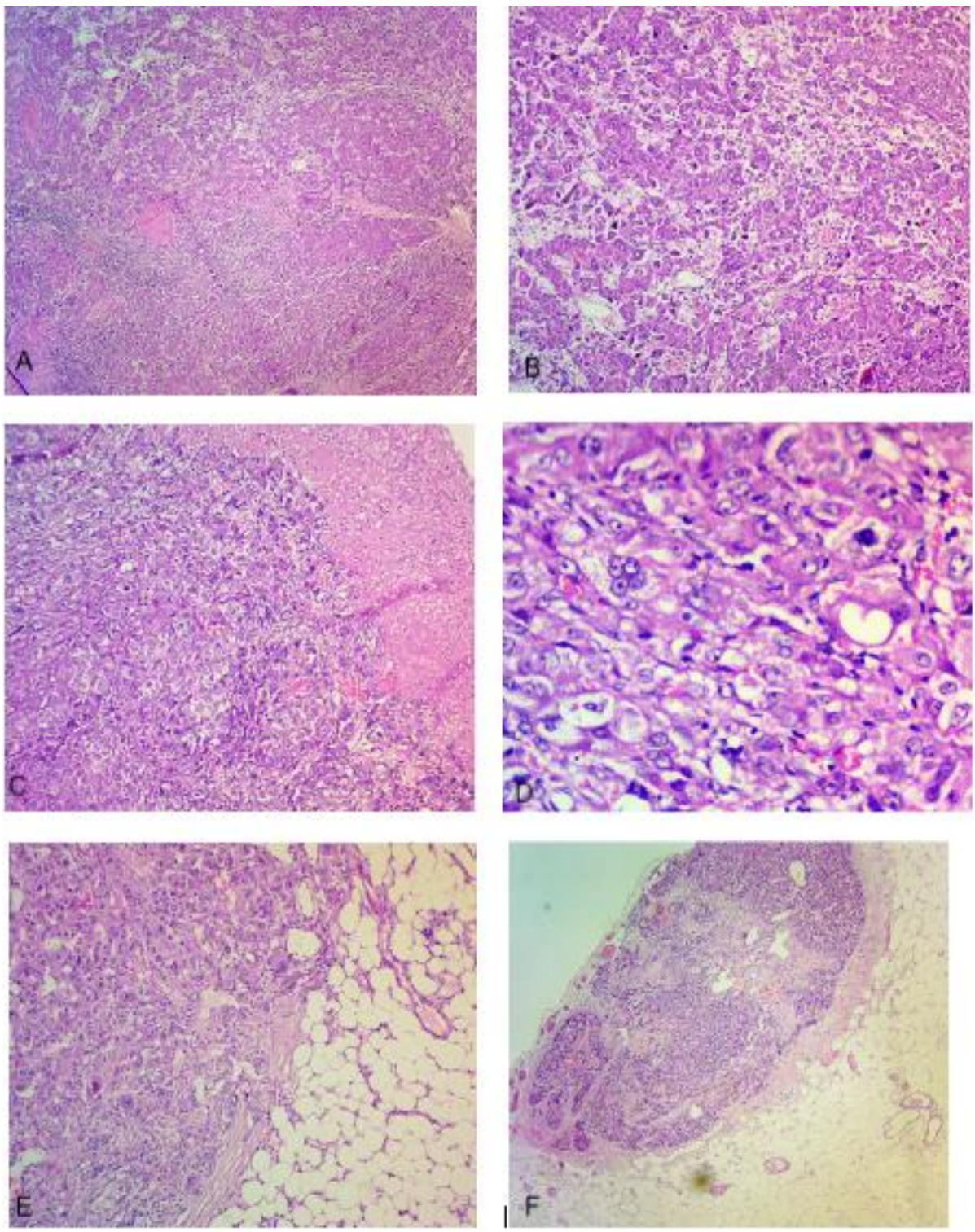

Figure 2. Tumour growing as solid nests and trabeculae of large polygonal epithelial cells with abundant eosinophilic cytoplasm ulcerating the mucosa (A-D), involving the omentum and mesentery (E) and lymph node (F).

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counselled, informed consent was obtained, and he subsequently underwent surgery. Intraoperative findings were a large tumour in the mid-transverse colon infiltrating the distal third of the stomach along the greater curvature, multiple tumour deposits on the mesentery of the small bowel ranging from 0.1 cm to 3cm (Figure 1), and on the liver and ascitic fluid measuring 1.5litres. The surgical team decided to proceed with the resection of the tumour, guided by the patient's condition and the intraoperative findings. An extended right hemicolectomy with en-bloc partial resection of the stomach was performed successfully. The pathological findings were an 8.5 cm poorly differentiated tumour involving the stomach and transverse colon, fungating into the lumen of each organ, and multiple tumour nodules on the serosa of the bowel. Histologically, the tumour in the transverse colon exhibited solid nests and trabeculae of large polygonal epithelial cells invading the colon transmurally, along with stomach involvement and lymph node metastasis (Figure 2). Perineural invasion and mild to moderate intra-tumoral lymphocytic infiltrates were observed. Among 26 retrieved lymph nodes, 11 were tumour-positive, leading to the diagnosis of hepatoid adenocarcinoma, pT4N3M1.

Four weeks post-surgery, the patient experienced sudden right hip pain and inability to walk after a clicking sound while picking up an object. A pelvic X-ray revealed a fractured base of the right femoral neck with varus deformity. He had closed reduction and internal fixation with a proximal femoral nail, followed by radiotherapy 8Gy to the femur. He subsequently could bear weight on the right leg without any pain. Histologically, the fractured bone ends showed an epithelioid malignant neoplasm. He had palliative chemotherapy with a single agent of capecitabine 1500 mg twelve-hourly in a 2-weekly cycle. The serum alpha-fetoprotein (AFP) levels, four weeks post transverse colectomy, was 726 ng/mL (normal value, <20 ng/mL), and after three cycles of chemotherapy, increased to 3485 ng/mL. The disease progressed, and he developed bone metastasis to the thoracic spine, for which he had more radiotherapy.

DISCUSSION

Diagnosing hepatoid adenocarcinoma involves a multidisciplinary approach that integrates clinical evaluation, imaging studies, laboratory investigations, histopathological examination, and immunohistochemical analysis [5]. Hepatoid adenocarcinoma (HAC) presents differently depending on its primary location, but there are common symptoms shared across organ systems. Gastric HAC often causes abdominal pain, dyspepsia, weight loss, nausea, vomiting, and gastrointestinal bleeding [6]. Pulmonary HAC is characterised by cough, dyspnoea, chest pain, haemoptysis, and recurrent pneumonia. Ovarian HAC, although rare, may lead to abdominal pain, bloating, and pelvic mass [2]. HAC originating in other organs like the pancreas, uterus, gallbladder, or colon may have specific clinical presentations related to their sites. Colorectal HAC, for instance, can manifest as rectal bleeding, changes in bowel habits, abdominal pain, and anaemia [7]. Notably, many HAC patients have a history of inflammatory bowel disease (IBD) [8].

In this report, the patient experienced persistent anaemia, rectal bleeding, epigastric mass sensation, unintentional weight loss, and abdominal distention. Interestingly, despite extensive pulmonary metastasis, he did not exhibit respiratory symptoms, and he had no evidence of IBD. He had metastasis to the liver, lung, stomach, small bowel, and peritoneum, each of which can be the primary location of the tumour, but the bulk of the tumour was in the transverse colon, which was the primary site. There are no specific symptoms or signs that suggest HAC. Imaging methods like abdominopelvic ultrasound, CT scans, and X-rays are essential in locating and assessing tumour size, lymph nodes, and distant organ involvement [6]. Abdominopelvic ultrasound revealed intra-abdominal nodules with ascites, and the CT scan showed a significant mid-transverse colon mass with mesenteric and liver metastasis, causing an impending obstruction. Chest X-ray revealed cannonball lesions. These findings guided surgical planning, resulting in an extended right hemicolectomy with en-bloc partial stomach resection, addressing obstruction and rectal bleeding despite challenges from extensive metastasis.

Laboratory tests, including liver function assessment and tumour markers, such as serum alpha-fetoprotein (AFP), are valuable. AFP levels are often elevated in HAC, though not specific [5], and can be used to monitor disease progression. In the discussed case, AFP levels were unknown before surgery due to the lack of pre-operative HAC diagnosis, but they significantly increased four weeks after surgery and during therapy, suggesting possible disease progression. Diagnosing hepatoid adenocarcinoma (HAC) can be challenging, often requiring a high index of suspicion [9]. In some cases, a definite diagnosis is only established after the primary tumour has been resected, as seen in this report, where an initial diagnosis of undifferentiated colon carcinoma was made from colonic biopsies. Armaghani et al. reported a diagnosis of HAC from a lymph node biopsy from a recurrence following sigmoid colectomy [7]. Microscopic examination is crucial for identifying HAC, characterised by hepatocellular-like growth patterns and cytomorphology, with tumour cells forming trabecular or glandular structures resembling hepatocytes [10]. Distinct cytological features include polygonal or cuboidal-shaped cells with eosinophilic or granular cytoplasm, round or oval nuclei with prominent nucleoli, and the presence of nuclear pleomorphism and atypical mitotic figures [11,12]. Tumour differentiation, depth of invasion, and lymphovascular or perineural invasion presence are also assessed [13].

Immunohistochemistry is essential for confirming HAC diagnosis and differentiating it from other malignancies. Commonly used markers include HepPar-1, alpha-fetoprotein, glypican-3, arginase-1, and CDX2 [14].

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Positive staining, combined with morphological features, strongly suggests HAC [4]. Additional markers like cytokeratin 8/18, cytokeratin 7, and CEA may be variably expressed [11,15]. In this report, glypican-3 was strongly positive in tumour cells, and the CEA levels were low. Molecular profiling techniques can identify genetic alterations and specific molecular targets in HAC, paving the way for targeted therapies [16]. Sorafenib, a multikinase inhibitor, has shown efficacy in HAC cases with overexpression of vascular endothelial growth factor receptors [3,17]. Immune checkpoint inhibitors, including pembrolizumab or nivolumab, have demonstrated promise in certain advanced or metastatic HAC cases, particularly those with PD-L1 expression or microsatellite instability-high status [18,19,20]. However, the patient in this report did not express PD-L1 or receive immunotherapy or targeted therapy.

Treatment

Hepatoid adenocarcinoma (HAC) lacks a standardised treatment guideline, making management challenging. Surgical resection is the primary approach for localised HAC when feasible [21]. For cases with liver metastases, surgical resection may be considered if the disease is limited, with hepatic resection or liver transplantation as options in select cases. Unresectable cases may undergo surgical debulking or palliative procedures to alleviate symptoms and improve quality of life [22]. The reported patient had stage IV HAC, necessitating surgery to prevent intestinal obstruction and manage anaemia. However, extensive liver and small bowel involvement posed resection risks. Systemic chemotherapeutic choices in HAC depend on the primary tumour site and molecular targets [23]. Regimens often include platinum-based drugs like cisplatin or carboplatin combined with paclitaxel, gemcitabine, or 5-fluorouracil [24]. Responses to chemotherapy can vary due to the aggressive nature of the disease. The patient received single-agent chemotherapy due to poor performance status, but rising AFP levels during treatment suggested disease progression, highlighting its aggressive nature.

In advanced or metastatic cases with no curative options, palliative care is essential. The patient underwent palliative surgery, chemotherapy, and symptom-based supportive care, including closed reduction and internal fixation with radiotherapy for a pathological femur fracture, improving mobility with reduced pain. Managing symptoms, optimising quality of life, and supporting patients and families are critical in advanced HAC cases.

Conclusion

Hepatoid adenocarcinoma is a rare but aggressive disease, and even more rare is hepatoid adenocarcinoma of the colon. There is no specific treatment for this disease, though knowledge of clinicopathology and histopathology is growing as reports of cases are documented. This case report highlights one of the youngest diagnosed cases, emphasising the aggressive nature of the disease and metastasis to various organs, including bone.

DECLARATIONS

Ethical consideration

Informed consent for publication was obtained from the patient. However, ethical approval from the institutional review board was not sought for this case report.

Consent to publish

All authors agreed on the content of the final paper.

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Competing Interest

The authors declare that there is no conflict of interest regarding the publication of this article.

Author contributions

CAL, ABB, MD, VN, and PAK contributed to the initial draft. VV and JCD reviewed the manuscript for intellectual property. All authors reviewed the final manuscript.

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Availability of data

Data is available upon request to the corresponding author.

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