# Case Report Hepatoid adenocarcinoma of the colon: a rare case report and review of the literature

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**Abstract:** Hepatoid adenocarcinoma is a rare subtype of adenocarcinoma, which usually occurs in the stomach. The occurrence of this adenocarcinoma in the colon is even less common. Herein, we presented an extremely rare case of hepatoid adenocarcinoma in the colon. The patient was a 54-year-old male, who had hematochezia for three months. Enteroscopy detected a mass in his transverse colon. No mass was detected in the patient's liver by ultrasound scan. Histologically, tumor cells were observed to form solid-cell nests or cords. The tumor cells were polygonal, with abundant eosinophilic or clear cytoplasm, which mimicked hepatocytes. The tumor cells had marked atypia, with an active mitotic index, and large nucleoli. Necrosis was common in the tumor tissues, and focal hemorrhage was observed. Immunostaining showed expression of CK and GPC-3 in the tumor cells. The tumor cells were negative for CK7, CK20, CDX-2, hepatocytes, synaptophysin, and carcinoembryonic antigen (CEA). The Ki-67 index was 80%. As such, the tumor was diagnosed as hepatoid adenocarcinoma according to the clinical, microscopic and immunostaining findings. The patient underwent surgery and chemotherapy and had no recurrence at the four-month follow-up. Hepatoid adenocarcinoma in the colon is extremely rare and needs to be differentiated from metastatic hepatocellular carcinoma to improve patient clinical outcomes.

Keywords: Hepatoid adenocarcinoma, colon, case report, review

#### Introduction

Hepatoid adenocarcinoma is a rare adenocarcinoma subtype, which has pathological features similar to hepatocellular carcinoma [1]. Hepatoid adenocarcinomas most often occur in the stomach [2]. Other rare sites of this adenocarcinoma include papilla of Vater, extrahepatic duct, gallbladder, intestine, appendix, lung renal pelvis, urinary bladder, ureter, pancreas, endometrium, uterus, uterine cervix, esophagus, and urachus. Because of the histological similarities between the two carcinomas and diversity of tumor origin sites, pathological diagnosis of hepatoid adenocarcinoma can be very complicated, especially for metastatic tumors. Prognosis of hepatoid adenocarcinoma is poor due to frequent metastasis and recurrence [2, 3]. In the report by Lin and researchers, the median survival time of patients with gastric hepatoid adenocarcinoma was only 7.2 months [4]. In the study by Qu and colleagues, metastasis was reported to be the most important factor affecting the outcomes of patients with gastric hepatoid adenocarcinoma [3]. Gastric hepatoid adenocarcinoma most often metastasized to the liver [4]. Hepatoid adenocarcinoma in the colon is extremely rare; as such, there are only a few published reports to date [5-7]. Currently, no targeted treatment for this tumor type has been developed, and early discovery is important to improve the survival rate of patients. To date, there have been no systematic analysis of the clinical pathological features of hepatoid adenocarcinoma in the colon. Therefore, in this study, we report a rare case of colonic hepatoid adenocarcinoma along with a review of the literature.

#### **Case presentation**

#### Clinical history

The patient was a 54-year-old male. He had hematochezia, which presented as black stool from three months ago. He had also developed symptoms of anemia. He had no abdominal pain. Colonoscopy revealed a mass in his trans-



**Figure 1.** Microscopic features of the tumor. The tumor cells formed solid cell nests or cords (A,  $\times 200$ ). The tumor cells were polygonal with abundant clear (B,  $\times 400$ ) or eosinophilic cytoplasm (C,  $\times 400$ ). Cancer cells had high mitotic index (D, white arrow,  $\times 400$ ) and large nucleoli (E, black arrow,  $\times 400$ ). There were many small blood vessels around the tumor cells (F, the arrow,  $\times 400$ ). Hemorrhage (G,  $\times 200$ ) and necrosis H,  $\times 100$ ) were found in the tumor tissues. The cancer cells invaded the serous membrane (I). (A, G, I:  $\times 200$ ; B-F:  $\times 400$ ; H:  $\times 100$ ).

verse colon. Ultrasound scan did not show a mass in the patient's liver. The patient received surgery and chemotherapy, and he had no recurrence at a four-month follow-up.

## Materials and methods

The tumor samples were examined by hematoxylin-eosin (HE) and immunohistochemicalstry staining according to the manusfacturere's instruction and as described previously [8]. The study was performed and approved by the institutional Ethics Committees of China Medical University and conducted in accordance with the ethical guidelines of the Declaration of Helsinki.

## Results

#### Histopathological features

The microscopic findings were as shown in Figure 1. The tumor cells formed solid-cell

nests and cords without obvious glandular structure (A). The cells were polygonal with abundant clear (B) or eosinophilic cytoplasm (C). Mitosis was common (D) and higher than 10/10 HPF. Some tumor cells had big large nucleoli (E). Abundant small blood vessels was were seen around the tumor cells (F). A fFocal hemorrhage (G) and a large area of necrosis (H) was were found in the tumor tissues. The tumor cells invaded the whole layer of the intestinal wall and penetrated deep into the serous coat (I).

#### Immunophenotype

Immunostaining of the tumor cells was as shown in **Figure 2**. The tumor cells were positive for CK and GPC-3. The immunostaining was strong and diffuse. The tumor cells were negative for synaptophysin, CDX-2, CK7, CK20, carcinoembryonic antigen (CEA), and hHepatocytes. The Ki67 index was 80%.



**Figure 2.** Immunostaining of tumor cells. Synaptophysin, CDX-2 and CEA were negative. CK was diffusely positive. CK7 and CK20 was negative. GPC-3 were diffusely positive. Hepatocyte was negative. The Ki67 index was 80%. (×400).

## Discussion

Bourreille reported the first case of hepatoid adenocarcinoma, and the site of its occurrence was the stomach [9]. The stomach is the common site of hepatoid adenocarcinoma; however, this rare subtype of adenocarcinoma can also occur in many other organs, including the colon, bile duct, esophagus, urinary and reproductive systems, and lung [5]. Chen reported a hepatoid adenocarcinoma in the colon with high serum AFP levels, and the paper suggested that hepatoid adenocarcinoma should be differentiated due to the increased AFP level [5]. While serum AFP levels were commonly increased in patients with hepatoid adenocarcinoma, there have also been cases of the disease without increased AFP levels [4, 10]. In the report by Lin and colleagues, 7 of 8 cases had increased serum AFP levels [4]. Hepatoid adenocarcinomas in the intestine are less common than in the stomach. Hepatoid adenocarcinomas in the duodenum, small intestine, colon, and rectum have been reported [6, 11-14], but the cases were very few.

Histologically, this tumor is similar to hepatocellular carcinoma in many aspects [1, 15]. First, both tumors form solid-cell nests or cords without obvious glandular structures. Second, the tumor cells are large, polygonal-shaped, with abundant eosinophilic or translucent cytoplasm, which is similar to that of hepatocytes. In addition, there are abundant small blood vessels around tumor cells in both tumors. In the current report, the tumor was also composed of these tumor cells with abundant small blood vessels in the tumor tissues.

The cause and molecular mechanism of oncogenesis of hepatoid adenocarcinoma in the colon are not clear, like in many other organs. In the paper by Chen and investigators, the patient with colonic hepatoid adenocarcinoma also had long-standing ulcerative colitis [5]. Kochar reported a case of hepatoid adenocarcinoma in the small intestine and Crohn's disease [13]. To date, most tumors reported in the bowels occurred along with inflammatory diseases [5, 11, 12, 16], which strongly indicate a correlation between them. However, it is unclear whether the inflammatory disease caused the cancer. Avan reported a case in the colon without inflammatory bowel disease [6]. Kuroda, Tanigawa, and Chiba reported hepatoid adenocarcinomas in the Barrett's esophagus, which indicated a possible association between them [17-19]. It is generally considered that the stomach and liver both differentiate from the foregut of the embryo, so that hepatoid adenocarcinoma is relatively common in the stomach [5]. The study by Akiyama indicated that the origin of hepatoid adenocarcinoma in the stomach combined with tubular carcinoma was the same as the component of tubular adenocarcinoma [20]. Some studies focused on gene abnormalities, and Her2 amplification and p53 mutations were detected in some gastric hepatoid adenocarcinomas [21].

AFP is usually, but not always, positive in tumor cells of hepatoid adenocarcinoma [5, 6]. GPC-3, a marker of hepatocellular differentiation, is also commonly positive in hepatoid adenocarcinoma [6], as in the current case. CEA serum level was normal in the case reported by Armaghani; however, in the current case, CEA was negative in tumor cells. In addition, CDX-2 was positive in tumor cells of the case reported by Armaghani [6], which was different from our study. In the case reported by Terracciano, CK7 was negative [22], as in the current case. According to study by Xiao, both CK7 and CK20 immunostaining in hepatoid adenocarcinomas were not constant [23].

Hepatoid adenocarcinoma is highly aggressive. Armaghani reported a case that metastasized to the lung and liver rapidly after sigmoid colectomy and chemotherapy [6]. In the case reported by Cappetta, the patient with hepatoid adenocarcinoma in the transverse colon died from the tumor after six recurrences and 8 months after diagnosis [7]. Because the tumor is rare and knowledge about its molecular biology is limited, there are currently no targeted therapies that differ from treatments for a common adenocarcinoma [6].

# Conclusion

In summary, hepatoid adenocarcinoma is very rare tumor and requires differentiation from hepatocellular carcinoma. The tumor is very aggressive with frequent early metastasis; therefore, timely and correct diagnosis is important to improve patient prognosis.

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# Disclosure of conflict of interest

None.

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