RARE PRESENTATION OF HEMANGIOMA-LIKE HEPATOCELLULAR CARCINOMA WITH INFREQUENT SYMPTOMS OF LOWER GASTROINTESTINAL BLEEDING AND ATYPICAL RADIOLOGICAL FEATURES-A CASE REPORT

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ABSTRACT Hepatocellular carcinoma can mimic benign lesions like liver haemangioma with atypical image findings. It can manifest in an acute emergency where a diagnostic dilemma can alter the management phase. We, at this moment, present a case of a 70-year-old male patient with multiple medical comorbidities who presented to us initially in June 2021 with a history of blunt trauma abdomen. Ultrasound abdomen imaging was suggestive of bleeding from liver hemangioma. The patient underwent emergency exploratory laparotomy, and hemostasis was achieved. After being clinically better, he underwent angioembolisation of the bleeding vessels; unfortunately, he presented with bleeding per rectum one year later. On re-evaluation, imaging features were again consistent with giant liver hemangioma infiltrating ascending and transverse colon. Tumour markers were negative. Being nonamenable to angioembolisation at this setting, he underwent exploratory laparotomy enblock right hemicolectomy + non-anatomical liver resection (segment 6, part of 5,7) on October 2022 based on intraoperative findings. Surprisingly the histopathology report was that of hepatocellular carcinoma (HCC). Detailed searching allowed us to find these discordant presentations of HCC with negative tumour markers and atypical imaging findings. The patient was referred to our medical oncology department for expert management. The incidence of direct invasion of HCC to the gastrointestinal tract is approximately 0.5–2%. Colonic metastasis is uncommon in patients with HCC. Radiologic hallmarks generally make the diagnosis of HCC of dynamic contrast imaging. Sometimes large HCCs may have atypical radiological contrast enhancement patterns, thus mimicking hemangioma.

KEYWORDS HCC-Hepatocellular carcinoma, CT- Computed tomography, MRI- magnetic resonance imaging, TACE-Transarterial Chemoembolisation, GI- gastrointestinal, PLB-Percutaneous liver biopsy, AFP-Alpha fetoprotein

Introduction

HCC is usually diagnosed by dynamic contrast computed tomography (CT) or magnetic resonance imaging (MRI), showing a typical contrast enhancement pattern in the arterial phase and rapid washout in the portovenous phase. However, large HCC may present atypical contrast enhancement patterns mimicking benign liver masses(1).

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Bleeding liver hemangioma can be intervened by angioembolisation. HCC-mimicking benign hemangiomas may undergo hematogenous metastasis after Transarterial Chemoembolisation (TACE). In the case of hematogenous metastasis, the venous flow from the colon to the liver is reversed, possibly because of the increase in portal pressure in patients with cirrhosis and during TACE(2).

Lungs, abdominal lymph nodes, and bones are the most common sites of extrahepatic metastasis in HCC(3). Most of the extrahepatic metastasis of HCC occurs in patients with advanced-stage intrahepatic tumours (4). Colonic involvement by HCC has been reported in scanty case reports wherein HCC directly invaded the transverse colon/hepatic flexure and presented with a GI bleed (4). Direct invasion of the gastrointestinal (GI) tract by HCC is uncommon, with a reported incidence of approximately 0.5–2% among clinical HCC cases (5,6). The most common clinical presentation is frank GI bleeding, and the most common site of involvement is the stomach, followed by the duodenum and colon (5,6). Surgical intervention may be the optimal choice for the palliative treatment of HCC with GI involvement (5). We at this moment present a case of a 70-year-old male with discordant imaging features of HCC mimicking hemangioma liver initially managed with surgery and TACE in whom later presentation of lower GI bleed lead to a diagnosis of HCC liver infiltrating colon, a rare and uncommon extrahepatic manifestation.

Case report

Presenting Complaints

A 70-year-old male patient presented in the emergency department with complaints of bleeding per rectum for 2 weeks. Initially, he had maelena and later hematochezia. He has no history of bleeding per rectum, no h/o intake of Anticoagulant or Antiplatelet agents, no h/o intake of NSAIDs, and no h/o loss of appetite and weight. He had multiple medical comorbidities-Type 2 Diabetes, Hypertension, Chronic obstructive pulmonary disease, Chronic kidney disease and Secondary Polycythemia.

Past Surgical History

The patient had a history of blunt abdominal trauma in June 2021 and then presented to the casualty one week later with features of hypovolemic shock. After initial stabilization, the Ultrasound abdomen revealed gross hemoperitoneum secondary to ruptured liver hemangioma. Since the patient's general condition was deteriorating over time, He underwent Emergency Exploratory laparotomy, hemostasis was achieved, and omentum was kept over the ruptured hemangioma site. Postoperatively, the TACE of the feeder's vessel was done 2 weeks later.

Personal, Family History and Physical Examination

The patient was a smoker who stopped 12 years back and an occasional alcoholic, consuming a mixed diet—no family history of malignancy. On Physical examination, He had pallor, No jaundice, clubbing, or generalised lymphadenopathy. He is moderately built and nourished with BMI=21.2kg/m2. A digital rectal examination revealed Blood clots. There was no active bleeding and No palpable mass. Proctoscopy also showed blood clots. No haemorrhoids or masses were visible. The abdomen was soft and non-tender. A vague mass was palpable below the right costal margin. A laparotomy scar was present along with divarication of recti.

Routine Laboratory Blood Investigations

The patient had Severe anaemia [Hb-6.8], for which multiple blood transfusions were given. His Prothrombin time/INR was 14/1.48, RFT - 56/1.8, Total Bilirubin/Conjugated Bilirubin - 1.2/0.8, Total Protein /Albumin - 5.2/3.0, AST/ALT/ALP - 22/24/122. He belonged to CHILD PUGH A.

Imaging studies

Plain and Contrast CT Abdomen revealed a Large ill-defined partially exophytic lesion with heterogeneous areas within the right lobe of the liver measuring 9.8 x 6 x 8.3 cm with communication with an ascending colon. Multiple renal cortical cysts of varying sizes. Divarication of recti with protrusion of bowel and Splenomegaly was noted. Interventional Radiology advised proceeding with Triple phase CT of the Abdomen.

Triple phase CT abdomen

A large ill-defined, partially exophytic hetero-dense lesion measuring 10.2 x 6.2 x 6.5 cm was noted in segment VI of the liver. In the Arterial phase, the lesion had Peripheral nodular enhancement. The Venous phase showed progressive filling—small arterial feeders to the lesion noted from the gastroduodenal artery and proper hepatic artery. A small direct branch from the aorta was noted, supplying the lesion below the renal artery. Prominent veins were noted in the peripheral posterior aspect of the lesion draining to the inferior vena cava and superior mesenteric vein. The lesion is communicating with ascending colon; the impression was hemangioma liver eroding into the ascending colon and hepatic flexure. Interventional radiology review consultation was sent with a triple-phase report. Advised that the lesion was not amenable for embolization since there were only tiny feeders from mesenteric and hepatic vessels.

Surgical management

The patient underwent exploratory laparotomy Enblock Right Hemicolectomy + Non-anatomical Liver Resection (Segment 6, part of 5,7)

Post-operative care

The patient was kept on elective mechanical ventilation for a postoperative day and extubated uneventfully. Further postoperative period was uneventful except for wound infections.

Histopathology of resected surgical specimen

(R) 6th Segmentectomy (Liver) (R) Hemicolectomy Received adherent and distorted segment of liver, measures 12.5x9x7cm, ileum measures 17.5 cm length, appendix measures 7 cm length, and Colon measures 50 cm length.-Hepatocellular Carcinoma Moderately differentiated

Lesion measures 11.5 x 7.5x33 cm with extensive areas of necrosis and fixation -Segment of Colon, appendix and intestine-histologically unremarkable Because of extensive necrosis, resected end of the liver cannot be assessed.No lymphovascular emboli seen. No lymph nodes identified

Immunohistochemistry study-Tumour cells are positive for Hepar-1, and CK7 showed positivity in normal bile ducts—CD 31-Negative.

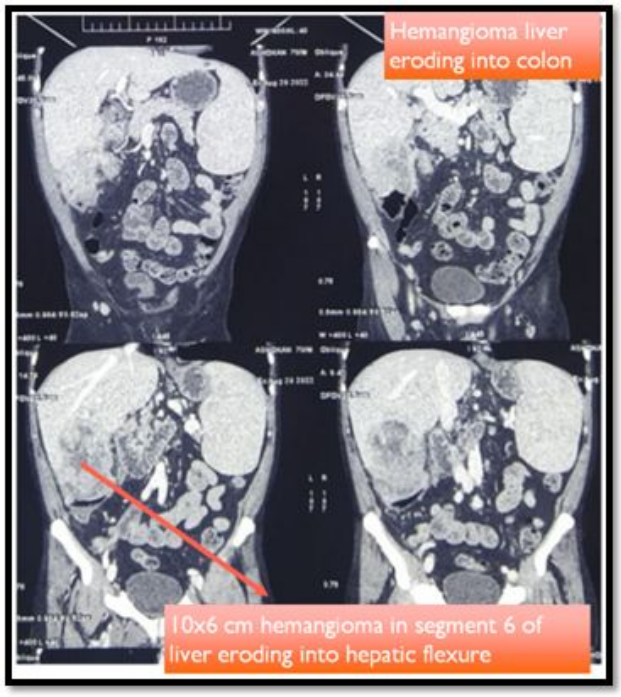

Figure 1 TRIPLE PHASE CT ABDOMEN-HEMANGIOMA IN SEGMENT6 OF LIVER ERODING INTO ASCENDING COLON AND HEPATIC FLEXURE

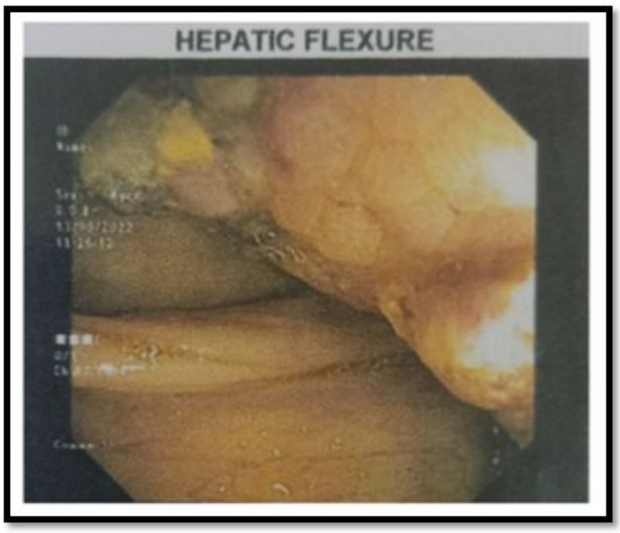

Figure 3 HEPATIC FLEXURE- A LARGE MASS WITH FRIABLE MUCOSA AND MINIMAL OOZING WITH COMPLETE LUMINAL NARROWING

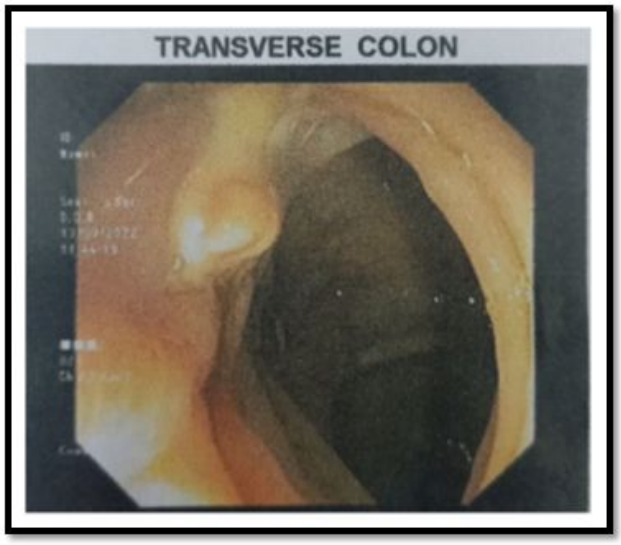

Figure 2 TRANSVERSE COLON- AT MIDTRANSVERSE COLON SUPERFICIAL ULCER WITH MUCOSAL IRREGULARITIES INVOLVING <30 % OF CIRCUMFERENCE.

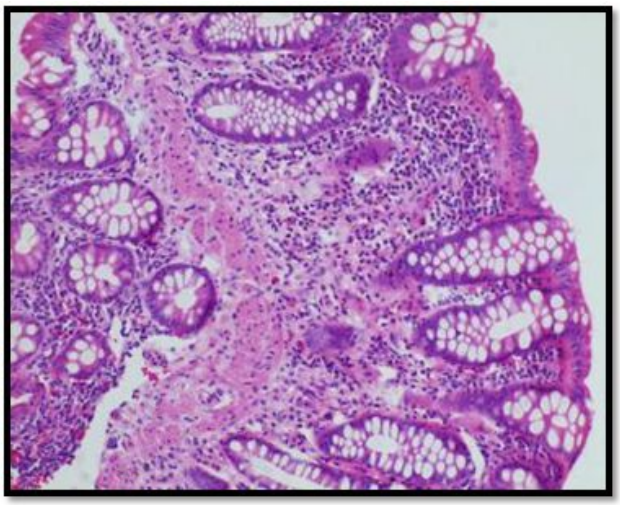

Figure 4 TRANSVERSE COLON BIOPSY-SHOWING MILD CHRONIC INFLAMMATORY INFILTRATE IN LAMINA PROPRIA.NO DYSPLASIA SEEN

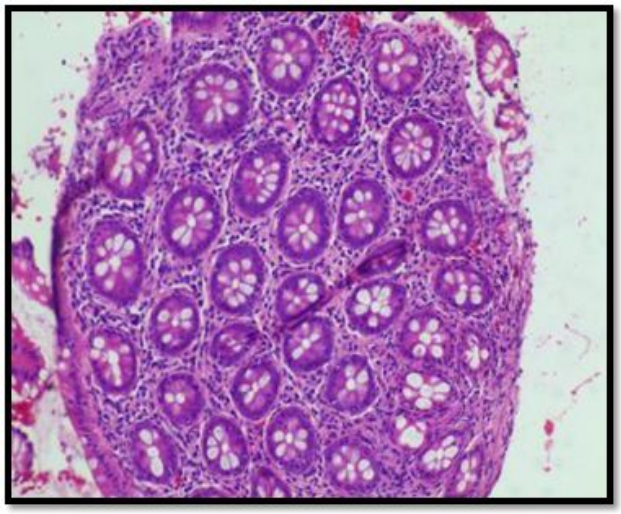

Figure 5 HEPATIC FLEXURE BIOPSY-SHOWING MILD CHRONIC INFLAMMATION IN LAMINA PROPRIA.NO CRYPTITIS AND CRYPT ABSCESS.NO EVIDENCE OF DYSPLASIA/NEOPLASIA

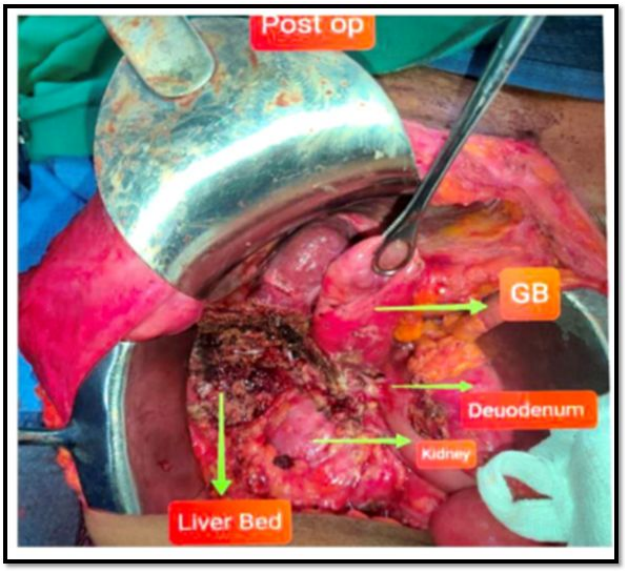

Figure 7 POST OPERATIVE IMAGES AFTER NON-ANATOMICAL LIVER RESECTION AND RIGHT HEMI-COLECTOMY

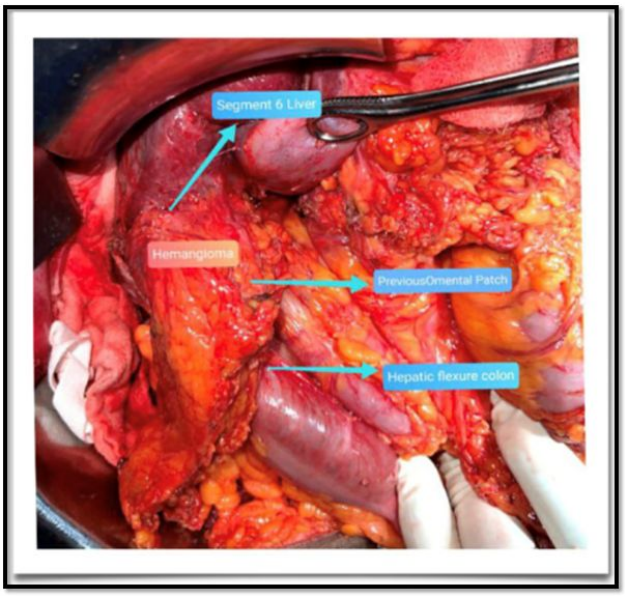

Figure 6 INTRAOPERATIVE FINDINGS-1.LIVER HEMANGIOMA ARISING FROM SEGMENT 6 ABUTTING THE HEPATIC FLEXURE WITH CLUMPED UP OMENTUM, ILEUM, ASCENDING COLON AND PART OF TRANSVERSE COLON.

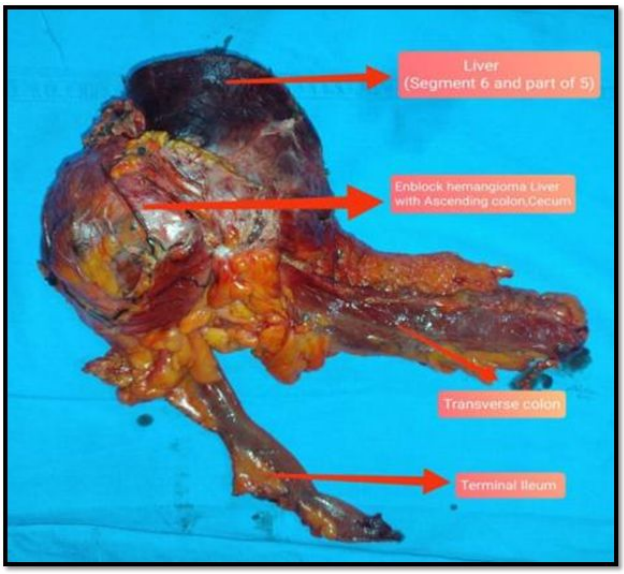

Figure 8 GROSS SPECIMEN AFTER RESECTION

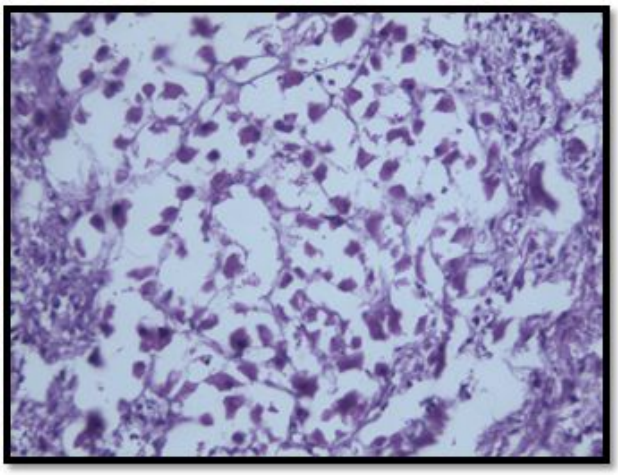

Figure 9 HISTOPATHOLOGICAL IMAGE SHOWING A) MALIGNANT HEPATOCYTES

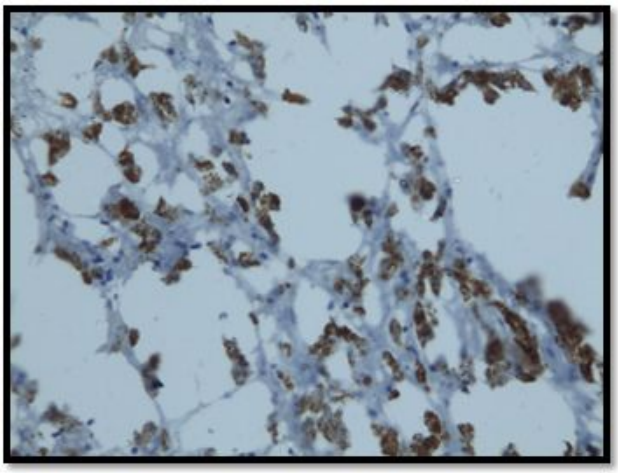

Figure 10 HEPAR 1 POSITIVE

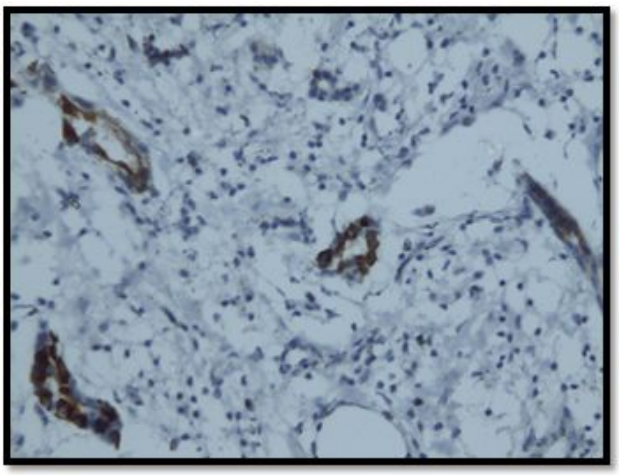

Figure 11 CK 7 POSITIVE

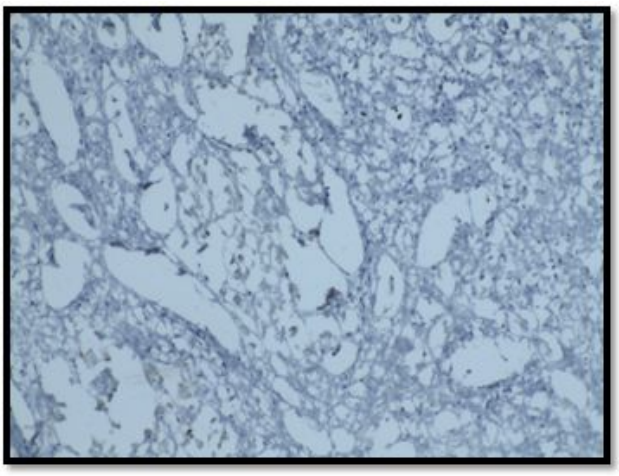

Figure 12 CD 31 NEGATVE

Discussion

An unusual cause of gross hemoperitoneum, wherein a patient is evaluated and managed for a bleeding giant liver hemangioma having undergone TACE, later presenting as a case of lower GI bleeding, with atypical imaging features and surprising histopathological findings of HCC is the peculiar rare case we report here. Hepatic hemangioma is the most common benign neoplasm of the liver. Patients with this condition are typically asymptomatic (7). The prevalence of hepatic hemangiomas ranges from 1% to 20% in the general population(8,9).

Hepatic hemangioma is primarily diagnosed via imaging studies or autopsies and mainly presents in middle-aged females. Cavernous hemangioma is a common type of hepatic hemangioma, which usually presents as a solitary, well-delineated, subcapsular, disclosed nodule. These distinctive structures show a characteristic hemodynamic pattern on enhanced CT and MRI. However, an atypical hemangioma may lack the imaging features characteristic of a typical hemangioma. A hepatic hemangioma can therefore be difficult to distinguish from other lesions such as HCC, intrahepatic cholangiocarcinoma (ICC), and mixed hepatocellular cholangiocarcinoma (HCC-CC) (7).

In our patient, HCC mimics Giant hemangioma, was misdiagnosed due to its atypical imaging features, negative tumour markers, negative histopathological reports from biopsies of colonic infiltrate, and later being diagnosed as HCC only after histopathological examination of non-anatomical segmental liver resection and right hemicolectomy specimen, which was indicated due to massive bleeding per rectum.

Our patient was normal 2 years back. He was a cattleman who accidentally slipped and fell down at a worksite during his work. The patient was apparently normal for 2 days. Later he presented to the emergency surgical causality with tachycardia, hypotension and anuria. Ultrasound abdomen revealed a well-defined exophytic lesion from segment 6 of the liver measuring 9.4 x 7.3 x 6.5 cm. The lesion is hyperechoic with a central hypoechoic area-Most likely ruptured liver hemangioma. Since the patient's clinical condition, the deteriorating patient underwent exploratory laparotomy. Intraoperative gross hemoperitoneum was present. 2.5 litres of blood was evacuated. Bleeding was noted from a lesion measuring 7x6x3 cm, which was arrested with bipolar diathermy and liver sutures. The specimen was sent for histopathological examination. After attaining hemosta-

sis, omentum was placed over the raw area. The postoperative period was uneventful. Gradually patient's general condition improved. Haemoglobin levels improved—histopathological examination showed tissue sections with extensive areas of necrosis without any identifiable viable tissue. Given the liver lesion's atypical size, we consulted the interventional radiology department.

Meanwhile, the tumour marker Alpha-fetoprotein (AFP) was sent and was negative. An angiogram of the hepatic artery showed a tumour blush in the posterior segment of the right lobe of the liver. Elective cannulation of the culprit feeder of the tumour was accessed with a great microcatheter and embolised with polyvinyl alcohol. Postembolisation angiogram showed no tumour blush. The post-procedure patient was normal and was discharged. The second visit after 1 year was more challenging, and now the patient presented with severe anaemia secondary to lower GI bleeding. The patient was given multiple packed red blood transfusions. In view of the previous history, a triple-phase abdomen CT was again done. A large ill-defined partially exophytic heterodense lesion measuring 10.2 x 6.2 x 6.5 cm was noted in segment VI of the liver. In the arterial phase, the lesion had peripheral nodular enhancement, and in the venous phase, it showed progressive filling. Small arterial feeders to the lesion were noted from the gastroduodenal artery, a proper hepatic artery. A small direct branch from the aorta was noted, supplying the lesion arising below the renal artery. Prominent veins were noted in the peripheral posterior aspect of the lesion draining to the inferior vena cava and superior mesenteric vein. The lesion is communicating with ascending colon; the impression was hemangioma liver eroding into the ascending colon and hepatic flexure. Interventional radiology review consultation was sent with a triple-phase report. Advised that the lesion was not amenable for embolization since there were only tiny feeders from mesenteric and hepatic vessels. Colonoscopy and biopsy from the transverse colon and hepatic flexure were negative for malignancy. AFP was within normal. Hence our clinical judgment was more towards liver hemangioma infiltrating the colon and presenting as bleeding per rectum.

Recurrent bleeding episodes and multiple blood transfusion requirements made us plan for segmental liver resection and segmental colectomy. Intraoperatively, liver haemangioma was seen arising from segment 6 abutting the hepatic flexure with clumped up omentum, ileum, ascending colon and part of the transverse colon. We performed Enblock Right Hemicolectomy + Non-anatomical Liver Resection (Segment 6, part of 5,7) and ileotransverse anastomosis. Multiple comorbidities were a hindrance to immediate post-operative extubation. The patient was electively ventilated for 2 days and weaned off to room air. The immediate postoperative period was uneventful except for minor surgical site infections. Nevertheless, all of the surprise histopathological findings of the gross specimen and its immunohistochemical analysis led to the diagnosis of hepatocellular carcinoma.

Literature conveys that imaging findings are not always correct for some atypical hemangiomas. Furthermore, when the patient concomitantly had high AFP, a risk factor for tumour malignancy, we should attribute the symptoms to a single disease: HCC (7).

Many HCCs do not have the classic imaging characteristics, especially when larger than 3 cm. The typical imaging findings in HCC are arterial hyperenhancement with washout on portal venous and/or equilibrium phases. Larger HCCs can have atypical imaging findings, including fibrous capsule or mosaic appearance. As imaging modalities continue to improve, fewer biopsies are required for diagnosing benign and malignant lesions. HCC, in particular, has very well-defined imaging features and a clear imaging algorithm for making a noninvasive diagnosis. The features are so well recognized that the imaging appearance is sufficient for directing treatment and transplant allocation. A diagnosis based on the enhancement features alone would have led to a misdiagnosis(10). Radiologic hallmarks generally make the diagnosis of HCC of dynamic contrast imaging. However, large HCCs may have atypical radiologic contrast enhancement patterns due to tumour necrosis, fibrosis, fatty change, calcification, peliosis, or portal vein thrombosis. HCCs with atypical radiologic characteristics could mimic other benign hepatic masses like hemangioma, large regenerative nodules or abscesses (1). The gold standard for diagnosing lesions is the pathological diagnosis, which requires liver resection or PLB (Percutaneous liver biopsy). PLB is an important tool for the diagnosis and treatment of liver lesions. This approach provides tissue for histopathological observation (7). However, as an invasive procedure, PLB risks certain complications, such as abdominal dissemination by needle-tract implantation(11).

AFP is a kind of fetal-specific glycoprotein produced by the fetal liver, which has a normal range in adults of less than 20ng/mL. Serum AFP is elevated in cases such as HCC, seminoma, and pancreatic cancer (7). According to the conclusions of the Barcelona-2000 EASL Conference (EASL: European Association for the Study of the Liver), the diagnostic criteria of HCC include AFP levels>400ng/ mL and focal lesion >2cm with arterial hypervascularization(12).

In our case, AFP and CEA(Carcinoembryonic antigen) levels were within normal range. As per the literature, the incidence of gastrointestinal metastasis in HCC is 0.5-2%, and among GI metastasis, the stomach and duodenum comprise the site of distant metastasis. Infiltration and metastasis to the colon are extremely rare. Negative colonic biopsies, negative tumour markers and image findings made us stick on with diagnosing a giant liver hemangioma. The predisposing factors for GI tract involvement were large liver lesions (>5 cm), subcapsular location and exophytic growth pattern (13). Colonic involvement by HCC has been reported in scanty case reports wherein HCC directly invaded the transverse colon/hepatic flexure and presented with GI bleed. Rare reports of hematogenous spread of HCC to other parts of the colon are also available(4).

Hirashita et al. described 2 similar HCC cases directly invading the colon. Both patients underwent partial liver and colon resection but had limited survival (1 month and 6 months, respectively)(14). Lin et al. reported 11 cases of GI metastasis in HCC and concluded that the prognosis in all the patients was extremely poor(5). The authors also added that surgical intervention may be the optimal choice for the palliative treatment of HCC with GI involvement(4).

The possibility of metastases to colon may also be attributed to TACE, which was performed in the patient's first presentation of bleeding hemangioma(15). The literature says that, In the case of hematogenous metastasis, the venous flow from the colon to the liver is reversed, possibly because of the increase in the portal pressure in patients with cirrhosis and during TACE(16). Several cases of hematogenous metastasis after TACE were reported (17). The median time from initial HCC to colorectal metastasis is 30 months, so continuous follow-up is necessary. Although the median survival time after colorectal metastasis

in the cases reported in the literature is 5.5 months, some studies have reported longer periods of over 1 year. In most cases, surgery was performed to control bleeding rather than cure the cancer. However, aggressive metastasis resection may lead to a prolonged prognosis if the general condition is acceptable and complete resection is possible(2).

According to the Japanese guidelines for treating HCC (18), the administration of molecularly targeted drugs is strongly recommended to treat extrahepatic metastases of HCC. In contrast, local therapy, such as resection, is only weakly recommended when intrahepatic lesions are absent or well controlled(2).

Despite a definitive diagnosis, surgery was performed to control the bleeding(2).In one study, the 1-year cumulative survival rate was reported to be 20%, and the 3-year cumulative survival rate in the extrahepatic metastasis non-resection group was not reported (19).

Our patient is still alive, and resection of the metastases might have contributed to the improved prognosis. Chemotherapy may prolong survival if there are no indications for surgical resection, such as metastasis. However, several studies must be performed, and data must be collected and analysed to determine which is better.

When a ruptured tumour accompanied by retroperitoneal haemorrhage is found, HCC colonic metastasis should be ruled out(2).

Although a preoperative diagnosis was not possible in this case, the use of Tc-99 m for the diagnosis of colorectal metastasis of HCC has been reported previously (20), which might prove useful for diagnosis when extrahepatic metastasis of HCC is suspected based on the patient's medical history(2).

Conclusion

Large hemangiomas can create a diagnostic dilemma in which clinicians find it difficult to diagnose because of atypical image findings, negative tumour markers and unusual clinical presentation. From our experience, we have concluded that large hemangiomas have to be considered hepatocellular carcinomas unless otherwise proven. Wherever in doubt, it's better to obtain a tissue diagnosis in the form of a percutaneous liver biopsy or a diagnosis of HCC, especially if a large hemangioma presents in the background of chronic liver disease.

Declarations

Patient informed consent

Written informed consent was taken from the patient.

Conflict of Interest

The authors declare no conflict or competing interests.

Ethics committee approval:

Consent of Ethicks taken.

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