

Primary Hepatic Carcinoid Tumor with Poor Outcome

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ABSTRACT

Primary Hepatic Carcinoid Tumor (PHCT) represents an extremely rare clinical entity with only a few cases reported to date. These tumors are rarely associated with metastasis and surgical resection is usually curative. Herein, we report two cases of PHCT associated with poor outcomes due to late diagnosis. Both cases presented late with non-specific symptoms. One patient presented after a 2-week history of symptoms and the second case had a longstanding two years symptomatic interval during which he remained undiagnosed and not properly worked up. Both these cases were diagnosed with hepatic carcinoid tumor, which originates from neuroendocrine cells. Case 1 opted for palliative care and expired in one month's time. Surgical resection was advised to the second case, but he left against medical advice.

Key Words: Neuroendocrine tumor. Primary hepatic carcinoid. Liver metastasis.

INTRODUCTION

Carcinoid tumors originate from neuroendocrine cells and are usually well-differentiated, low-grade malignant neoplasms, mostly occurring in the gastrointestinal tract.¹ Primary Hepatic Carcinoid Tumor (PHCT) is a rarity and represents only 0.3% of all neuroendocrine tumors. Diagnosis of PHCT is challenging due to its radiological similarity to other hepatic lesions and mild non-specific symptomatology. Histology is the gold standard to confirm and exclude other tumors including hepatocellular carcinoma, cholangiocarcinoma and metastatic lesions.² PHCT usually follows a slow growth and inert pattern and surgical resection is the treatment of choice in most cases. For unresectable lesions, transarterial chemoembolization (TACE) or long acting somatostatin analogue can be considered.³ Early diagnosis is associated with good long term outcome and requires a high index of suspicion and histological confirmation.

We are reporting two cases of a rare liver tumor from South Asia, which is very infrequently reported from this region.

CASE REPORT

Case 1: The patient was a 60-year gentleman who presented with history of abdominal discomfort, nausea and vomiting for 15 days. Abdominal examination revealed a palpable mass in the right upper quadrant. Biochemical parameters showed low Hb (8.5 gm/dl), high serum total bilirubin of 2.8 mg/dl (direct 1.62,

indirect 1.18) and raised alkaline phosphatase (1062 IU). Viral serology was negative for hepatitis B and C. Serum alpha-fetoprotein levels were normal and there were no signs of chronic liver disease.

Diagnostic imaging included an abdominal ultrasound, which revealed a large hypoechoic mass in the right lobe of the liver. CT abdomen (Figure 1a) showed an enlarged liver and a well circumscribed, hypodense mass measuring 13 x 10 x 8 cm with homogeneous contrast enhancement. He underwent an ultrasound guided liver biopsy and histology (Figure 2), which confirmed the diagnosis of a neuroendocrine tumor. Metastatic workup including upper and lower gastrointestinal endoscopy and CT chest were performed, which were normal and ruled out the possibility of a metastatic carcinoid tumor.

The patient was advised oncological consultation and surgical resection of the tumor, which he refused and was, therefore, discharged on palliative care. One month later, he presented again with progressive abdominal distension, shortness of breath and two episodes of bleeding per rectum. Chest X-ray demonstrated bilateral pleural effusion with basilar atelectasis. Patient was started on broad-spectrum antibiotics and intravenous (IV) fluids, but despite all the supportive measures, his condition deteriorated and he developed severe urinary tract infection and sepsis leading to his death.

Case 2: This was a 59-year male who presented with a two-year history of central, dull, non-radiating abdominal pain. On examination, he had right upper quadrant tenderness and mild hepatomegaly. Abdominal ultrasound revealed mildly enlarged liver and two well-defined hyper-echoic lesions in segment VI of right lobe. Biochemical results showed normal alpha-fetoprotein level and negative hepatitis serology. CT abdomen showed two well-defined heterogeneously enhanced lesions with the largest one measuring 2.8 x 3.2 cm in

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Received: February 03, 2015; Accepted: August 27, 2015.

segment VI of the liver (Figure 1b). The lesions showed enhancement on early arterial phase and washout on portal venous and delayed phase. Liver biopsy was performed and histology confirmed the diagnosis of carcinoma with neuroendocrine differentiation (Figure 2).

The case was discussed in Tumor Board and patient was advised surgical resection of the tumor, which he refused due to financial constraints. The patient was started on palliative care but he left against medical advice.

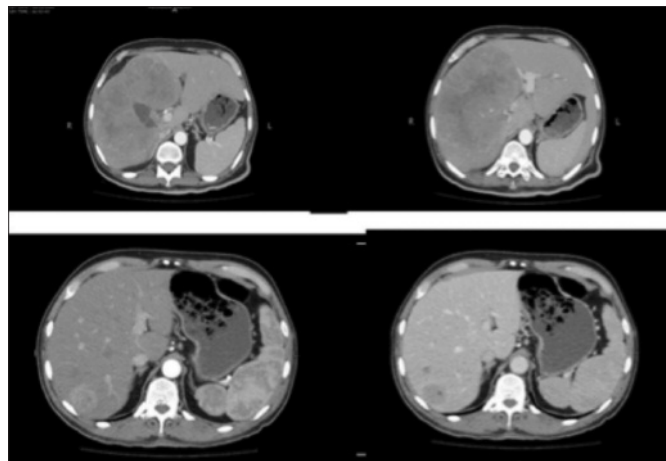


Figure 1 (a): Case 1: CT scan showing a large heterogeneously enhancing lesion in the right liver lobe with filling defect right branch of portal vein representing thrombosis. **(b)** (Case 2) Two, well-defined, heterogeneously enhancing lesions are identified in segment VI of right lobe of liver. These lesions show enhancement on early arterial phase and washout on portal venous and delayed phase.

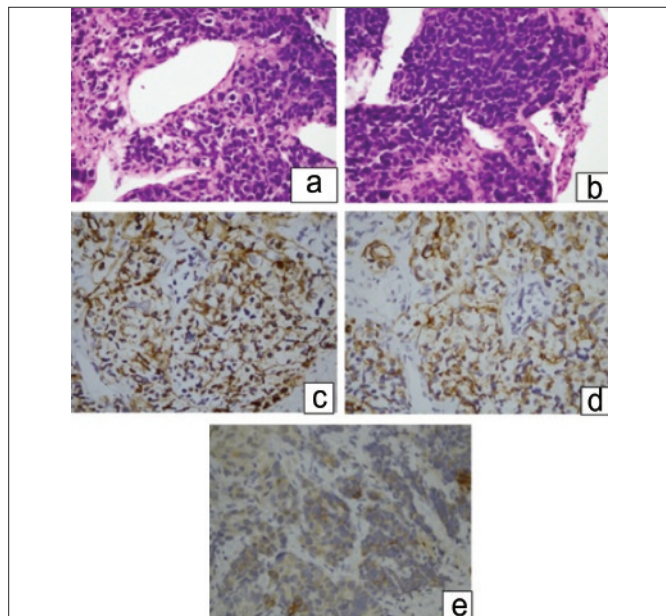


Figure 2: (a) Aggregates and sheets of tumour cells with pleomorphic. **(b)** Tumour cells arranged around blood vessels (H&E x 20). **(c)** Tumor cells showing positivity for immunohistochemical stain CK CAM5.2 (X20). **(d)** Tumor cells showing positivity for immunohistochemical stain CK AE1/AE3 (X20). **(e)** Tumor cells showing positivity for immunohistochemical stain CD56 (X20).

DISCUSSION

Carcinoid tumors are rare, slow-growing neuroendocrine tumors, which were previously reported mainly within the gastrointestinal tract (GIT). Recent literature, however, reports frequent involvement of lungs, pancreas and reproductive system.⁴ Liver is usually a common site for metastasis of GIT neuroendocrine tumor and Primary Hepatic Carcinoids Tumors (PHCT) are extremely rare. The exact histogenesis is not known; however, it is hypothesized that they may arise from scattered neuroendocrine cells in the intrahepatic biliary epithelium or could be due to intestinal metaplasia as a result of chronic inflammation of biliary system.⁵

PHCT are reported mainly in adult population (mean age 49.8 years) and are slightly more common in females (58.5%).⁶ They can be clinically silent, possibly due to spillage of neoplastic derived products into the portal vein and subsequent degradation by the liver enzymes. When symptomatic, patients usually present with weight loss, abdominal pain, jaundice and a palpable mass on examination. Classic carcinoid syndrome with skin flushing, wheezing and diarrhea is mainly associated with metastatic neuroendocrine tumors and may be present in around 5% of patients PHCT.⁷

The diagnostic dilemma affiliated with this disease, which was also apparent in our cases, is attributed to its rarity, mild symptomatology and close resemblance to other hepatic lesions (hepatocellular carcinoma, cholangiocarcinoma, metastatic liver disease, etc.). Imaging modalities, such as ultrasound, CT and MRI, have a low specificity for carcinoid tumor due to similarity with hemangioma and HCC.⁸ Octreoscan scintigraphy is more specific compared to CT and MRI in detecting both primary carcinoids and metastatic lesions, but has very limited availability especially in remote centers. Assertive diagnosis was made only on the basis of immunohistochemistry, which verifies the neuroendocrine origin of PHCT by detecting markers such as CgA, NSE, chromogranin, CEA and synaptophysin.⁴

The definitive management of PHCT is surgical resection, which is very effective when tumor is confined to a single lobe. A postoperative 5-year survival rate of 74% has been reported with early resection. In cases of multilobar and non-resectable lesions, palliative cytoreduction surgery with TACE can be effective.⁵ For metastatic hepatic carcinoids, therapy with radionuclides and the somatostatin analogs can be a reasonable option.⁹

Both of these cases were diagnosed very late and had a poor outcome. This implies the importance of early diagnosis and management of PHCT, which in itself follows an inert course if treated timely. However, living in a region with high prevalence of HBV and HCV, hepatocellular carcinoma (HCC) is usually a strong initial suspect in patients with liver tumors and must be

excluded via histology, since both HCC and PHCT have completely different management. The authors also imply on the competence of histopathologist and availability of CD markers for diagnosis of PHCT.

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