Case Report

Primary neuroendocrine tumor of liver: An eye opener for a pathologist

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Abstract

Introduction: Neuroendocrine tumors (NETs) are neoplasms that arise from cells of the endocrine (hormonal) and nervous systems. Many are benign, while some are malignant. They most commonly occur in the intestine. While the liver is a common site of metastases.
Case Presentation: We describe a 73-year-old female who reported to our center with complains of swelling and pain in the right upper quadrant of stomach. CECT revealed large well-localized multicystic mass in the right lobe of the liver. A suspicion of hydatid cyst was given. However, immunogenic tests results were negative for hydatid cyst. The AFP level was also unremarkable.
Conclusion: Histopathological examination with immunohistochemical panel along with other serological and radiological investigations made the diagnosis possible due to its vague clinical presentation.

Keywords: Liver, neuroendocrine neoplasm, primary

Introduction

Primary neuroendocrine tumor (NET) originating in the liver is quite rare.[1] Less than 200 cases have been reported throughout the English-language literature since Edmondson first described this disease in 1958. It most commonly arises in the bronchopulmonary or gastrointestinal tract but can originate from almost any organ.[2] Initial differential diagnosis was kept as hydatid cyst on imaging study. There is a paucity about the clinical course of the disease and surgical outcome; however, a surgical resection has become the mainstay of the treatment. To the best of our knowledge, this the first case from India reported in a woman >70 years of age. Hence, it is a rare case of a non-secretory primary hepatic neuroendocrine tumor in elderly lady who was successfully managed with surgical resection. Since this tumor may remain asymptomatic for years, only pressure effects make it to be notified. Hence, it is relevant to report this tumor in the context of primary care.

Case Presentation

A 73-year old female referred to surgery OPD with complaints of right hypochondrium pain along with abdominal swelling for the past 3 months. Physical examination showed mild tender and distended abdomen with icteric sclera. Relevant negative findings were also noted as no cervical or inguinal lymphadenopathy and breast lump found and there is negative history of postmenopausal bleeding. Blood investigation revealed mild anemia with elevated total bilirubin and liver enzymes. Biomarkers such as carcinoembryonic antigen (CEA), CA19,-9 and Ca125 also came within normal limits. Chest X-ray was unremarkable. Ultrasonography (USG) of the abdomen revealed two heterogeneous enhancing space-occupying lesions (SOL) in the right lobe of the liver with normal study of uterus and bilateral ovaries. Contrast-enhanced computed tomography (CECT) further confirmed two large multilocular cystic SOLs measuring 11.6 × 11.5 × 13.4 cm and 8.6 × 7.2 × 8.3 cm noted in the right lobe liver with multiple feeding vessels [Figure 1a and b].

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Gall bladder was normal and deviated to the left side. No lymphadenopathy was present. On the basis of these findings, three differential diagnoses were made: hemangioma, biliary cystadenoma, and hydatid cyst.

Right hepatectomy with gall bladder was sent for histopathological examination. Gross specimen showed markedly enlarged liver weighing 1.0 kg. The outer surface showed vague cystic nodules. The cut surface of mass mainly exhibited multiple cystic areas varying in size and filled with brownish black hemorrhagic fluid and necrotic material. A thin rim of normal brownish black liver parenchyma was also noted [Figure 2a]. Microscopy showed multiple cystic structures comprising tumor cells arranged in cords, acinar pattern, and papillaroid fragments along with large areas of hemorrhage and necrosis. Tumor was seen infiltrating into the normal liver parenchyma at the periphery. The tumor cells were round to oval nucleus exhibiting fine granular chromatin, conspicuous nucleoli, and moderate amount of eosinophilic cytoplasm [Figure 2b and c]. Further immunohistochemical (IHC) stain was applied on the viable tumor away from necrosis. IHC showed tumor cells positive for Panck, CK-19, Synaptophysin, and Ki-67 labeling index of 4% and negative for HepPar-1, CEA, arginase, CDX-2, CD-10, CK-7, CK-20, chromogranin, PR, and TTF-1 [Figure 2d-f]. Hence, finally on the basis of morphology and immunohistochemistry, a diagnosis to neuroendocrine tumor grade 2 was made.

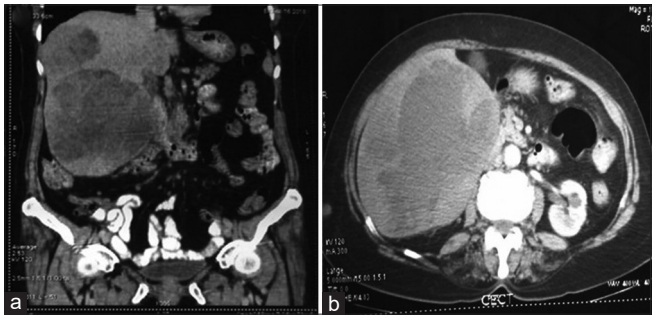

Figure 1: CECT (a) coronal view (b) axial view of the abdomen showing multilocular cystic space-occupying lesion in the right lobe liver

Discussion

Neuroendocrine tumor of liver is known as a rare tumor of liver.[1,7] However, carcinoid syndrome which is characterized by flushing and diarrhea due to endogenous secretion of serotonin and kallikrein rarely observed in patients having primary hepatic neuroendocrine tumor (PHNET).[2] Their pathogenesis is thought to be secondary to the unrestricted proliferation of neuroendocrine cells. Usually, they are asymptomatic and picked up as incidental finding.[3] Females in the age group above 50 years (age range, 8–83 years) are more prone to develop this disease . However, in our case, the patient presented with abdominal pain with swelling without skin flushing, abdominal pain, and episodic diarrhea. In the past 3 months she started feeling significant pain. Neuroendocrine tumors most commonly originate in the gastrointestinal system, mostly in the appendix or small bowel.[4] Liver is the affected organ in this case presentation. PHNETs typically grow slowly and become clinically obvious only at an advanced stage.[5] That is a relevant finding in this case. Most tumors are solitary (76.6%) but could be multicentric, with right lobar preference (46.8%).[6] Solitary multiloculated cystic lesion was noted in USG in this patient which made suspicious for hyadatid cyst. However, various biomarkers were also investigated such as CEA, CA19-9, and CA125 which are supportive in other malignancies like gastrointestinal tumor, pancreas, and ovary which came within normal limits. Immunogenic test was also negative for hydatid cyst. The cut surface of gross showed a variegated appearance comprising variable solid cystic change with large areas of hemorrhage and necrosis that further increases the suspicion of high-grade malignancy. Microscopic examination showed trabecular and glandular cell arrangements with round to oval nucleus and fine granular chromatin on hematoxylin and eosin (H and E) staining which is indicative of

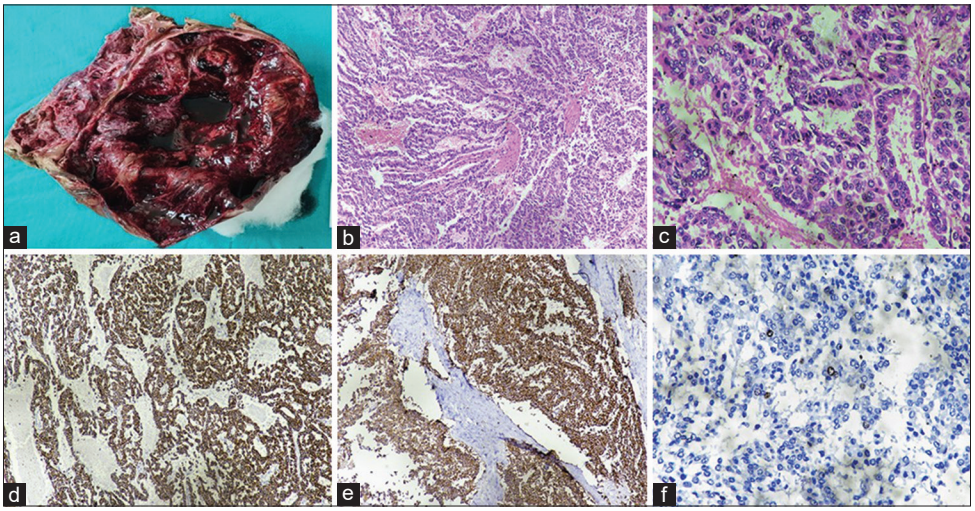

Figure 2: (a) Gross features shows predominently cystic tumor with areas of hemorrhage, (b) papillaroid arrangement of tumor with numerous interspersed dilated and congest blood vessels (H and E, 100×), (c) fine granular chromatin and conspicuous nucleoli and moderate amount of eosinophilic cytoplasm. (H and E, 200×), (d) Diffuse positive synaptophysin immunoreactivity (IHC,100×), and (e) pan cytokeratin immunoreactivity (IHC,100×), and (f) Ki67 proliferation marker is 4% (IHC,400×)

an PHNET. Combination of histomorphological features and immunohistochemical results ultimately support the diagnosis of PHNET as in our case presentation.[7] However, a diagnosis of PHNET largely depends on ruling out non-hepatic origins (6). Categorization of PHNETs according to the 2010 WHO classification of GEP-NETs is useful for the assessment of the prognosis and malignant potential of the tumors.[8] Other factors such as age, gender, presence of extrahepatic metastasis, number of tumors, or distribution of the tumor within the liver have not been shown to impact long-term patient survival.[9] The prognosis of PHNET depends on the size of the tumor, degree of differentiation (well, moderately, or poorly differentiated), histologic grade, Ki-67 index, and status of metastasis.[10,11] Even patients with positive tumor margins on biopsy have been shown to benefit from surgical resection.[9] Surgical treatment is the only curative method, with 5- and 10-year survival rates of 78% and 59%, respectively.[12]

Conclusion

Histomorphology with immunohistochemistry is the key for diagnosis. However, an initial thorough search should be done to rule out any possibility of metastatic disease in liver. Since clinical presentation and radiological findings may be misleading in case of primary hepatic neuroendocrine tumor (PHNET).

Ethical clearance

NOT REQUIRED. Institutional ethical clearance is not required in case report in which only paraffin block was required.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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