Neuroendocrine tumor of the gallbladder metastatic to Liver

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<th>KEYWORDS</th>
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<td>Gallbladder, Neuroendocrine tumor</td>
<td>Primary gallbladder and biliary duct system neuroendocrine (NE) tumors comprise less than 1% of all NE tumors arising from any tissue or organ in the body. We describe a case of NE tumor of the gallbladder in a 39-year-old man. There have been only 32 cases described in the literature but with metastasis is never reported.</td>
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Introduction

The Neuroendocrine(NE) tumor is a relatively rare type of endocrine tumor, which arises mainly in the gastrointestinal tract.\(^1\) Primary gallbladder and biliary duct system comprise less than 1% of all NE tumors arising from any tissue or organ in the body. We describe a case of carcinoid tumor of the gallbladder in a 39-year-old man with a metastatic nodule in the liver. There have been only 32 cases of gallbladder NE tumors described in the literature but with metastasis is rare.\(^1\)-\(^3\)

Case report

A 39-year-old man presented a six year history of mild abdominal distension associated with fat intolerance. There was no pertinent past medical or surgical history. His vital signs were normal and his sclera were anicteric. Abdominal examination revealed no tenderness, organomegaly, or abnormal mass.

Laboratory data included normal hematological findings and serum electrolyte levels. Liver function studies revealed the following values: total bilirubin, 0.8 mg/dl; direct bilirubin 0.2 mg/dl; alkaline phosphatase, 89 IU/L (normal level: 60 to 170 IU/L); aspartate aminotransferase, 10 IU/L (normal level: 0 to 18 IU/L); and alanine aminotransferase, 18 IU/L (normal level: 0 to 18 IU/L).
Abdominal ultrasound revealed a 6.4 cm soft tissue mass that appeared to arise from the wall of the gallbladder. CT scan showed a large tumor with soft tissue density in the gallbladder without evidence of calcification. The patient was referred for surgical opinion and laparotomy was subsequently performed. At laparotomy a 3 x 3 cm hypervascularized nodule was found in the liver.

The tumor appeared to extend from gallbladder into the liver. The nodule was excised which on histopathological analysis showed a tumor in nests and cords with tumor cells having stippled chromatin pattern “salt and pepper” appearance. (Fig 1). Gallbladder tumor showed a neuroendocrine tumor with tumor cells in nests and cords. On Immunohistochemistry tumor cells were positive for NSE, Chromogranin and Synaptophysin (Fig 2). MIB1 index was high. Patient is receiving Palliative Chemotherapy and is under follow up at 1 year of diagnosis.

The gallbladder is extremely rare site for NE and represents less than 1% of all NE tumors. The first case of primary carcinoid tumor of the gallbladder was reported in 1929 and since then a further 32 cases have been reported in Western literature. (1,2,3) and metastatic gallbladder neuroendocrine tumor is never reported in literature.

Preoperative diagnosis of NE tumor of the gallbladder is difficult, mainly because of its small size and limitations in the resolution of available radiological techniques. (1) In some patients, as in the present case, a mass in the gallbladder was identified but determination of histologic type of tumor and diagnosis to differentiate from gallbladder adenocarcinoma is often difficult.

The survival rate of patients with NE tumors is most directly related to the malignant potential of the tumors. Several factors have been found to be important in determining malignancy. First of all, the site of origin, because 60% of colonic NE tumors demonstrate metastases at the time of diagnosis whereas only 2% of appendiceal carcinoids have metastases. Second, the size of the tumor is important, because only 6% of primary tumors less than 1 cm in diameter are associated with metastases, whereas 70% of tumors 2 cm or larger have metastases. Third, the presence of multicentric primary tumors is associated with an increased malignancy risk. Fourth, the depth of penetration into the organ wall is important, with increased malignancy rates noted as the tumor invades beyond the submucosa to the muscle itself, the serosa and beyond. Other factors associated with determination of malignancy potential include the histologic growth pattern and the nuclear DNA content. (1)

Specific prognostic factors have not been identified in patients with gallbladder carcinoids and the usual criteria for judging malignancy, such as anaplasia and mitotic figures, are unreliable in these sites of carcinoid tumor. (3) Malignancy is well determined from evidence of tumor invasion into adjacent structures. If the tumor is localized to the gallbladder wall, with no evidence of intraperitoneal or metastatic spread, these patients have a better prognosis. But, if there is deep invasion in the organ wall, as in our case, the prognosis is uncertain. (3)
Fig. 1 showing neuroendocrine tumor in liver

Fig. 2 showing tumor cells diffusely positive for NSE

References