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Neuroendocrine tumor of the common bile duct: A case report

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Abstract
Neuroendocrine tumors (NETs) are rare neoplasms that originate from the neuroendocrine cells and peptidergic neurons. They occur at multiple organs, including the digestive tract, lung and thymus. Neuroendocrine tumors in the common bile duct (CBD) are a very rare entity. Here, we present a case of a 32 year old female with NET of the common bile duct who presented to the hospital with complaints of jaundice and loss of weight since 4 months. Histopathological report of the endoscopic biopsy raised the possibility of a malignant neoplasm. Resection of the tumor was done. The histomorphology and the immunohistochemistry (IHC) studies done on the same were consistent with the diagnosis of a grade 2 neuroendocrine tumor.

Keywords: Neuroendocrine tumors, Common bile duct, ERCP

Introduction
Neuroendocrine tumors (NET) are a subset of neoplasms originating from the chromaffin cells and Kulchitsky cells [1]. They were initially known as carcinoid tumors. However, this term has been replaced by the term 'NET' in the world health organization (WHO). NETs more commonly occur in the gastrointestinal tract and the pancreas. However, other sites of occurrence include lung, thymus and uterus. Common Bile Duct (CBD) is an extremely rare site for primary NETs. The originating cells i.e the chromaffin cells are rarely found in the biliary ducts. Most common clinical presentation of a NET in CBD is painless jaundice. Pain in the right upper abdomen and weight loss may also be the initiating symptoms at times [2]. Most common age group affected is 37-67 years old female patients as found from the scant data available on the NETs in CBD [3].

Case presentation
A 32-year-old female patient presented to the Gastroenterology OPD of St. John's Medical College and Hospital, Bangalore with history of four months of weight loss and yellowish discolouration of eyes. Intermittent pain abdomen followed the above symptoms in the last two months. General physical examination revealed icterus. Systemic examination revealed no significant abnormality. Laboratory investigations revelaed serum total bilirubin level of 10.5 mg/dL, direct bilirubin: 7 mg/dL, alkaline phosphatase level of 900 IU/L, aspartate aminotransferase of 50 IU/L and alanine aminotransferase of 44 IU/L. An abdominal ultrasoung was done which revealed 3x2 cm mass lesion in the CBD. As the hemodynamic variables were stable, she was taken up for endoscopic retrograde cholangiopancreatography (ERCP). Prior to that, she underwent Magnetic Resonance Cholangiopancreatography (MRCP) and it revealed a filling defect at the mid CBD with proximal of the CBD being dilated to 10 mm. ERCP was done which revealed stenosis of CBD. Further, an endoscopic Ultrasound (EUS) examination was performed which reported 16 × 12 mm isoechoic lesion in the middle of the CBD. In this regard, it was decided to perform an ERCP-guided biopsy of the lesion. The histopathology report was as follows: clusters of atypical cells with high nucleus to cytoplasmic ratio with hyperchromatic nuclei which was highly suggestive for malignancy. In accordance with the further protocol of workup, a thoraco-abdominopelvic computed tomography scan was done to evaluate the extent of local invasion and distant metastasis. Apart from the previously detected tumor, there was a 20x28 mm low attenuated mass like lesion at antero-posterior aspect of pancreatic tail with normal splenic vasculatures and no regional lymphadenopathy. The scan was reported negative for liver or any other organ metastasis. The patient improved symptomatically and was discharged on request. The patient was admitted again after 6 weeks and underwent pancreaticoduodenectomy and

resection of the mid portion ofthe CBD with portahepatis lymph node dissection and excisional biopsy of the lesion. The postoperative session was uneventful and she was discharged one week after surgery. The resected specimen was examined at the Department of Pathology, St. John's Medical College and Hospital after proper fixation. The gross appearance of the tumor was that of a polypoidal growth measuring 4x1x0.5 cm. On microscopy, the tumor was found to have trabecular pattern predominantly, (Figure 1), apart from nests and cords. The tumor cells had round to oval nuclei with stippled chromatin and moderate granular cytoplasm. The immunohistochemistry study done was positive for Synaptophysin (Figure 2) and Chromogranin A. Ki-67 index came in the range of 14-16%. One out of seven dissected lymph nodes was involved by the tumor. The tumor was seen extending till the serosa. Foci of lymphovascular and perineural invasion were seen. Finally a diagnosis of well-differentiated neuroendocrine tumor grade II with perineural and lympho-vascular invasion was made, in accordance with the WHO 2019 Classification of the neuroendocrine neoplasms of the digestive system. The patient was referred to oncologist for further adjuvant therapy based on cisplatin and etoposide. Follow up after six months revealed patient to be doing well symptomatically. PET scan and a contrast enhanced Computerised tomography (CT) scan revealed no reoccurrence of the lesion. (Fig 1 and 2).

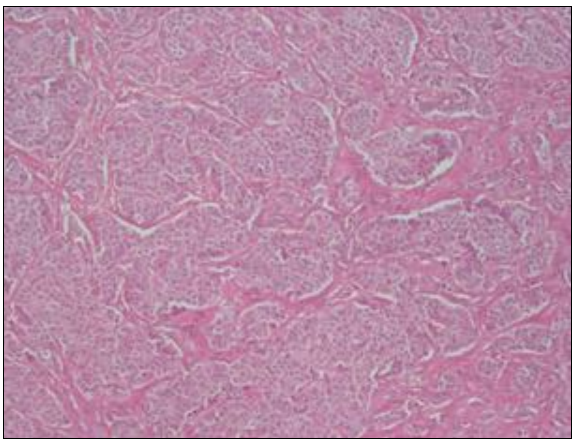

Fig 1: Trabecular arrangement of NET in common bile duct with stippled chromatin, round nuclei and granular cytoplasm. H&E: 10x magnification

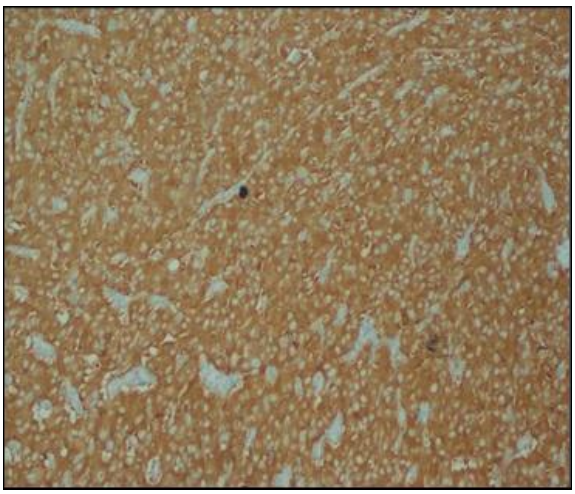

Fig 2: Synaptophysin positivity in NET. H&E: 20x magnification

Discussion

The World Health Organization (WHO) 2019 classification and grading crietria for neuroendocrine neoplasms of the gastrointestinal tract categorized neuroendocrine neoplasms of digestive tract into three major subtypes: well differentiated neuroendocrine tumor (NET), poorly differentiated neuroendocrine carcinoma (NEC) and mixed neuroendocrine-non neuroendocrine neoplasms (MiNEN). These neoplasms are different in histologic features and proliferation factor. Well differentiated NETs are arranged in nests, clusters and trabeculae and are composed of cells with uniform round nuclei, stippled chromatin and eosinophilic to clear cytoplasm. They are divided into three grades, including grade 1 (<2 mitoses/2mm^2, Ki-67 index: < 3%), grade 2 (2–20 mitoses/2mm^2, Ki-67:3% to 20%), grade 3 (>20 mitoses/2mm2, Ki-67 > 20%). A NEC is a poorly differentiated, high grade malignant neuroendocrine neoplasm composed of either small or intermediate to large cells with marked nuclear atypia and a high proliferation fraction (>20 mitoses/2 mm^2 and > 20% of Ki67 index). Mixed neuroendocrine-non neuroendocrine neoplasms (MiNEN) have histological features of both gland-forming epithelial and neuroendocrine neoplasms [4].

Biliary duct is a rare site for the NENs. In the biliary system, the incidence of NET accounts for 0.2%–2.0% of tumors [5] and NEC accounts for 0.19% of bile duct tumors. NETs of CBD may be presumed to be cholangiocarcinoma initially based on imaging findings. It is only the histopathological examination and immunohistochemistry that finally confirms the diagnosis of NET [6]. The diagnosis of such a tumor preoperatively is a challenging task due to its extremely rare incidence.

Conclusion

Although current knowledge about NETs of the CBD is limited but it seems that combination of radical surgical resection and lymph node dissection followed by chemotherapy provides substantial prognosis.

Conflict of Interest

Not available

Financial Support

Not available

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