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Case Report

Neuroendocrine tumor of distal bile duct

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Introduction

Neuroendocrine tumors (NET) are rare, albeit, well known in gastrointestinal tract (GIT).¹ However, in GIT, biliary tree (BT) is an unusual site for NET.² Further, in BT, distal common bile duct (CBD) is a very rare site indeed, as we report the 8th case in literature.² Ours is the first case where tangential portal vein excision was employed for its radical resection.

Case Report

A 45-year-old female patient presented with 2-month history of painless progressive jaundice, pruritus, and clay-colored stools with associated weight loss. On examination, she had the following: performance status ECOG-0; no pallor, icterus +; no generalized lymphadenopathy; palpable distended gall-bladder. Relevant laboratory results were as follows: serum bilirubin – 7.9 mg% (direct – 6.9 mg%); SGOT – 41 IU/L; SGPT – 54 IU/L; ALP – 188 IU/L; CEA – 0.2 ng/ml and CA 19.9 was

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Fig. 1 – Axial CT image showing metallic stent in CBD. (SMV – superior mesenteric vein.)

Fig. 2 – Resected pancreatoduodenectomy specimen with metal stent protruding from cut end of common bile duct (CBD).

marginally raised at 39.9 U/ml. Ultrasonography showed dilated intrahepatic biliary radicals with dilated CBD with abrupt cutoff in its terminal part along with gallbladder calculi. Contrast-enhanced computerized tomogram (CECT) showed the same. Endoscopic ultrasonography (EUS) showed a 3 cm × 2 cm hypoechoic mass in terminal CBD. The patient was inappropriately stented with a metal stent at a different center (Fig. 1). Brush cytology was negative for malignant cells. Whipple's pancreatoduodenectomy with tangential portal vein (PV) excision and primary repair was done, with tumor being operable but densely adherent to PV (Fig. 2). Patient had an uneventful recovery. Cut specimen revealed 3.2 cm × 2.7 cm × 1.8 cm tumor in distal CBD. Histopathology showed tumor cells, originating from distal bile duct, arranged in trabeculae, ribbons, nests, and islands separated by fibrous tissue. Few mitoses were seen along with infiltration of duodenum and pancreas with perineural invasion and dense surrounding desmoplasia (Fig. 3). One, out of 15 nodes dissected, was found metastatic. Immunohistochemistry (IHC) stained positive for neuron-specific enolase (NSE) and synaptophysin but negative for chromogranin (Figs. 4 and 5). Ki67 was <1%. The pathologic

Fig. 3 – Tumor cells arranged in cords and trabeculae infiltrating the stroma. H&E stain (100×).

Fig. 4 – Immunohistochemistry with Neuron-specific enolase (NSE) positivity in tumor cells (100×).

Fig. 5 – Immunohistochemistry showing synaptophysin positivity in tumor cells (100×).

diagnosis was well-differentiated NET of distal bile duct origin pT3N1 Mo.

Discussion

Neuroendocrine system is structured into two distinct forms. Namely, the glandular system, in which the neuroendocrine cells aggregate together to form glands, such as, pituitary, parathyroid, etc., and the diffuse system, in which the cells are diffusely dispersed throughout the body.³ The GIT has the lion's share of neuroendocrine cells of the diffuse system, making it the largest neuroendocrine organ.³ However, the distribution of neuroendocrine cells in GIT is uneven. The cells are liberally spread in gut, whilst, sparingly so in the BT.² As the occurrence of NET parallels the distribution of neuroendocrine cells in the body, therefore, they are, although well known in gut, exceptional in BT (<80 documented cases).^{2,4} Even in the BT, the distribution of NET in BT is variable. It occurs in the ampulla, gallbladder, middle CBD, proximal CBD, distal CBD, and hepatic duct/cystic duct in decreasing order of incidence.^{2,4}

These tumors are known to occur in the background of chronic inflammation with consequent metaplasia^{2,4}; however, gallstones and choledochal cyst have been associated only in a minority of cases.^{2,5} These tumors are known to occur in middle age (median age 47 years) with slight female preponderance, as in our case.² Most tumors are nonfunctional with only four reported functional cases – one case had diarrhea and other three had recurrent peptic ulceration due to secretion of serotonin and gastrin, respectively.^{2,4} Elevated 5-hydroxy indole acetic acid (HIAA) in urine has been reported in three cases.^{2,4} Painless jaundice is the main presenting symptom followed by right upper quadrant pain and lethargy.^{2,4} Most symptoms are attributable to compression/invasion of adjacent organs.^{2,4}

Preoperative diagnosis is an exception than a rule. Laboratory tests, which may give a clue, are the urinary HIAA and serum chromogranin.^{2,4} In addition, tests for serum gastrin, serotonin, pancreatic polypeptide, etc. may be employed based on the functional characteristics/symptoms.^{2–4}

Transabdominal ultrasonography can only reveal features of biliary obstruction and of metastasis, if any, as distal CBD is obscured by overlying bowel gas. However, EUS may prove more helpful, as in our case, by revealing a polypoidal mass in the CBD. CECT, although, did not reveal the tumor in our case, NET do have some characteristic features, which may help in distinguishing them from the more common cholangiocarcinomas in the location.⁶ These characteristic features are marked enhancement during arterial phase, polypoid shape, and small tumor size (2–4.5 cm). Lymphatic/hepatic metastasis suggests higher grade of tumor.⁶ In contrast, the commoner infiltrating cholangiocarcinoma is evident as high-attenuation mass surrounding the lumen or as wall thickening.⁶ Less common polypoidal cholangiocarcinoma manifests as low-attenuation mass within the dilated bile duct and may show extensive spread/diffuse involvement.⁶ Magnetic resonance imaging may also reveal similar picture. Positron emission tomogram CT generally shows lower

fluoro-deoxy-glucose (FDG) uptake than a cholangiocarcinoma.⁶ Endoscopic retrograde cholangio pancreatography (ERCP) with brush cytology is possible but is unlikely to yield results due to submucosal location of the tumor.² Somatostatin receptor scintigraphy may be utilized due to presence of somatostatin receptors.⁴

Most cases, as ours, are diagnosed retrospectively by histopathologic and IHC examination of operative specimen.^{2,4} Microscopically, these neoplasms exhibit trabeculae, ribbons, nests, and occasional tubule formation with intervening fibrous septae.² Tumor cells may variably stain positive for chromogranin, NSE, synaptophysin, cytokeratin, CD56, and peptides/hormones, such as, gastrin, somatostatin, pancreatic polypeptide, and serotonin.⁷ Mitosis and Ki67 index are, along with tumor differentiation, grade, and lymphovascular/perineural invasion, important factors that determine the nature/malignant potential of these tumors.^{3,7} Size of the tumor >2 cm has also been found to correlate with aggressive biology.^{2,7}

Recommended treatment is radical excision, with pancreatoduodenectomy being the commonest surgery.² Our case was the first one necessitating tangential PV excision, as the dense desmoplasia precluded safe dissection of PV from the pancreatic head. However, pancreas preserving CBD excision alone has been described for distal CBD benign NET.⁸ Most mid and proximal CBD NET have been managed by CBD excision and hepaticojejunostomy.^{2,4} Left hepatic duct NET mandated left hepatectomy in one case.⁴

Metastasis to liver, pancreas, lymph nodes, or perineural invasion is seen in a third of the cases.^{2,4,6,7} Our understanding of management of metastatic disease stems from extrapolating the management strategies employed in gastroenteropancreatic NETs.^{1,3} Liver metastasis may be dealt with by excision, embolization/chemoembolization, or ablation.^{1,3} Long-acting somatostatin analogs, such as, pasireotide, serotonin antagonist, such as, ketanserin, and interferon α can be used in cases of carcinoid syndrome.^{1,3} Combination chemotherapy using 5-fluorouracil, cisplatin, etoposide, chlorambucil, streptozocin, and dacarbazine may be employed in metastatic disease.^{1,3} Being hypervascular, antiangiogenesis factor, such as, bevacizumab, may be added to the chemotherapy.^{1,3} Tyrosine kinase inhibitor, such as, sunitinib, mTOR inhibitors, such as, everolimus, and radiolabeled somatostatin analogs can also be used in metastatic settings.^{1,3}

Prognosis is, in completely resected BT NET, good with 5 years survival approaching 60–100%, due to indolent nature of the tumor.^{2,4} Death due to advanced tumor is rare.²

Conclusion

Neuroendocrine tumor of distal CBD is a rare cause of obstructive jaundice. Radical excision is its apt management.

Conflicts of interest

The authors have none to declare.

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