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Case Report

CASE REPORT

Neuroendocrine carcinoma of the ampulla of Vater: a case report, review and recommendations

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Abstract

Neuroendocrine tumor (NET) of the ampulla of Vater is a rare presentation of biliary obstruction. Here, we present a case of NET and discuss the current recommendations that necessitate different management and surgical treatment than other sites. A 56-year-old Caucasian female presented with 2 years of right upper quadrant pain. Workup revealed a well-differentiated 2.2 cm NET at the ampulla with 0 MF/10 HPF, Stage 1A T2NOMO. Whipple procedure performed with 2.2 cm ampullary NET with 1 of the 15 lymph node metastases and <2 mitoses in 10 HPF. TNM classification: Stage IV T2N1MO. Regardless of tumor size, NETs metastasize in half of cases. Local excisions including endoscopic and laparoscopic ampullectomy were recommended only for poor surgical candidates. Ampullary NETs behave more aggressively than nonampullary NETs and their biological behaviors are irrespective of size. For patients of acceptable surgical risk, we recommend radical resection utilizing Whipple procedure.

BACKGROUND

The ampulla of Vater is the well-vascularized epidermal mucosa overlying the Sphincter of Oddi and is highly regulated to release bile and pancreatic enzymes and proenzymes. During normal resting state the ampulla prevents reflux of enteric contents into the biliary system. Neuroendocrine cells are derived from the enterochromaffin cells from the crypts of Leiberkuhn and are found in the gastrointestinal mucosa and submucosa.

Neuroendocrine tumors (NETs) are classified into three categories with tumor grade having the most influence. These categories are: well-differentiated tumors, well-differentiated carcinomas with low grade malignant potential and poorly differentiated neuroendocrine carcinomas. NETs are also classified based on their mitotic activity and presence of necrosis. Well-differentiated Grade 1 have <2 mitotic figures per 10 HPF and lack of necrosis. Grade 2 has 2–20 mitotic figures per 10 HPF OR the presence of necrosis and High Grade 3 tumors have >20 mitotic figures and the presence of necrosis. Histopathology is essential and the expression of neuroendocrine markers chromogranin A, neuron-specific enolase and synaptophysin, either isolated or in combination, provides the diagnosis. The cell proliferation marker Ki-67 may be present and may indicate a more aggressive tumor.

NET of the ampulla of Vater is an exceedingly rare presentation of biliary obstruction as much <1% of GI NETs originate in the ampulla [1–3]. In total, <150 cases have been reported [4]. Most of the cases occur in the 5th–6th decades of life with a 3:1 predominance of women to men [5]. Their clinical picture is more similar to adenocarcinoma, which makes preoperative diagnosis difficult. Because of the rarity of the disease, relatively

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little is understood about the clinical significance and the prognostic factors of this tumor [4, 6]. There is a wide diversity of their clinical presentation, hormone production, morphologic characteristics and biological behavior based on their site of origin [1].

Here, we present a case of NET originating in the ampulla of Vater and discuss the current recommendations that make this site of origin require different management and surgical treatment than other sites of origin.

CASE REPORT

A 56-year-old Caucasian female with past medical history (PMHx) of pulmonic stenosis, supraventricular tachycardia and gastroesophageal reflux disease (GERD) presented to our ER with biliary leak and complaints of right upper quadrant (RUQ) pain after recent cholecystectomy with normal intraoperative cholangiogram for presumed gallstone pancreatitis. Computed tomography (CT) scan and hepatic 2,6-dimethyliminodiacetic acid (HIDA) upon admission confirmed a biliary leak from her recent surgery. An IR drain was placed and endoscopic retrograde cholangiopancreatography/endoscopic ultrasound (ERCP/EUS) with biopsy showed a well- differentiated (Low Grade, G1) 2.2 cm diameter NET staining positive for both cytokeratin and synaptophysin. The mitotic rate was 0 per 10 HPF with preoperative stage 1A and TNM classification T2N0M0. No suspicious lymph nodes were seen on EUS.

The patient was taken for laparoscopic washout for biliary leak control and 4 days later underwent a subsequent Whipple procedure with final pathologic examination confirming low grade neuroendocrine carcinoma with a diameter of 2.2 cm with 1 of 15 lymph node metastases and <2 mitosis in 10 HPF. The TNM classification of the tumor was Stage IV with T2N1M0. The tumor expressed Ki-67 3–20%. Patient was discharged POD5 from Whipple procedure tolerating a regular diet with planned follow-up.

RESULTS AND DISCUSSION

Neuroendocrine carcinoma most commonly presents with jaundice (60%), abdominal pain (40%) and less commonly with weight loss (10%) [7]. Presentation with acute pancreatitis is rare (3–6%) [7]. Carcinoid syndrome does not occur often as most primary tumors are nonfunctional, but the tumor cells may express somatostatin, insulin, serotonin and cholecystokinin. The ampulla of Vater is highly vascularized, which contributes to the dissemination of metastases. Owing to the often small size of the primary tumors, CT scan and magnetic resonance imaging (MRI) capabilities only have a 33% sensitivity of diagnosing the primary tumor [8]. ERCP/EUS is the most useful modality for diagnosis but so far no sensitivities have been reported in the literature. Regardless of tumor size, all published data show that tumors metastasize in half of cases, specifically 66% for tumor < 1 cm, 50% for tumor 1–2 cm and 46% for tumor > 2 cm in a small retrospective case series of roughly 20 patients [9]. Because of this, in 2016, recommendations were made that all ampullary NETs be treated by Whipple with lymphadenectomy. No updated official guidelines exist. Local excisions including endoscopic and laparoscopic ampullectomy were recommended only for those who could not tolerate a more extensive operation [9].

Follow-up with yearly serum chromogranin A levels were recommended to detect disease response to treatment. Overall, 10-year survival for resected ampullary NETs with and without spread to nearby lymph nodes is 71% for well-differentiated tumors but only 15% survival at 10 years for poorly differentiated tumors [10]. In patients with hepatic metastases and carcinoid syndrome, radiofrequency ablation and/or chemoembolization and somatostatin analogs such as octreotide may provide symptomatic relief.

CONCLUSIONS

In conclusion, ampullary NETs are more aggressive than nonampullary NETs and their biological behaviors are irrespective of size. The low accuracy of 33% of preoperative radiographic evidence with both CT and MRI at staging makes surgical management of these tumors quite difficult. Based on the literature, for patients who are not high surgical risk and can tolerate the procedure, we recommend radical resection utilizing Whipple procedure even for preoperative tumors < 2 cm in size. Endoscopic and laparoscopic therapies should be reserved for patients who cannot tolerate Whipple procedure.

CONFLICT OF INTEREST STATEMENT

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REFERENCES

1. Han SL, Cheng J, Zhou HZ, Guo SC, Jia ZR, Wang PF. Surgically treated primary malignant tumor of small bowel: a clinical analysis. *World J Gastroenterol* 2010;**16**: 1527–32.
2. Rohan VS, Narendra H, Patel JJ, Tankshali RA. Carcinoid of ampulla of Vater. *Indian J Cancer* 2007;**44**:90–2.
3. Waisberg J, Joppert-Netto G, Vasconcellos C, Sartini GH, Miranda LS, Franco MI. Carcinoid tumor of the duodenum: a rare tumor at an unusual site. Case series from a single institution. *Arq Gastroenterol* 2013;**50**:3–9.
4. Randle RW, Ahmed S, Newman NA, Clark CJ. Clinical outcomes for neuroendocrine tumors of the duodenum and ampulla of Vater: a population-based study. *J Gastrointest Surg* 2014;**18**:354–62.
5. Albores-Saavedra J, Hart A, Chablé-Montero F, Henson DE. Carcinoids and high-grade neuroendocrine carcinomas of the ampulla of Vater: a comparative analysis of 139 cases from the surveillance, epidemiology, and end results program—a population based study. *Arch Pathol Lab Med* 2010;**134**:1692–6.
6. Terada T. Pathologic observations of the duodenum in 615 consecutive duodenal specimens in a single Japanese hospital: II. Malignant lesions. *Int J Clin Exp Pathol* 2012;**5**: 52–7.
7. Jayant M, Punia R, Kaushik R, Sharma R, Sachdev A, Nadkarni NK, et al. Neuroendocrine tumors of the ampulla of Vater: presentation, pathology and prognosis. *JOP* 2012;**13**: 263–7.
8. Selvakumar E, Rajendran S, Balachandar TG, Kannan DG, Jeswanth S, Ravichandran P, et al. Neuroendocrine

carcinoma of the ampulla of Vater: a clinicopathologic evaluation. *Hepatobiliary Pancreat Dis Int* 2008;**7**:422–5.
9. Krishna SG, Lamps LW, Rego RF. Ampullary carcinoid: diagnostic challenges and update on management. *Clin Gastroenterol Hepatol* 2010;**8**:e5–6.
10. Yao JC, Hassan M, Phan A, Dagohoy C, Leary C, Mares JE, et al. One hundred years after "carcinoid": epidemiology of and prognostic factors for neuroendocrine tumors in 35, 825 cases in the United States. *J Clin Oncol* 2008;**26**: 3063–72.