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Case Report

"Ampullary Gangliocytic Paraganglioma:" A Rare Neuroendocrine Tumor Can Be Safely Treated with Ampullectomy

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Abstract

Ampullary Gangliocytic paraganglioma is a rare gastro-entero-pancreatic neuroendocrine tumor with a characteristic histologic appearance involving epitheliod, spindle and ganglion cells. Endoscopic ultrasound is useful to determine depth of invasion and regional metastasis. Endoscopic resection, Ampullectomy and pancreato-duodenenectomy have been described as management options in literature but no consensus has been established. The index case describes an asymptomatic 42 y/o lady with a background of plexiform neurofibromatosis referred for cholestatic derangement of liver function. She was found to have a dilated biliary system with a periampullary mass which proved to be a Gangliocytic Paraganglioma without local lymph node metastasis. She underwent successful endoscopic ampullectomy with complete normalization of LFT and decompression of the biliary system with no clinical or endoscopic recurrence at 2 years follow up. We advocate that Partial Ampullectomy could be done safely as a treatment of localized Ampullary GP allowing long term resolution of symptoms.

Keywords: *Ampullary lesion, ampullectomy, biliary dilatation, endoscopic ultrasound, gangliocytic paraganglioma, neuroendocrine tumor, Whipples surgery*

Introduction

Ampullary gangliocytic paraganglioma (AGP) is a rare gastro-entero-pancreatic neuroendocrine tumor with a characteristic histologic appearance involving epithelioid, spindle, and ganglion cells. They are generally detected incidentally or when they present with upper gastrointestinal (GI) bleed. Most of these tumors are detected either on a contrast computed tomography or magnetic resonance imaging (MRI). Although this tumor is mostly considered benign, most of the patients undergo pancreatoduodenectomy (Whipple's operation).

Case Report

An asymptomatic 42-year-old female was referred for evaluation of abnormal liver functions tests. History included plexiform neurofibroma of foot and thigh at the of age 19 years, laparoscopic cholecystectomy at the age of 34 years and tonic–clonic seizures secondary to parieto-occipital gliosis at the age of 37 years. She was on treatment with levetiracetam as seizure prophylaxis.

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Laboratory investigations revealed mild hypochromic microcytic anemia (hemoglobin 10.3 g/dl, mean corpuscular volume-77.9) with low serum ferritin levels. Her serum bilirubin levels at presentation were 14 mmol/L (normal 4–24 mmol/L), alanine aminotransferase 120 IU/ml (normal <30 IU/ml), aspartate aminotransferase 77 IU/ml (normal <31 IU/ml), and Alkaline phosphatase 296 IU/ml (normal <124). Carbonic anhydrase 19–9 levels were normal. MRI of the abdomen revealed intra- and extra-hepatic biliary dilatation with soft-tissue lesion demonstrating low signal on T2-weighted images [Figure 1c]. Gastroscopy and ileocolonoscopy were normal with normal duodenal biopsies. Side view endoscopy revealed nonulcerated bulky ampulla. Endoscopic ultrasound (EUS) revealed dilated common bile duct (CBD) (12 mm) and pancreatic duct (PD) (4 mm)

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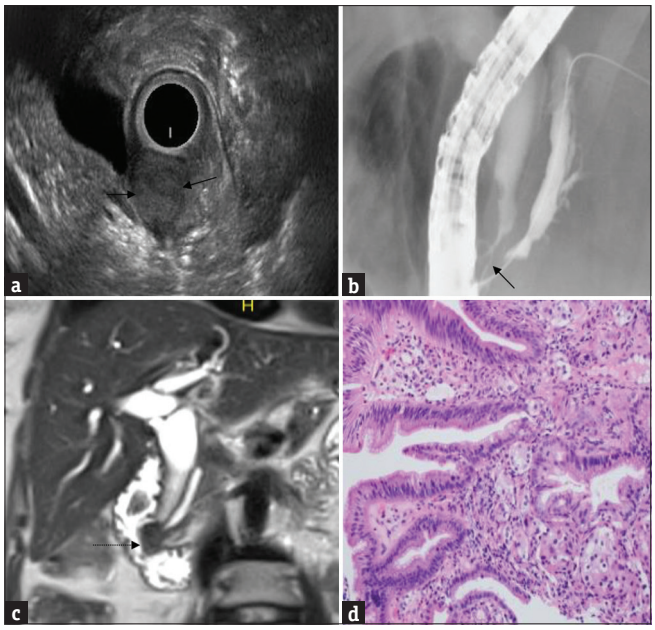

Figure 1: (a) Endoscopic ultrasound revealing biliary dilatation with a hypoechoic lesion at the ampulla (marked among arrows) with dilated upstream common bile duct. (b) Endoscopic retrograde cholangiopancreatography revealing dilated common bile duct and pancreatic duct with a hypoechoic soft-tissue mass at the ampulla (arrow). (c) Magnetic resonance imaging (sagittal view) revealing evidence of biliary dilatation with a soft-tissue lesion demonstrating low signal in T2-weighted images. (Arrow head with dotted line) (d) ampullary biopsy (H and E) revealing nest of epithelial cells (×10)

with a 14 mm hypoechoic submucosal lesion at the ampulla without any local lymph nodes [Figure 1a]. Biopsy from the ampullary specimen revealed nests of epithelial cells without significant pleomorphism with occasional ganglion-like cells with large and oval nucleus [Figure 1d]. Immunohistochemistry revealed epithelial cells stained positive for cytokeratin (CK) 7, synaptophysin, and chromogranin and were negative for S-100 and nonspecific enolase (NSE). The ganglion cells stained positive for S-100, synaptophysin, chromogranin, and NSE and were negative for CK. A diagnosis of AGP was made.

The patient underwent ampullectomy with biliary sphincteroplasty with 5 Fr prophylactic stent into the PD [Figure 1b]. The resected specimen confirmed the previous diagnosis of AGP, a benign lesion without malignant potential. There were no signs of cellular atypia or mitotic figures.

On the last follow-up at 2-year postsurgery, the patient was doing well with complete normalization of liver function tests with repeat biopsies from the ampulla being negative for dysplasia or malignancy.

Discussion

AGP is a rare gastro-entero-pancreatic neuroendocrine tumor with a characteristic histologic appearance involving epithelioid, spindle, and ganglion cells.[1] Paragangliomas of GI tract have been described in association with neurofibromatosis Type 1 or Von Recklinghausen's Disease.[2,3] The patient in the index case had a background of plexiform neurofibromatosis, a form of neurofibromatosis Type 1 diagnosed at a young age. Burke and Helwig described a review of 51 patients with gangliocytic paragangliomas of GI tract with 49 of them occurring in the duodenum.[4] Although patients may present with abdominal pain or GI bleeding due to mucosal or submucosal invasion, patients may often remain asymptomatic;[5] as in our patient. Histological diagnosis is based on the presence of admixture of epithelioid, ganglion, and spindle-shaped cells. Immunohistochemical staining shows positive reaction for neuron-specific enolase, chromogranin A, and S-100 protein.[4]

The first step in the management of ampullary lesions is to determine the depth of invasion using an EUS and cross-sectional imaging. EUS findings were first described by Smithline *et al*. in 1993.[5] AGPs have been described as isoechoic or hypoechoic, round well-demarcated submucosal tumors arising from the third or fourth layer[6] of duodenal wall. EUS not only detects these lesions with ease due to its anatomical position but also rules out its deeper penetration or involvement of regional lymph nodes. Regarding its treatment, endoscopic resection is the treatment of choice when the tumor is localized.[7] Long-term outcomes from such an approach have proven to be favorable with no recurrence or metastasis.[8] More recently, endoscopic mucosal resection (EMR) has been described for resection of such tumors.[9,10] Endoscopic ampullectomy offers a minimally invasive approach for treating peri-ampullary lesions.[11] Both EMR and ampullectomy are feasible options when lesion is limited to the ampulla and has no evidence of regional lymphatic spread. A surgical ampullectomy has also been described when tumor involves the CBD.[12] Endoscopic ampullectomy as a mode of tumor excision was chosen in the index case with dilated CBD and PD, after determining that there is no deeper invasion and there is a lack of lymph nodal involvement. A prophylactic pancreatic stent was placed to reduce the risk of postampullectomy pancreatitis.[13] Patient follow-up at 3 years has shown no tumor recurrence or metastatic disease. We recommend that a minimal risk endoscopic approach over a comparatively invasive surgical approach when choosing ampullectomy. Finally, more invasive procedures such as pancreatoduodenectomy may be reserved for cases with local or lymphovascular invasion.

Conclusion

The index case highlights the association of Neurofibromatosis with AGP and the role of EUS in the management of this condition. Based on the current report, we suggest that endoscopic ampullectomy could be done safely allowing long-term resolution of symptoms in cases of AGP without local metastasis.

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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