

Neuroendocrine tumour of the ampulla of Vater: A rare neoplasm at an atypical site

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Abstract

The periampullary neuroendocrine tumour is an infrequently occurring tumour. Its prevalence among gastrointestinal neuroendocrine neoplasms is less than 0.3%, and less than 2% out of periampullary tumours. These neoplasms have relatively poor prognosis. Jaundice and pain in the abdomen are the early and most commonly occurring symptoms with weight loss being a late event. The carcinoid syndrome presents infrequently in periampullary neuroendocrine tumour and happens only if hepatic metastasis occurs. In this scenario, histopathology plays a paramount role in the diagnosis. Specific immunohistochemical staining is used for diagnosis while the treatment options are local excision, endoscopic excision and pancreaticoduodenectomy. Here is a case report of a 42-year-old patient who presented with complaint of obstructive jaundice for one month. Periampullary carcinoid tumour was diagnosed on biopsy, and she underwent Pancreaticoduodenectomy as treatment. Literature shows that there is poor precision of preoperative and intraoperative lymph node metastatic involvement regardless of the size of the tumour. Hence, radical resection must be considered the standard approach.

Keywords: Carcinoid Tumour, Periampullary growth, Pancreaticoduodenectomy, Pancreatic Neoplasms, Ampullary growth.

DOI: <https://doi.org/10.47391/JPMA.1231>

Introduction

Neuroendocrine tumours (NETs) are slow-growing neoplasms of enterochromaffin cells. Gastrointestinal NETs are a group of neuroendocrine tumours which originate from varied amount of mucosal and submucosal neuroendocrine cells of the gastrointestinal tract.¹ Therefore, there is heterogeneity in their clinical presentation, morphologic characteristics, immunophenotyped, incidence, production of hormones and how they behave biologically.² The Neuroendocrine tumour at ampulla of Vater is an infrequent entity and there is little information

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regarding its demographics, how it behaves biologically and performs clinically. Moreover, the specific factors determining prognosis of this tumour have not yet been established.² These tumours constitute less than 1% of all gastrointestinal NETs, and have a prevalence of less than 2% among periampullary tumours.¹ Females are three times more prone to develop this tumour as compared to males,³ with incidence being highest in the age group of 50 to 60 years. Here we present a case report, of a woman, who had pancreaticoduodenectomy for a neuroendocrine tumour of the ampulla of Vater, a rare neoplasm at an atypical site.

Case Report

A 42-year-old woman presented in the Surgical OPD of Lahore General Hospital, Lahore on January 19, 2019 with complaint of yellow discoloration of the skin, eyes and urine, and clay coloured stools for the past one month. Generalised pruritus was present for the last 20 days. She did not report any loss of weight, abdominal pain, loss of appetite or vomiting. On examination, she had jaundice and scratch marks on her body. The abdomen was soft with no tenderness; there was neither any palpable mass nor lymph nodes. There was no significant finding on systemic

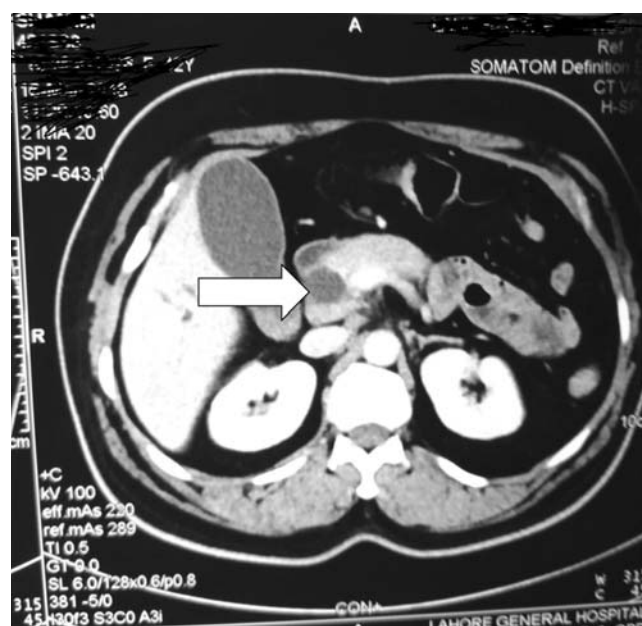


Figure-1: CT scan of patient shows tumour at ampulla of Vater. (white arrow).



Figure-2: MRCP of patients Abdomen shows stricture at distal CBD (white arrow) along with dilatation of the intra and extrahepatic biliary channels (blue arrow).

examination. Her laboratory tests revealed normal Hb (11.2 g/dl) and raised levels of TLC (17.3), bilirubin (8.7mg/dl), and ALP (512U/L). Viral markers (HBV, HCV) were negative. Abdominal USG, revealed dilated intra and extrahepatic biliary channels without any evidence of CBD stone or mass. Subsequently, MRCP was done, that indicated stricture at distal CBD along with dilatation of the intra and extrahepatic biliary channels (Figure-1). Based on the above investigations, ERCP was planned, which revealed an ulcerated, tumorous-looking ampulla. A plastic stent was put in the CBD and biopsies from the growth were taken for histopathology. Later, it was diagnosed as a high-grade neuroendocrine tumour, which was positive for chromogranin and synaptophysin. Her CA19-9 was also slightly raised (50 units/ ml). There was no metastasis on staging computed tomography scan of the chest, abdomen and pelvis (Figure-2). After reviewing in MDT, surgical resection was planned. The patient underwent a diagnostic laparoscopy and proceeded after taking an informed consent. She had a pylorus-preserving Whipple's procedure (gastrojejunostomy, hepaticojejunostomy and pancreatojejunostomy). Her immediate post-operative period was uneventful, but after one month she developed a pancreatic fistula, which was managed conservatively. At the six-month follow up, she was doing well and no recurrence was noted.

Discussion

There are three main categories of NETs as claimed by WHO on the basis of the tumour grade: "well-

differentiated neuroendocrine tumours, well-differentiated (low grade) neuroendocrine tumours and poorly differentiated (high grade) NETS".⁴ Previously, "well-differentiated neuroendocrine neoplasms were considered the same as carcinoid neoplasms". This expression is confusing because when it comes to clinical presentation, "a carcinoid tumour produces serotonin related with symptoms of the carcinoid syndrome".⁴ WHO has classified duodenal neoplasms and neuroendocrine ampullary into the same category, but literature shows that these tumours are distinct from each other. Perampullary neuroendocrine tumours manifest no concordance to the extent of the non-ampullary duodenal NETs neoplasms, and behave more aggressively. Moreover, they often express somatostatin and are associated with NF1.^{4,5} Presence of NF1 increases the risk of gastrointestinal tract neoplasms, including neuromas, somatostatin rich ampullary carcinoids and gastrointestinal stromal tumours (GIST)⁵ The duodenal papilla is a highly vascular area, and even small tumours are likely to spread. Published data shows metastasis in 66% of neoplasms that were less than 1cm, in half of neoplasms between 1cm and 2cm and 46% of neoplasms which were more than 2cm.⁶ Lymph nodes and liver are the commonest regions of metastasis. Yellowish discoloration (60%) and pain in the abdomen (40%) are the commonest symptoms of ampullary NETs, with weight loss (10%) being a late and relatively uncommon symptom.⁷ Majority of perampullary neuroendocrine tumours are diagnosed coincidentally during duodenoscopy. Similar symptoms were also observed in this patient and she was diagnosed incidentally on duodenoscopy. Establishment of the histopathology is of utmost importance and can be achieved by specific immunohistochemical stains.⁴ Most of the ampullary NETs usually express neuroendocrine markers such as synaptophysin, chromogranin A and NSE. Synaptophysin and chromogranin A were positive in this patient. The presence of cell proliferation markers such as PCNA and Ki-67 may lead to increased metastatic potential of the ampullary neoplasms and to more advanced and invasive biological behaviour.⁷ Workup including abdominal CT and MRI, duodenal endosonography (EUS) and endoscopic retrograde cholangiopancreatography (ERCP) conclude the workup of a neuroendocrine tumour of the ampulla.⁷ In the present case, no metastases in the liver or mesentery could be seen on CT and MRI. MRCP showed no sub mucosal mass but stricture of CBD. ERCP and EUS clarified the ampullary NET. The differential diagnosis of an ampullary neuroendocrine tumour include non-ampullary neuroendocrine tumour, gangliocytic paraganglioma, a Brunner's gland hamartoma, gastric tissues and

heterotopic pancreas. Similarly, adenoma, adenocarcinoma, lymphoid hyperplasia, gastrointestinal stromal tumour (GIST) and mesenchymal tumours, such as neurofibromas and Schwannomas are some differentials of ampullary NETs.⁷ Literature shows that, irrespective of the primary tumour's size, these neoplasms metastasise in 50% of the patients.⁸ Hence, keeping in view this factor, radical excision (pancreaticoduodenectomy with lymphadenectomy) is the treatment of choice. Local removal can be the treatment of choice in highly differentiated, slow-growing neoplasms with a diameter of less than 2cm, and in high surgical risk patients as well as for patients who are unable to bear a more extensive operation. However, chances of incomplete removal still remain high.⁹ Another treatment option is endoscopic ampullectomy. It is appropriate in well-differentiated, superficial and mobile tumours that are restricted to the mucosal layer without lymphatic or vascular involvement.⁹ Laparoscopic trans-duodenal resection is another viable procedure suggested in patients with ampullary neuroendocrine tumours.¹¹ For tumours with metastasis, the removal of the primary tumour, followed by management through somatostatin analogues such as Octreotide or Lanreotide analogues decrease the enlargement of metastatic lesions via cytotoxic effect and improve quality of life.⁹ Similarly, for hepatic metastases in these tumours, surgical removal or cytoreductive procedures like radio frequency ablation and chemoembolisation have shown to ameliorate the condition. The serum chromogranin A levels can be used to monitor the disease response to the treatment, progression and recurrence.¹⁰ It was negative in our patient's follow-up. As far as survival rate is concerned, distant metastasis is an important prognostic factor. Involvement of lymph nodes, size of the tumour and resection margins are of minor importance in the long-term endurance. Five-year survival rate is 80% and 10-year survival rate is 71% in low grade tumours. Whereas, high-grade neuroendocrine tumours have 15% 10-year survival rate.¹⁰

Conclusion

Despite being a rare entity, many cases of periampullary NET have been reported in recent years. These neoplasms have comparatively poor prognosis. However, neuroendocrine tumours with diameter less than 2cm and without invasion have a better prognosis. There is high incidence of metastases in lymph nodes, regardless of the extent of neoplasm. Even a mass as small as 2cm

has shown lymph node metastasis. Because of imperfect precision of preoperative and per-operative evaluation of lymph node engagement, radical resection should be the usual treatment strategy.

Disclaimer: Informed consent from the patient and approval from ethical committee was obtained before publication.

Conflict of Interest: None.

Disclosure: None.

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