

Periampullary Neuroendocrine (Carcinoid) Tumor in a Patient with Neurofibromatosis Type I

Abdul Qaiyoume Amini, Naveed Ali Khan, Jawed Ahmad and Amjad Siraj Memon

ABSTRACT

Neurofibromatosis type 1 (NF-1) is a genetic disease with autosomal dominant pattern which is associated with a large number of tumors especially of Gastro-Intestinal origin. These tumors have neurogenic or neuroendocrine origin (carcinoid tumors) and cause symptoms due to secretion of somatostatin or local pressure effects. Here we report the case of a patient with Neurofibromatosis Type-1 who had a periampullary Neuroendocrine (Carcinoid) Tumor and presented with upper abdominal pain and mild jaundice. An initial diagnosis of carcinoma of head of pancreas was made based on CT scan and Whipple's Pancreaticoduodenectomy performed. On histopathology, it was revealed as a neuroendocrine tumor with carcinoid features. Patient recovered well and became symptom free after surgery. This concludes that the pancreaticoduodenectomy (Whipple's procedure) is the current standard management in periampullary neuroendocrine tumors.

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INTRODUCTION

Carcinoid tumors are low grade malignant neoplasms that have a slow growth rate, are highly invasive and have metastasizing properties¹. These are rare tumors, with an incidence at all locations of 1 in 1200^{2,3}. These tumors are commonly found within the gastrointestinal tract (about 67%) but the incidence in periampullary region is less than 1%⁴. Although the periampullary neuroendocrine (carcinoid) tumors are very uncommon in general population but they have a well-known association with neurofibromatosis type 1 (NF1) which is also known as Von Recklinghausen's disease^{5,6}. Patients with NF 1 also have increased risk to develop tumors throughout the gastrointestinal tract including neuromas, GIST and periampullary somatostatin rich carcinoid⁷.

Here, we report a rare case of a patient with periampullary carcinoid tumor that was associated with neurofibromatosis type 1.

Case Report:

A 45 year old woman who was a known case of Neurofibromatosis Type 1 presented with upper

abdominal pain, jaundice and history of weight loss to out-patient clinic. She had no symptoms related to oversecretion of hormones. On examination she was a female of average height and built, having numerous soft nodules on skin (neuromas) all over the body along with café au lait spots. She was mildly anemic and jaundiced but had normal vital parameters. She had normal hearing and vision but clinically obvious squint in her right eye. Abdominal examination was unremarkable as was the rest of clinical examination. Initial laboratory investigations were all within the normal limits except slightly deranged LFTs (Serum total bilirubin 6.6, Direct 4.8). Tumor markers were negative. Serum levels of several hormones including insulin, glucagon, gastrin, somatostatin and 24 hours urinary 5-HIAA were also within the normal ranges.

Ultrasound examination revealed a dilated CBD measuring 2.1cm along with dilated intrahepatic ducts. Upper GI endoscopy showed gastritis with some mass effect from outside the duodenum. Computed Tomography (CT) examination showed a nodular mass in the region of the head of pancreas measuring 1.7x1.3cm (Figure 1), which was focally indenting the contiguous 2nd part of duodenum. The mass was causing encasement of common bile duct (CBD) and the pancreatic duct resulting in proximal dilatation of the CBD (2.0cm), intrahepatic biliary ducts and pancreatic duct (0.5cm). A diagnosis of carcinoma of head of pancreas was made and she underwent Whipple's Procedure.

Surgical Unit V, Dow University of Health Sciences, Civil Hospital, Karachi, Pakistan.

Correspondence: Dr. Abdul Qaiyoume Amini, Surgical Unit V, Dow University of Health Sciences, Civil Hospital, Karachi, Pakistan.

E-mail: aqamini@yahoo.com

On gross pathological examination a firm grey white mass is seen arising from the ampulla of Vater measuring 2.5x2.5cm along with dilated CBD and distended Gall Bladder. Histologically the lesion had a trabecular arrangement of cells that were round with abundant eosinophilic cytoplasm. The nuclei were round with stippled chromatin and inconspicuous nucleoli. Abundant stromal sclerosis was also noted. A total of five lymph nodes were recovered which were all negative for metastatic disease. On immunohistochemical staining, the tumor cells were found to be strongly positive for neuroendocrine markers. So on the basis of above mentioned features, the final diagnosis of a neuroendocrine tumor was made along with morphological characteristics of carcinoid.

Patient recovered well from surgery and was discharged on 10th post op day. On follow up visits she found to have no symptoms related to disease and gained weight.

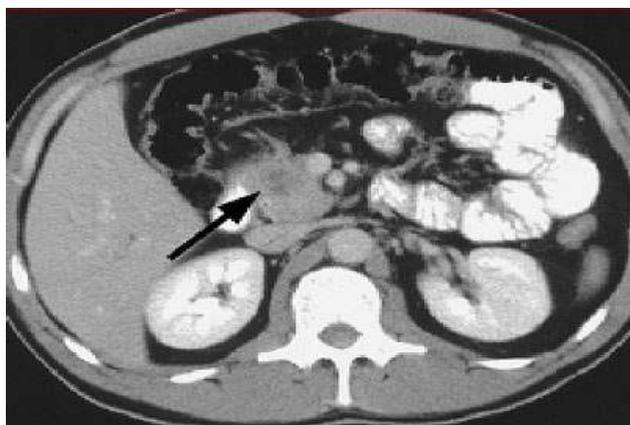


Figure 1: CT Scan showing lesion in periampullary region (Arrow)

DISCUSSION

Neurofibromatosis Type 1 (NF1) is an autosomal dominant genetic disorder with a reported incidence of 1 in 2500-3000 live births⁴. The disease is characterized morphologically by cutaneous neurofibromas, café-au-lait spots, freckling of axillary and inguinal skin and Lisch nodules. NF1 is also associated with several tumors of neurogenic or neuroendocrine tissue, 3 to 5% of which may develop malignancy during the lifetime¹⁰. Such tumors may develop in central and peripheral nervous system (neuromas, neurofibromas, peripheral nerve sheath tumors, schwannomas etc.) and in Gastro-intestinal system including gastro-intestinal stromal tumor, tumors of intestinal neural tissue and neuroendocrine cell tumors of periampullary region (duodenum and pancreas)⁷. Frequently these tumors are non-functional and have no symptoms associated with excess hormone secretion.

The symptoms are mainly the pressure symptoms due to local mass effect such as obstructive jaundice, bleeding, intestinal obstruction and cholangitis¹¹.

Our case is of surgical interest because of its rarity and its atypical presentation. She had no symptoms associated with oversecretion of hormones and was only mildly jaundiced. She never had any episode of intestinal obstruction or gastro-intestinal bleeding. Serum level of hormones including somatostatin was normal. A diagnosis of adenocarcinoma of head of pancreas (peri-ampullary) was made based on CT scan findings and pancreatoduodenectomy (Whipple's procedure) was done. On histopathological examination it came out to be a neuroendocrine tumor with carcinoid features. Immunohistochemical assay was positive for many neuroendocrine markers (Cytokeratin AE1/AE3, Synaptophysin, Chromogranin-A) but negative for somatostatin. All resection margins were free of tumor and the lymph nodes recovered were also tumor free. Patient had a smooth and uneventful post operative recovery.

There are specific guidelines or protocol in literature for treatment of such periampullary neoplasm although complete surgical resection is the mainstay of treatment. The Whipple procedure is the standard choice and is preferred over local excision when tumor is more than 2.0 cm³ in diameter. The other point in favour of Whipple's procedure is that unlike carcinoids at other anatomical sites, the size tumor does not correlate with metastatic potential in periampullary region. There are cases reported in which metastasis to lymph nodes and even liver metastasis was found from a primary tumour of less than 1 cm in size.⁶ Due to this, many surgeons favor Whipple's resection for all periampullary carcinoids, irrespective of the size.^{4,9}

A thorough evaluation for periampullary tumors in NF-1 patients is important with subsequent surgical management which is curative in most of the cases without distant metastasis^{7,8}. These tumours also have a good prognosis even when there is metastasis with a 5 year survival rate of almost 90%² after surgical resection

CONCLUSION

In patients with NF1 (Von Recklinghausen's Disease) who present with gastrointestinal symptoms like abdominal pain and jaundice, a high index of suspicion is required along with thorough clinical examination and detailed investigations. Thereafter an aggressive surgical approach seems to give a symptom free survival for longer duration.

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