

PANCREATICO DUODENAL NEUROENDOCRINE TUMOURS – OUR EXPERIENCE OVER THE PAST 2 YEARS

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ABSTRACT: INTRODUCTION: Pancreaticoduodenal Neuroendocrine tumours are a heterogeneous group of tumours with their origin in neuroendocrine cells of the embryological gut which are positive for 'Pan-neuroendocrine' markers including chromogranin A and synaptophysin. The estimated incidence is 5.25/100,000/year. They appear at all ages with the highest incidence from the 5th decade onwards. This article presents a review of our experience with pancreaticoduodenal neuroendocrine tumours over the past 2 years (2012 to 2014). **Description of Cases:** Over a period of 2 years from 2012 to 2014 we came across 5 cases of pancreaticoduodenal neuroendocrine tumours with age group ranging from 38 to 70 years. Of the 5 patients 3 cases (60%) were males and the remaining 2 cases were females (40%). 4 out of 5 patients underwent Whipples procedure. 1 case was stage 4 disease at presentation and inoperable. **DISCUSSION:** Pancreaticoduodenal NET present with varying signs and symptoms. Routine workup includes USG, CECT, USG / CT guided FNAC- tissue diagnosis, Somatostatin Receptor Scintigraphy, EUS – Most sensitive for small tumours, Serum tumor markers: Cg A; NSE. Surgery is the primary modality of treatment. The goal of surgery is local disease control. **CONCLUSION:** All patients are to be considered potential candidates for curative surgery especially duodenal NET. Curative resection of the primary tumour and loco regional lymph node metastases improves outcomes in these patients.

KEYWORDS: Net- Neuroendocrine Tumour.

INTRODUCTION: Neuroendocrine tumours (NET) comprise a rare group of neoplasms that arise from the neuroendocrine system of the intestine. Also known as pancreatic endocrine tumour or langerhan cell tumour or islet cell tumour.¹ Median age of incidence as per SEER data is 59 years They have an incidence of 1 in 100,0001 and it is estimated that at least 3% of primary neoplasms are derived from the pancreas and more than 10% are associated with genetic syndromes such as MEN – 1, VHL, Tuberous Sclerosis. They may be functional (IHC positive with hormonal symptoms) or may be Non-functional (IHC positive without hormonal symptoms)². By definition all NET express neuroendocrine markers such as synaptophysin, Neuron-specific enolase and Chromogranin. Chromogranin positivity favours well differentiated variety. Synaptophysin positive tumours can be well differentiated or poorly differentiated. Other IHC markers include SSR2A, CD 34 (denotes vascular density of the tumour). At least 14 different types of cells have been implicated to date in their pathogenesis.³

Symptoms can be caused by tumour growth. Among these is abdominal pain (40–60%), weight loss (25–50%) and jaundice (30–40%). In recent years there has been an increase in the incidental diagnosis of neuroendocrine tumours with imaging studies because of their nonspecific symptoms (over 35% of patients in some series). Screening asymptomatic individuals result in lower rates of metastasis, increased resectability, and improved survival.⁴

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Description of Cases:

CASE 1: A 38 year old male who presented with complaints of abdominal pain, loss of weight and loss of appetite of 2 months duration. On per -abdomen examination was detected to have a hard mass occupying the epigastrium and right hypochondrium. Contrast Enhanced CT Scan of the abdomen showed a mass arising from the head of pancreas and also a paraaortic mass on the left side. USG guided FNAC which was done elsewhere was reported as Neuroendocrine Tumour; IHC - CK, Synaptophysin and Chromogranin positive; Ki 67-10%. DOTOAC scan revealed similar findings. Preoperative staging was done; as it was a non-metastatic disease, the patient underwent Whipples's procedure along with resection of para-aortic mass. HPE report: 8*8*5.5 cm Whipple's specimen and 18* 16 * 6 cm para-aortic mass specimen; Grade II Neuroendocrine tumour, margins negative, positive lymphovascular invasion. pT1N1Mx; STAGE II B.



FIGURE 1

CASE 1: 38 yr / male;
Abdominal Pain;
Loss of Weight
Loss of Appetite
(2 months)
Mass Per abdomen;
CECT-Suggestive of mass arising from head of pancreas.

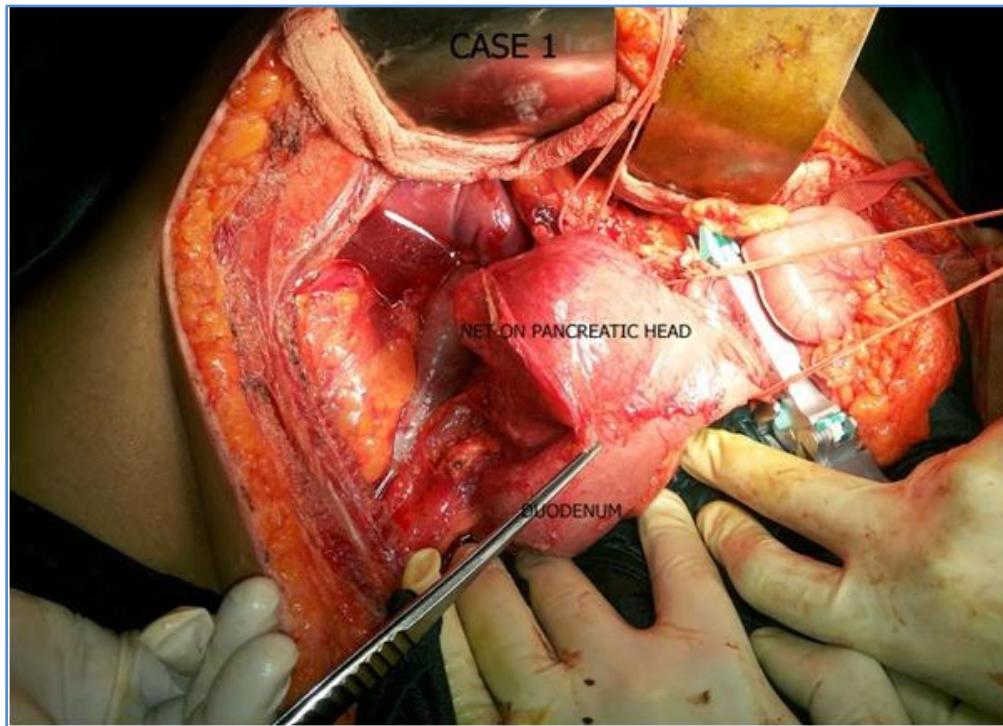


FIGURE 2

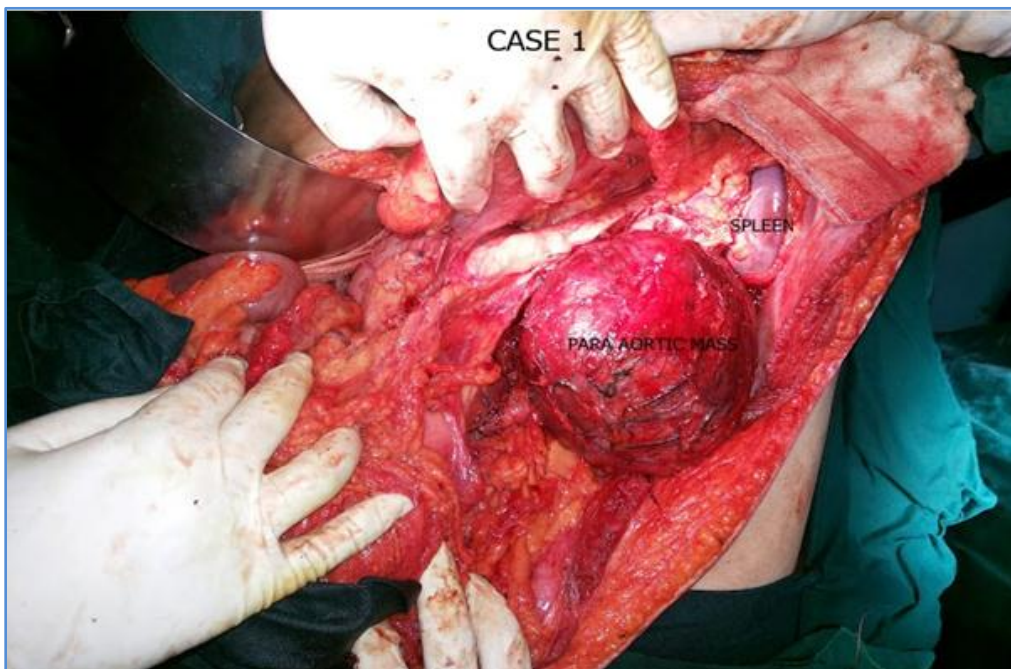


FIGURE 3

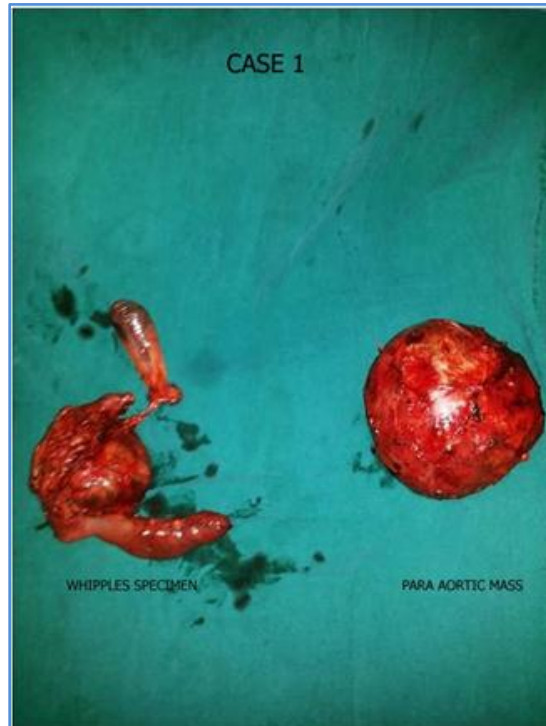


FIGURE 4

CASE 2: A 38 year old male who was incidentally detected to have a pancreatic mass on USG abdomen during a routine health check-up. USG guided FNAC in outside hospital reported as Adenocarcinoma Pancreas. CECT abdomen showed a heterogeneously enhancing mass with necrotic areas in the uncinata process of pancreas – 5.5 * 4.7 * 5.5 cm. Preoperative staging was done, as it was a non-metastatic disease, patient underwent Whipple's procedure. HPE report : Tumour of size 4.5 * 4.5 * 2 cm arising from the uncinata process of pancreas. Moderately differentiated, lymphovascular and perineural invasion present. Grade II. SATGE 2 B. Pt3N1Mx. IHC – Chromogranin positive, Synaptophysin > 3%, Ki 67 > 3 % CK – strongly positive. One month following the surgery the patient developed a biliary fistula which subsided with conservative management.

CASE 3: A 50 year old female who presented with diarrhoea, vomiting, loss of weight and loss of appetite of 3 months duration. Upper Gastrointestinal Endoscopy revealed duodenal nodules in the 2nd and 3rd part of duodenum which were biopsied. CECT abdomen showed tiny enhancing polypoidal lesions in the D2 and D3 (2nd and 3rd part of duodenum)? Polyp? Carcinoid. Upper Gastrointestinal Endoscopy biopsy was reported as Neuroendocrine tumour. Serum Chromogranin level was elevated (1052.2ng/ml). DOTONAC scan showed 9 *9 mm enhancing nodule on the medial wall of D2, no lymph node or distant metastasis. Preoperative staging was done, patient underwent Whipple's procedure. HPE showed a well differentiated carcinoid tumour of size 1 * 1 * 1 cm in duodenum with pancreatic head infiltration, no lymphovascular or perineural invasion, 1 out of 3 lymph nodes involved, surgical margins uninvolved. IHC – CK, Synaptophysin and Chromogranin positive; Ki 67- 10 %. pT3N1M0; Grade -1; Stage- 2B.

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CASE 4: A 70 year old male who presented with bloating sensation, dyspepsia and constipation of 1 month duration. Abdominal clinical examination was normal but per rectal examination revealed a palpable extramural mass with normal rectal mucosa. Upper gastrointestinal endoscopy revealed nodules in the D1 and D2 (1st and 2nd part of duodenum) from which biopsy was taken. CECT abdomen and pelvis showed a pelvic mass measuring 10*7*10 cm located in the presacral region with sclerotic areas in the spine and pubic suggestive of metastasis. The upper gastrointestinal endoscopy biopsy was reported as neuroendocrine tumour Grade I (advised Ki 67 for precise grading and IHC). As it was a metastatic stage 4 disease, not feasible for resection, no surgical intervention was contemplated.

CASE 5: A 60 year old female, known case of CKD, who presented with Jaundice, loss of weight and loss of appetite of 3 months duration. Upper gastrointestinal endoscopy showed a periampullary growth. MRI showed terminal CBD stricture with severe biliary dilatation. Stenting was not done as bilirubin level was only 3 mg %. Upper gastrointestinal endoscopy biopsy was reported as neuroendocrine tumour. Pre-operative staging was done. As it was a non-metastatic disease, patient underwent Whipple's procedure. HPE showed a well differentiated periampullary Grade I carcinoid tumour of size 1 * 1 * 0.5 cm, with no lymphovascular or neural invasion. pT1N0Mx. Stage I.

A total no of 5 cases were evaluated in our institution between 2012 and 2014 of which 4 were operated. The age group of the patients ranged from 38 to 70 years of which 3 were males and 2 were females. Majority of the patients that presented to us had complaints of loss of weight and appetite – 3 patients (60%), 2 patients presented with altered bowel habits (40%), 1 patient presented with abdominal pain (20%) and 1 patient presented with mass per abdomen (20%). All the patients who were operated underwent Whipples procedure. All the cases were non-functioning neuroendocrine tumours.

OUTCOME:

POST OPERATIVE RECOVERY: Case 2 patient, in the post op period developed enterocutaneous fistula – which resolved on conservative management.

Case 5 patient died on post-op day 1 due to Acute Myocardial Infarction.

DISEASE OUTCOME:

Case 1-Recurrence 4 months post-surgery on palliative care.

Case 2- Disease free till date – 9 months post op.

Case 3- Disease free till date – 1yr, 5 months post op.

Case 4- On palliative treatment – for past 1 1/2 months.

DISCUSSION: Neuroendocrine tumours are a heterogeneous group of tumours with their origin in neuroendocrine cells of the gut. They tend to appear at all ages, highest incidence 5th decade onwards. Slight overall higher incidence in seen in males than in females. Most tumours are low to Intermediate grade and non – functional.^{1, 5, 6} Most of the neuroendocrine tumours are malignant except insulinomas. The staging of these tumours are done with USG, CECT abdomen and pelvis, Endoscopic Ultrasonography (EUS), Somatostatin Receptor Scintigraphy or DOTONAC scan. CECT will help in assessing the location and size of the tumour and its resectability based on its relation to

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superior mesenteric artery and celiac axis. First establish diagnosis by FNAC (EUS /USG/CT guided). Non metastatic, localised disease may be resected.⁷ If liver metastasis of small volume is found, it may be resected. If metastatic disease or large borderline resectable primary tumour, initiate cytotoxic chemotherapy. If resectable tumour with liver metastasis, 2 stage procedure – remove primary tumour first and later the liver secondary. The goal of surgery is local disease control. In advanced disease, cytotoxic chemotherapy with streptozotocin, 5-fluorouracil and dacarbazine containing regimens are advised. Biological therapy with somatostatin analogues, interferons are other modalities. For pancreaticoduodenal neuroendocrine tumours, surgery is the primary modality of treatment. Haynes et al. in a case series of more than 139 patients concluded that those with incidental gastro-pancreatico duodenal neuroendocrine tumours should undergo tumour resection and careful postoperative surveillance even if pathological findings are suggestive of benign disease.^{1,9} Lee Moffitt Cancer Centre concluded that 26% of tumours were discovered incidentally and 55% of them were in stage I according to AJCC stratification. Moreover, the median patient survival in those who already had symptoms was 103 months versus 84 in those who did not.¹⁰

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