NEUROENDOCRINE TUMORS IN DECOMPENSATED LIVER DISEASE

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Abstract:
We report two cases of neuroendocrine tumors in patients with decompensated chronic liver disease. Neuroendocrine tumour in the setting of decompensated liver disease is a very rare entity thus the presentation. Patients who had decompensated chronic liver disease, diagnosed by clinical, laboratory and imaging criteria underwent upper gastrointestinal endoscopy. During endoscopy, polyps numbering one to numerous were found in the stomach and duodenum. Biopsy was taken from polyps and sent for histopathological examination. Histopathological examination was suggestive of neuroendocrine tumor. To confirm the diagnosis, Immunohistochemistry for neuroendocrine markers, chromogranin A, synaptophysin, Leu7, and neuronspecific enolase was done. After confirmation with positive immunohistochemistry, metastatic work-up was done using CECT abdomen and PET CT scan.

Keyword: Carcinoid tumour, PET CT Gallium 68 Dotatate

Case presentation Case 1 Mr. R 55 years male presented with abdominal distention and pedal oedema for 1 month, with no other significant positive history, clinically patient had anemia, icterus, pedal oedema and abdominal free fluid. Laboratory and radiological investigations confirmed the diagnosis of cirrhosis with portal hypertension, probable etiology being ethanol. Patient underwent upper gastrointestinal endoscopy done, which revealed Grade III oesophageal varices in two columns distal 7 cm without red signs. Duodenal bulb shows multiple polyps, one was large in size 2cm X 2cm with central ulceration (Fig.1). Biopsy was taken from large polyp. Histopathology showed fragments of duodenal mucosa with surface ulceration, dilated mucosal glands and ectatic blood vessel with hyperplastic island of neuroendocrine cells around blood vessels so Neuro endocrine tumour or Glomous tumour (Fig.2). Immunohistochemistry report revealed synaptophysin and chromogranin were positive while PAN CK negative (Fig.5). Impression favoured diagnosis of carcinoid tumour with aKi index of 2. Patient was not willing for a PET Scan so patient underwent Computed tomography (CT) scan which showed polypoid mucosal thickening in second part of...
duodenum, multiple mesenteric and retroperitoneal lymph node with adjacent fat stranding and cirrhosis with portal hypertension causing secondary Porto systemic collaterals along with moderate ascitis. Surgery was deferred due to Decompensated cirrhosis CTP C which is associated with a very high post operative morbidity and mortality. So the patient was planned for polypectomy. Polypectomy was done and send for histopathological examination which confirmed the diagnosis and showed the margins were free from tumour.(Fig 3&4). Patient is being treated symptomatically and is on regular follow up for the past 9 months.

Fig.1. **VOGD** Duodenal bulb shows, one was large in size 2cm X 2cm with central ulceration

Fig.2. **HPE Report:** showed fragments of duodenal mucosa with surface ulceration, dilated mucosal glands and ectatic blood vessel with hyperplastic island of neuroendocrine cells around blood vessels s/o Neuroendocrine tumour or glomous tumour

Fig.3. During polypectomy with snare

Fig.4. Post polypectomy duodenal polyp

Fig.5. Immunohistochemistry - synaptophysin - positive
Case 2. Mr G, a 40-year-old male referred from elsewhere as a case of Decompensated liver disease with portal hypertension ethanol related for upper gastrointestinal endoscopy. The endoscopy revealed Grade I oesophageal varices in one column and Grade II oesophageal varices in three columns in distal 13 cm with red wale signs. Multiple polypoid lesions were seen in fundus, proximal and mid body of stomach (Fig 6). Biopsy was taken from the polypoidal lesions and sent for Histopathology of the gastric mucosa showed gastric mucosal glands with hyperplastic foveolar epithelium, lamina propria showed oedema and inflammatory infiltrates. One of the fragments revealed submucosal nests of neoplastic cells. The neoplastic cells and vessels are with eosinophilic cytoplasm and uniform nuclei, so Neuroendocrine tumor. Immunohistochemistry report revealed that Neuron specific enalose and chromogranin was positive which favoured a diagnosis of neuroendocrine tumor. PET CT Gallium 68 Dotatate was done, which showed focal Gallium 68 Dotatate avid stomatostatin receptor expressing lesion in the multiple gastric polyps (Fig 7). No other abnormal uptake in the whole body survey (Fig 8). Surgery was deferred due to the decompensated liver disease. Patient is being treated symptomatically and is on regular follow up for the past one year.

**Discussion:**

**Introduction:**
Carcinoids are rare neuroendocrine tumors (NETs) derived from enterochromaffin or Kulchitsky cells, which are widely distributed in the gastrointestinal tract 1,2.

**Fig. 6.** VOGD Multiple polypoid lesions are seen in fundus, proximal and mid body of stomach.

**Fig. 7.** Focal GALLIUM 68 DOTATATE avid stomatostatin receptor expressing lesion in the multiple gastric polyps.

**Fig. 8.** Focal GALLIUM 68 DOTATATE avid stomatostatin receptor expressing lesion in the multiple gastric polyps. No other abnormal expressing lesion in the whole body survey.
Most NETs, like other neoplasms, are clinically silent, producing symptoms only as a consequence of growth. But silence should not be mistaken for a low disease prevalence. Neuroendocrine tumours account for only 0.5% of all malignancies. The incidence is approximately 2100,000 with a female preponderance under the age of 50 years due to appendiceal location. In our study a total of 3,621 upper GI endoscopies were done in one year of which 428 patients had portal hypertension. Polyps were noted in 9 patients (2.1%) this is in accordance with the study by Amrapukur et al. one patient was excluded due to the presence of a positive rapid urease test. There are no existing reports of NET in decompensated liver disease. Among the polyps studied we found that 2 were hyperplastic, 4 were portal hypertensive polyp and 2 were NETs (0.46%).

Ki-67 index 2 so high disease progression-free survival is seen. Although the incidence of NETs has increased over the past 30 years, survival has also improved (reviewed by Zuetenhorst and Taal). Surgical resection is the standard treatment approach for carcinoid tumours. Metastasis to mesenteric lymph node is common at presentation and the resection should be en bloc to include mesenteric lymph nodes. Complete resection results in improvement of symptoms and survival. Since the incidence of multicentric disease is 2040 and of a second primary malignancy is 2030, the entire bowel should be inspected. The five-year overall survival rates for small bowel carcinoid tumours with localised regional disease is 65, but falls to 36 when distant metastases are present. Treatment is altered and modified for NET with decompensated liver disease, in our patients were of CTP C Class of cirrhosis which has a mortality of 7682- as per published data. so surgery was deferred in our patients in consultation with the surgical oncologist. As these patients are not able to metabolise chemotherapeutic drugs effectively chemotherapy was also deferred. So patient was treated symptomatically and with supportive care. Here, we describe a two cases of incidental carcinoid tumor in decompensated liver disease.

**CONCLUSION:** Occurrence of neuroendocrine tumors is rare, and an association has not been documented decompensated liver disease. Treatment is quite difficult for neuroendocrine.
tumors with decompensated liver. Long-term studies are needed to characterise the significance and if it all an association between portal hypertensive polyps and NET in cirrhotics.

**References:**
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