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A Case of Neuroendocrine Carcinoma of the Stomach with Perforation.

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ABSTRACT

Also known as carcinoid tumours These neuroendocrine tumours occur throughout the gastrointestinal tract, most commonly in the appendix, ileum and rectum in decreasing order of frequency. They arise from the enterochromaffin cells (Kulchitsky cells) found in the crypts of Lieberkuhn, which are capable of secreting APUD (Amine precursor uptake and Decarboxylation) and can secrete vasoactive peptides. Other sites are—other parts of GIT (including pancreas and biliary tract), bronchus and testis. In the ileum it is almost always in the terminal 2 feet. Metastasis occurs in 3% of appendiceal carcinoid; 35% of ileum. Most of them are asymptomatic and found incidentally during routine investigations or post-op . Carcinoid tumours generally are slow growing .May present with abdominal pain, features of intestinal obstruction, diarrhoea..etc The clinical syndrome may consists of reddish-blue cyanosis, flushing attacks, diarrhoea, borborygmi, asthmatic attacks ..etc . The extent of disease can be assessed preoperatively using octreotide scanning, which may detect otherwise clinically apparent primary and secondary tumours. [1,2] Plasma markers of tumour bulk, such as chromogranin A concentrations, may be useful markers of disease recurrence, as well as of prognostic value. Here we present a case of a 65 year old male presenting with perforation of the stomach, with neuroendocrine tumour.

Keywords: neuroendocrine, carcinoma, stomac, perforation.

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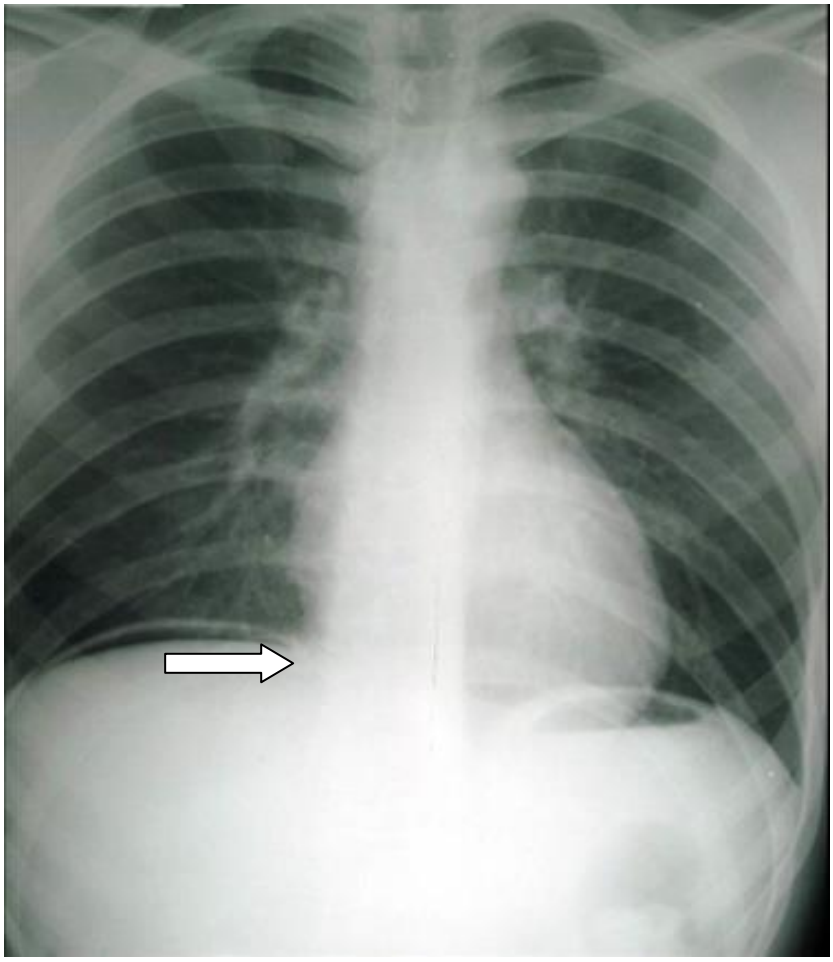
CASE HISTORY

65 year old male with complaints of diffuse abdominal pain since the past 2 days, associated with vomitting (3 episodes). Last episode contained blood. The patient gave h/o loss of weight and appetite since 6 months. No h/o malena/jaundice/ abdominal/ distension/ constipation . Bladder habits normal. Previous h/o alcohol consumption. k/c/o of DM on Rx since 2 years.

Clinical examination

Patient is moderately built and nourished. Toxic &Febrile. T-100*F. PR is 110/min.
No pallor/jaundice/cyanosis/clubbing/lymphadenopathy/pedal edema
P/A examination , there is diffuse tenderness, guarding & rigidity. No mass palpable.
PerRectal Examination : empty
All other systems examined and found to be normal

Investigations
Routine investigations were sent. TC was 14,560.
X-ray erect abdomen showed air under diaphragm.



Picture 1. Xray chest with abdomen showing air under diaphragm

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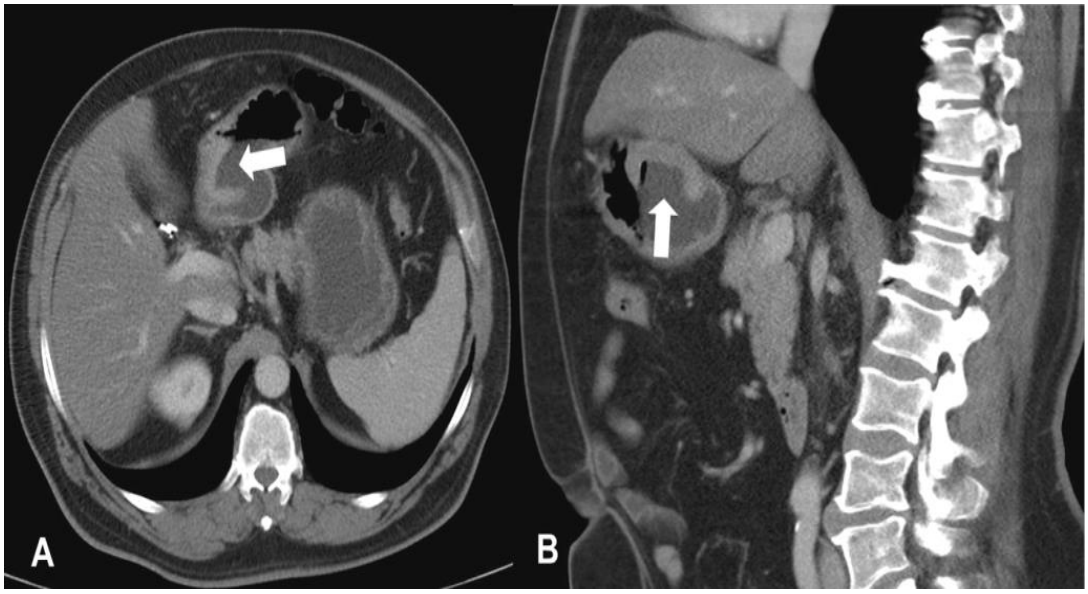
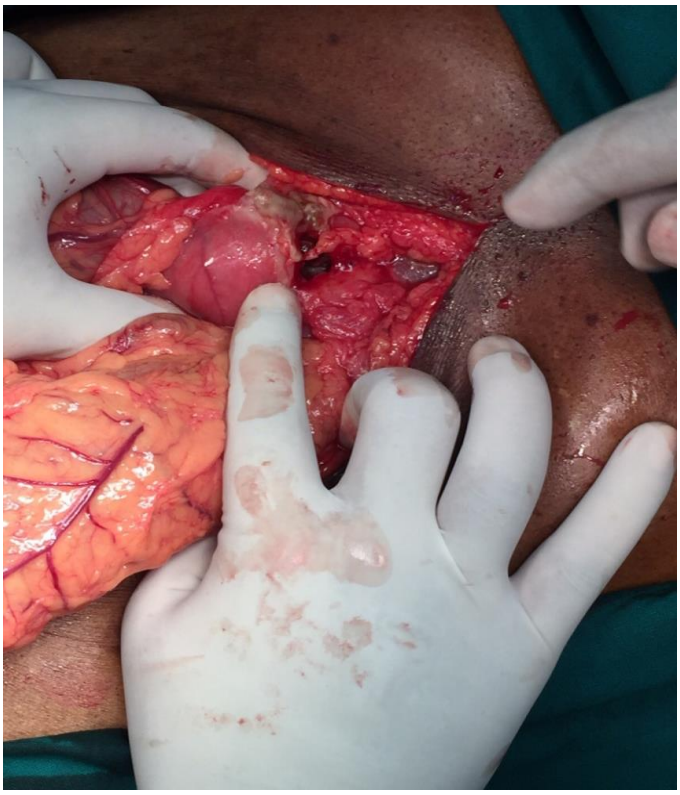


Picture 2 A & B. CT showed circumferential thickening in the pylorus, no e/o G.O.O. indicated by arrows

Procedure

Patient was put on NPO, RT, IVFs, Antibiotics and proceeded for an emergency exploratory laparatomy.

Findings: GROWTH in the PYLORUS of 4 x 3 cm gastric with PERFORATION of 2 x 2 cm. Minimal peritoneal contamination. bowel, omentum, liver, pelvis : NO deposits . SUBTOTAL GASTRECTOMY with ANTECOLIC GASTROJEJUNOSTOMY with JEJUNO-JEJUNOSTOMY was done.



Picture 3. Growth in pylorus with perforation Rest of the bowel & mesentery found to be normal. A drainage tube was kept. Abdomen closed in layers HPE turned out to be neuroendocrine carcinoma, with infiltration upto the serosa.

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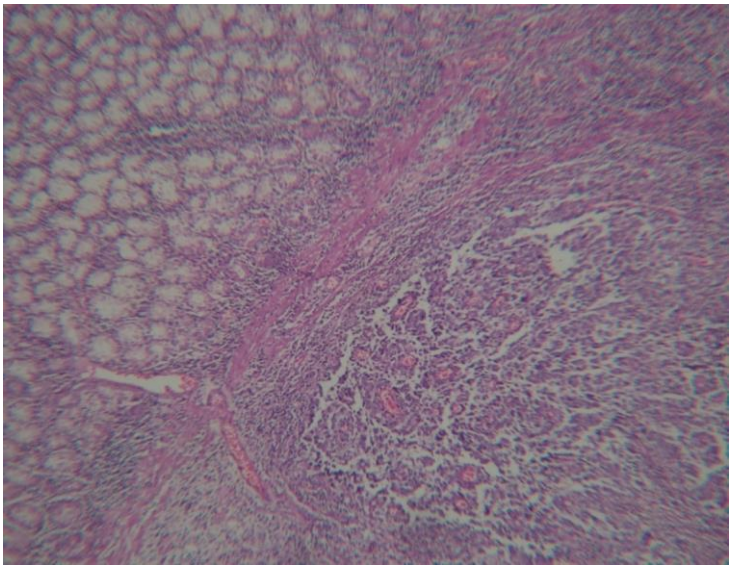

Picture 4. Round to Oval nuclei cells with vesicular nuclei, arranged in rossettes, papillary formations IHC reports showed increased chromogranin A.

Follow Up

Post-operatively patient recovered well and was discharged after 2 weeks. He was advised to come to OPD for check-up after a week, then after 2 weeks, after a month and then, 2 months following the last visit. He was asymptomatic and didn't have any complaints.

DISCUSSION

Also known as carcinoid tumours, these neuroendocrine tumours occur throughout the gastrointestinal tract, most commonly in the appendix, ileum and rectum in decreasing order of frequency. They arise from the enterochromaffin cells (Kulchitsky cells) found in the crypts of Lieberkuhn. These cells are capable of APUD (Amine precursor uptake and Decarboxylation) and can secrete vasoactive peptides. It commonly occurs in appendix (45%), ileum (25%) and rectum (15%). Other (15%) sites are—other parts of GIT (including pancreas and biliary tract), bronchus and testis.[**1,2]**

In the ileum it is almost always in the terminal 2 feet. Metastasis occurs in 3% of appendiceal carcinoid; 35% of ileum.75% of carcinoids are less than 1 cm and 2% of them will spread; carcinoid of 1-2 cm shows 50% chances of spread;more than 2 cm shows 85% chances to spread.75% of carcinoids are asymptomatic and found incidentally.

It secretes amines (5 HT, 5 HIAA, 5 HTP—85%, histamine,and dopamine), tachykinins (kallikrein, substance P, neuropeptide k), peptides (chromogranins—100%, pancreatic polypeptide—40%, neurotensin, HCG α, HCG β, motilin),prostaglandins.10% of cases are associated with MEN syndrome type I. Pathologically it is smooth, firm, yellowish submucosal nodule seen in antimesenteric border of bowel with mesenteric nodal mass having desmoplastic reaction.[**10]**

Carcinoid in appendix is usually single. But commonly it causes luminal obstruction and so presents with features of appendicitis. Common site is at tip/distal 2/3rd. Small bowel carcinoids are multiple in 40% cases. In 50% of cases other primary malignancy is observed like of breast and colon.Small bowel carcinoids (jejunoileal) < 1 cm incidence, of nodal and liver spread is 20-30%. If it is 1-2 cm, nodaspread is 60-80% and spread to liver is 20%. If it is > 2 cm, nodal spread is more than 80% and spread to liver is 50%.

CLASSIFICATION of Gastric neuroendocrine tumour [11]

- TYPE 1 :-75%, patients with c/c Hypergastrinemia 2* to pernicious anemia or c/c Atrophic Gastritis, low malignant potential (5%)

- TYPE II :- assoc. with MEN 1 & ZES, 10% malignant pot.
- TYPE III :- sporadic tumors, usually solitary, not assco. With hypergastrinemia

Clinical Features

Most often asymptomatic—an incidental finding. May present with abdominal pain, features of intestinal obstruction, diarrhoea.Hindgut carcinoids present with constipation, bleeding per rectum, rectal tenesmus. Once secondaries develop in the liver (which is yellowish)

Carcinoid syndrome develops (10%), which is due to release of 5-HT, kinins, prostag landins, histamine and indoles causing flushing, diarrhoea, cyanosis, asthmatic attacks, hepato megaly, cardiac lesion on right side. Attacks can be induced by alcohol.

Investigations

Urine shows increased 5-hydroxyindoleacetic acid (5HIAA) levels. (Normal value—2-8 mg/24 hours).111In-octreotide scintigraphy to detect the tumour.

ENDO-ULTRASONOGRAPHY
CT scan/MRI : very useful for staging, nodal involvement.
I131 MIBG scan is also done.

MARKERS: Plasma Chromogranin A
Urine 5-Hydoxyindoleacetic acid
Neuron-specific enolase
Synaptophysin

Plasma level of chromogranin A will be elevated in 80% of patients. Provocative tests using pentagastrin, calcium or epinephrine may be used. PET scan using 1C 5 HTP and 18 F L DOPA isotopes when fused with CT scan will give the best image; with urine 5 HIAA and serum chromogranin A, diagnosis will be accurate.

Surgical treatment [1,2,4]

-Appendix: Tip/lesion less than 2 cm but not involving base—appendicectomy.
Lesion more than 2 cm/involving base—right hemicolectomy.

-Gastroduodenum
Less than 1 cm—endoscopic resection
More than 1 cm—subtotal gastrectomy/pancreaticoduodenectomy

-Small bowel lesion
Less than 1 cm—segmental resection
More than 1 cm—radical resection with adjacent mesentery
Terminal ileum—right hemicolectomy

-Rectal lesion
Less than 1 cm—endoscopic resection
1 cm invasive—wide excision
More than 1 cm—anterior resection

-Debulking surgery as palliation in metastases [**3,7]**

Medical treatment

Mainly symptomatic. Long acting somatostatin analogue—octreotide can be given—90% symptom palliation is achieved. Slow release formulation of octreotide (Sandostatin LAR) is also used [**6**]. Pasireotide is

2nd generation octreotide which has got wide somatostatin receptor inhibition action (40 fold than octreotide) is said to be very effective. Ketanserin(tocontrol diarrhoea), cyproheptadine, ondansetron are also effective.Bevacizumab (antiangiogenesis factor), sunitinib (Tyrosine kinase inhibitor), everolimus (m TOR inhibitor) are other agents tried. [**4,5]**

Others: Serotonin antagonists, antihistamines, alpha methyl dopa, 5-fluorouracil, Bromocryptine, streptozocin, doxorubicin, dacarbazine, 5-FU, methylsergide, diphenoxylate hydrochloride, interferon, Radiolabelled somatostatin analogue. Indium 111 labelled pentetreotide is also effective [**4,5]**

Role of Chemotherapy: poor response, 10-20% rate, Cisplatin with etoposide may be used

PROGNOSIS:[**8]**

- Node negative : 90% 5-year survival rate
- Node positive : 50%
- Type III : 50%

CONCLUSION

Carcinoid tumours generally grow more slowly than most metastatic malignancies; the patients may live with the syndrome of metastatic disease for many years. Most of them are asymptomatic and found incidentally during routine investigations or post-op Histopathological analysis.Gastric carcinoid tumours constitute 1% of all Carcinoid tumors & < 1% of all gastric neoplasms [**11].** Development of tumor attributed to use of acid suppressing drugs .Many are benign, while some are malignant. They are not usually sensitive to chemo- or radiotherapy. Prognosis is usually very good.

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