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CARCINOID TUMOUR OF STOMACH IN A CASE OF MULTIPLE ENDOCRINE NEOPLASIA – 1 SYNDROME – A CASE REPORT

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ABSTRACT Multiple Endocrine Neoplasia (MEN) type 1 is characterised by occurrence of tumors in anterior pituitary, pancreas and parathyroid. Though rare, some of these patients may develop carcinoid tumors anywhere in the body.

Of the 3 types of gastric carcinoids, type 2 gastric carcinoid is rare representing 5% of all gastric carcinoids and is known to be associated with MEN 1 syndrome. Type 2 gastric carcinoid has low incidence of turning aggressive but there have been cases where the tumor behaved aggressive like in our case.

We are presenting one such rare case of malignant gastric carcinoid tumor in a 34 years old female with MEN 1 syndrome, who presented with metastasis to regional lymph nodes.

KEYWORDS : Carcinoid, MEN-1 Syndrome, Gastric tumor.

INTRODUCTION:

It is said that neuroendocrine tumors (NET) are tumours of the interface between nervous system and endocrine glands [1]. Endocrine tumors of the stomach are well differentiated, non-functioning enterochromaffin like (ECL) cell carcinoids that are known to arise from the oxyntic mucosa in the corpus or fundus [2]. Relatively rare, gastric carcinoids account for 7% of all carcinoid tumours [1].

Multiple endocrine neoplasia (MEN) syndrome is an inherited autosomal dominant disorder which is characterised by prolifera tion (neoplastic/ hyperplastic) of more than one endocrine gland. MEN type 1 also known as 'Werner Syndrome' is characterised by occurrence of tumours in the anterior pituitary, parathyroid and pancreas. Although uncommon, other abnormalities include thyroid and adrenocortical adenomas, carcinoid tumors, multiple soft tissue lipomas, multiple leiomyomas and Menetrier disease of stomach [3].Gastric carcinoid tumors may be associated with or without hypergastrinemic states. Those associated with hypergas trinemia and Zollinger-Ellison syndrome or MEN 1 is classified as type 2 4. MEN 1 associated with Gastrinoma, chronic atrophic gastritis, pernicious anaemia, auto-immune disease increase the risk of gastric carcinoids [5].

Type 2 gastric carcinoids are rare that are associated with gastrin omas accounts for less than 5%. Various studies have reported that gastric carcinoids comprise 8.7 to 80% of all carcinoids [5]. It has been reported that 0.6 to 2% of gastric polyp's accounts for gastric carcinoids 1. Even though it is reported that there is low incidence of malignancy (10-20%) in type 2 carcinoid tumors [4]. In our case the tumor behaved aggressively and therefore the need to recognise and characterise these tumors accurately.

Carcinoid tumors arising from the gastric mucosa may present as an isolated lesion or multiple lesions. Multiple gastric carcinoids due to hypergastrinemia has less chance for turning malignant and metastasize compared to solitary gastric carcinoid [5].

CASE REPORTS:

34 years old female came to emergency department with chief complains of loose stools and vomiting for the past 2 months. Patient gave history of intermittent fever for 1 month. Past history revealed that patient was a known case of MEN 1 syndrome with asymptomatic parathyroid adenoma, space occupying lesion in pancreas and a gastrin secreting tumor in duodenum diagnosed 10 years back. Previous endoscopy revealed polypoidal growth without any ulceration or fungation and biopsy from the same was suggestive of chronic duodenitis.

On examination, general condition of the patient was stable. Laboratory findings revealed, there was mild anaemia (Hb – 10.4gm/dL) with red blood cell morphology showing microcytic hypochromia with anisopoikilocytosis. Serum calcium levels were within normal limits i.e., 9.8 mg/dL (normal levels: 8.5- 10.2mg/dL). Serum gastrin and parathyroid hormone levels were highly elevated i.e., >1000pg/ml (normal levels >100pg/ml) and1207.0 pg/ml (normal levels: 10-65pg/ml) respectively.

Esophago-gastro-duodenoscopy (OGD) on present admission revealed multiple sessile polypoidal lesions scattered diffusely in fundus and body of the stomach. Computerised tomography (CT) scan revealed multiple diffuse polypoidal enhancing wall thickening involving entire stomach and first part of duodenum. Multiple enlarged lymph nodes in peri-gastric, peri-pancreatic, peri and para-aortic and aortocaval regions were also noted. Positron Emission Tomography (PET) scan revealed increased uptake of dye fluoro-deoxy-glucose (FDG) in stomach polyps and proximal duodenum with multiple FDG uptake in peri-gastric, peri-pancreatic and aortocaval lymph nodes.

Total gastrectomy specimen of stomach along with resected lymph nodes were received. External surface of the stomach was unremarkable. Cut section revealed multiple pedunculated as well as sessile polypoidal growths largest- 3 x 1 cm and smallest - 0.5 x 0.5 cm, covering entire mucosal surface of stomach diffusely (figure 1).

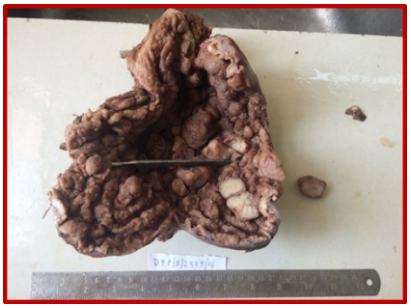

Figure 1: Gross showing multiple pedunculated as well as sessile polypoidal tumors on mucosal surface

Multiple sections studied from different polyps of stomach showed intact gastric mucosa and tumor composed of neuroendocrine cells arranged in micro-glandular, trabecular and insular pattern, predominantly seen in submucosa, not extending into muscularis propria (figure 2).

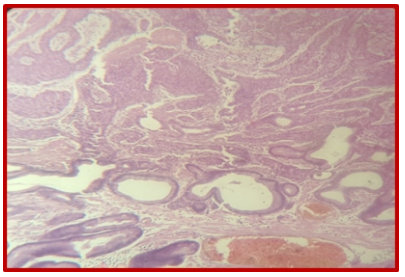

Figure 2: H and E, 10 X, tumor showing malignant tumor cells arrangedin micro-glandular, insular and trabecular pattern Individ ual tumor cells were round to oval, monomorphic with bland nuclei, salt and pepper chromatin, inconspicuous nucleoli and moderate amount of eosinophilic cytoplasm. There was no evidence of necrosis, haemorrhage or abnormal mitosis, lympho-vascular emboli and peri-neural invasion (figure 3).

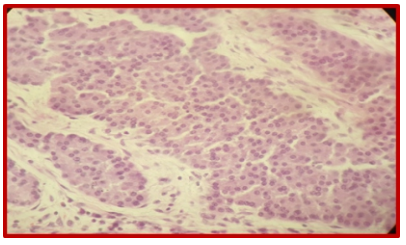

Figure 3: H and E, 40 X, tumor cells that are monomorphic, round to ovalwith bland nuclei and moderate eosinophilic cytoplasm.

All the resected margins were free of tumor. 11 out of 16 lymph nodes isolated showed tumor metastasis. Post operatively, patient was stable and free of disease on 3 month follow up.

DISCUSSION:

Multiple Endocrine Neoplasia (MEN) syndrome is an autosomal inherited dominant disorder characterised by proliferation of more than one endocrine glands. They are classified into 3 types; MEN type 1 also known as Werner syndrome, characterised by pituitary, pancreatic and parathyroid component. MEN type 2 is further subdivided as MEN 2a and MEN 2b. MEN 2a which is also known as Sipple syndrome is constituted by Medullary carcinoma of thyroid, parathyroid hyperplasia and pheochromocytoma of adrenal glands. MEN 2b known as Gorlin syndrome comprises of Medullary carcinoma of thyroid, mucosal neuromas, pheochromocytoma and Marfanoid habitus [3].

It is said that patients with MEN 1 develop clinical manifestations in >95% by 5th decade of life, although the earliest age of manifestation has been reported in child of 5 years [6]. In our case, clinical manifestations started in the 2nd decade (24 years).

In 95% of the patients with MEN, it is reported that the most common feature was hypercalcemia due to parathyroid tumors, 40% patients had pancreatic islet tumors comprising of gastrinomas, glucagonomas and vasoactive intestinal polypept idomas (VIPoma's) and about 30% patients having pituitary adenomas either functioning or non-functioning 6. However, in our case, patient had non-functioning pituitary adenoma, gastrin secreting tumor of pancreas and duodenum and also parathyroid tumor with normal calcium levels.

Gastric carcinoids account for about 7% of all carcinoid tumors and 1 % of all gastric neoplasms 1. It is reported that about 15 to 50% of the patients with MEN 1 develop gastric carcinoid tumor [4]. It has been stated that, gastric carcinoid tumors may be associated with or without hypergastrinemic states, which are sub-divided into three types; type 1 is associated with hypergastrinemic state and atrophic gastritis / pernicious anemia. Type 2 is associated with hypergas trinemia along with MEN and ZES. Type 3 is tumors associated without hypergastrinemia also known as sporadic 4. Our case was carcinoid with hypergastrinemia with MEN 1, so it was categorised under type [2].

Although 80-90% of type 2 carcinoid tumor are said to be non-invasive, few cases have been reported as aggressive cases as in our case and require surgical treatment. Grossly, type 2 gastric carcinoid tumors are typically said to show thickened gastric wall with multiple mucosal- submucosal nodules or polyps. In more than 75% cases, they reportedly are smaller than 1.5 cms with rare involvement of muscularis propria 2. Lymph node metastasis is reported in nearly 30% patients and 0 to 10 % were reported with liver metastasis [4].

In our case, total gastrectomy specimen showed multiple polyps of varying sizes diffusely scattered throughout the stomach without evidence of infiltration of the wall of stomach. Microscopically, Type 2 carcinoids are typically characterized by micro-lobular, trabecular aggregates formed by regularly distributed and aligned cells with monomorphic nuclei, abundant fairly eosinophilic cytoplasm with absent mitosis and infrequent angioinvasion [2]. In our case, microscopically the polyps showed typical features of carcinoid tumor and was limited only up to the submucosa, however, metastasis to regional lymph nodes characterized this tumor as malignant.

Immunohistochemistry shows tumor cells reactive for chromog ranin A and synaptophysin predominantly with minor sub-population of cells expressing serotonin, gastrin, somatostatin, pancreatic polypeptide 2. In our case, synaptophysin came strongly positive.

CONCLUSION:

This case report demonstrates the importance of recognizing that type 2 carcinoid tumor associated with MEN 1 may behave aggressively though majority of the cases behaved indolent.

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