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# **Diagnosing Multiple Endocrine Neoplasia Type1 in a Resource Limited Setting: A Case Report of Pancreatic Neuroendocrine Tumor Causing Gastric Outlet Obstruction**

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## **Abstract**

Gastric outlet obstruction (GOO) is a narrowing of the pyloric outlet of the stomach due to benign or malignant disease processes. Pancreatic neuro endocrine tumor (NET) as a cause of GOO is a rare etiology. Pancreatic neuroendocrine tumors are underdiagnosed pre-operatively in resource limited settings. The following case report is about unusual presentation of GOO which was clinically and radiologically diagnosed to be a pancreatic neuroendocrine tumor, more specifically a Gastrinoma. Further evaluation of the patient revealed the presence of Primary Hyperparathyroidism (PHPT) too. The constellation of the two clinical diagnoses, led to the consideration of Multiple Endocrine Neoplasia type 1(MEN1) syndrome which has not been previously reported in Ethiopia. High index of clinical suspicion is important to diagnose the MEN1 related endocrine tumors.

**Keywords:** Multiple Endocrine Neoplasia type 1; pancreatic neuroendocrine tumor; Gastrinoma; Primary Hyperparathyroidism.

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## **1. Introduction**

Gastric outlet obstruction (GOO) is a narrowing of the pyloric outlet of the stomach due to benign or malignant disease processes. In Ethiopia, chronic peptic duodenal ulcers, gastric cancers and pyloric tuberculosis are the prevalent etiologies. References [1]GOO resulting from mechanical impediment by pancreatic pathologies is also prevalent. Pancreatic neuro endocrine tumor (NET) as a cause of GOO is a rare etiology.

Pancreatic neuroendocrine tumors are underdiagnosed pre-operatively. The following case is about unusual presentation of GOO with high probability of being caused by pancreatic NET which was further evaluated and found to be part of Multiple Endocrine Neoplasia type 1 syndrome.

## **2. Case Report**

This is K.M a 40 years old man who presented with complaints of indigestion and weight loss of 2 years duration. The weight loss was quantified to be 16 kilos within 2 years. The patient had post-prandial sensation of bloating and dyspepsia for past 10 years which failed to respond to conventional medical treatment. Progressively his symptoms got worse and he developed foul smelling vomiting of ingested matter hours after ingestion of meals. He had restricted amount of food intake. He had no change of bowel habits except occasional bouts of voluminous diarrhea. Otherwise he has no known chronic medical or surgical illness and doesn't take any prescribed medications. There was no identified family history of a similar illness.

On examination he was a well looking man who grossly had non-impressive findings except a positive succession splash on abdominal examination. With impression of Gastric outlet obstruction from chronic PUD (peptic ulcer disease), the patient was investigated. His blood counts were within normal limits and hemoglobin was 14.9g/dL. He had moderate hypokalemia and hypochloremia which were corrected with intravenous fluids. Ionized calcium level was 2.27mmol/L, which was above normal limits (Reference range 1.1-1.3mmol/L). Organ function tests, glucose and lipid panel were determined to be normal. Abdominal ultrasound scan reported a dilated stomach with increased peristalsis and the absence of mass lesion in the stomach and peri-gastric lymphadenopathy. Stool was negative for occult blood and H. pylori antigen. There was no parasite in the stool. Viral markers were negative. Serum CEA and AFP were within normal limits.

A barium meal study showed a dilated stomach filled with food debris and loss of rugal folds. It also reported delay of contrast passage for more than an hour. There was no evidence of ulcer or filling defect seen along the outline of the stomach. Upper GI endoscopy confirmed the ultrasound findings and additionally showed inflamed esophagus throughout its length concluding the presence of chronic esophagitis. With the above impression, patient was admitted and prepared for surgery. Intraoperative exploration of the abdomen confirmed a hugely dilated stomach with thickened wall. There was significant adhesion in the vicinity of the pylorus and gentle release of adhesions was done to expose a moderately thickened pylorus without palpable mass lesion. However, there was an incidental finding of 3 by 2 cm hard mass arising from the pancreatic head. Additionally, there were few lymphadenopathies along the gastrohepatic ligament. With intraoperative impressions of GOO from chronic inflammatory adhesion of pylorus and pancreatic head mass, gastrojejunostomy and lymph node

biopsy were done. Biopsy of the lymph node showed a follicular hyperplasia with no visible neoplastic seeding or granulomatous process. Subsequently, patient had smooth postoperative course and was discharged from hospital with follow-up appointments.

A post-operative CT scan showed a calcified mass on the pancreatic head measuring 2.5 cm in diameter, which enhanced significantly during the arterial phase, and surrounding fibrotic changes. The pancreatic duct was not dilated. The body, tail and neck of pancreas had normal size and density. There were no peri-pancreatic enlarged lymph nodes. With this radiologic finding, neuroendocrine tumors of the pancreas were considered as the top differential and the patient's protracted illness was suggestive of Gastrinoma. There was no radiologic evidence of distant metastasis.



**Figure 1 A:** Axial contrast-enhanced CT of the abdomen demonstrating a 2.5 cm diameter sized calcified and hyperenhancing pancreatic head mass with surrounding fibrotic changes causing proximal dilatation of the duodenum. **B:** Coronal contrast-enhanced CT of the abdomen showing the hyperenhancing calcified pancreatic head mass.

Another peculiar laboratory finding was that Parathyroid hormone (PTH) was elevated at 72.4 pg/ml (Reference range 15-68.3 pg/mL) leading to the diagnosis of primary hyperparathyroidism (PHPT). After months of follow-up the laboratory was repeated and it still showed increased levels of PTH (132.5 pg/mL). Ultrasound scan of the neck failed to show any parathyroid nodules/mass. The constellation of the clinical evidences of neuroendocrine tumor of the pancreas and PHPT led to consideration of MEN 1 syndrome. Even though pituitary adenoma is the third entity that should be considered in MEN 1 syndrome, there was no suggestive clinical evidence. Patient refused to have further invasive procedures and thus was conservatively followed for 14 months.

### **3. Discussion**

This case illustrates uncommon presentation of MEN1 in a patient with GOO. Multiple Endocrine Neoplasia type 1 (MEN 1) is an autosomal dominant disorder of the tumor suppressor gene MEN1 which encodes the protein menin. The MEN1 gene mutation can be identified in 70-95% of patients with the syndrome. References [2] The clinical diagnosis is made with either of the following conditions:

- The presence of two of three principal MEN1 related NETs, including parathyroid, gastro-entropancreatic (GEP) tract neuroendocrine and anterior pituitary tumors.
- Presence of one of the tumors and a first-degree-relative with MEN1 [2, 3].

MEN type 1 syndrome was initially described in the beginning of the 20th century in a patient exhibiting acromegaly and multi-glandular parathyroid abnormalities. References [4] The classic triad of Parathyroid, Pituitary and Pancreatic adenomas was reported in another patient. References [5] In 1954, Wermer suggested that this triad could be from an autosomal dominant inherited trait [2, 6].

Familial form is defined as the syndrome in an individual who has either at least one first-degree relative with at least one of the main endocrine tumors, or only one organ involvement and presence of MEN1 disease-causing germline mutation. References [7] Familial form of MEN1 occurs in approximately 90% while the sporadic is estimated to account for 10% [3, 8].

Out of the three endocrine tumors Primary hyperparathyroidism is the main endocrinopathy occurring as multi-glandular disease in 90-100% of cases. The second commonest is GEP tract neuroendocrine tumors occurring in 30-80% of patients with MEN1. Anterior pituitary tumors are the least common constituting 15-90% of cases. References [2] Outside the three main entities, there are other 20 endocrine and non-endocrine tumors that have been recognized to be part of the syndrome. The list includes but is not limited to foregut carcinoids, adrenocortical gland tumors, cutaneous and CNS tumors [2, 3].

Regarding the clinical presentation of MEN1, many tumors tend to be benign and present at a younger age (than their sporadic counterparts) with symptoms associated with overproduction of hormones or with local mass/pressure effects. Based on their ability to secrete hormones, they can be classified as functional and non-functional tumors. Of note is that some of the tumors may have a malignant tendency contributing to a high morbidity and mortality associated with the syndrome.

Primary hyperparathyroidism (PHPT) which is due to over production of Parathyroid hormone is said to manifest as hypercalcemia in 100% of MEN1 affected individuals by age 50 years, although the hypercalcemia can be asymptomatic. PHPT associated with MEN1 is characterized by earlier age of onset of hypercalcemia and multi-glandular hyper functioning of the parathyroid glands. References [2] Imaging is not a requirement to make a diagnosis of PHPT in MEN 1, since the hypertrophied glands may not be well visualized. References [2, 3] In the current patient, there was sub-clinical hypercalcemia. Ultrasound scan of the neck also failed to show any delineable nodule or mass in the vicinity of the thyroid. However, laboratory assays of the PTH repeatedly showed elevations suggesting the presence of functional hypertrophied parathyroid glands.

GEP as part of MEN1 are well-differentiated endocrine tumors of the gastro-entero-pancreatic (GEP) tract characterized by multiple scattered adenomas and earlier age of onset than their sporadic counterparts. References [2] Gastrinoma is the most common pathology (40%) followed by Insulinoma (10%). References [8] Other pathologies include VIPoma, glucagonoma, somatostatinoma. References [8] Although majority of GEP tract neuroendocrine tumors are non-functioning, patients may come with hyper secreting functional tumors and their respective clinical symptoms. Gastrinoma is said to present with Zollinger-Ellison syndrome, peptic ulcer with or without chronic diarrhea. Peculiarly, Gastrinomas are known for their malignant potential presenting with metastasis at the time of diagnosis in 50% of cases. References [2, 3, 8] Presentation secondary to mass effect of the neuroendocrine tumors is also not uncommon.

The evidences that suggested the diagnosis of Gastrinoma in the current patient are the clinical history, intraoperative findings, and radiologic findings. Clinically, ZES as manifestation of Gastrinoma in MEN1 usually occurs before age 40 years (a decade earlier than their sporadic counter parts [2]) and clinical manifestations may include upper abdominal pain, diarrhea, esophageal reflux, ulcers, and ulcer related complications. References [9] Weight loss and vomiting are also reported. The age of the current patient, and the long standing dyspepsia symptoms associated with diarrhea, are clinical clues to the presence of ZES. Radiologically, CT scan of the abdomen has confirmed the presence of a focal calcified mass of the pancreatic head sparing the remaining parts of the gland. The arterial enhancement pattern of the lesion was typical of pancreatic NET. Pancreatic neuroendocrine tumors are best visualized in arterial phase of contrast-enhanced CT as well-circumscribed hyperenhancing masses that are less conspicuous during the venous phase. References [10] This is in contradistinction to pancreatic ductal carcinomas that typically have a hypoenhancing appearance. References [8] The hyper enhancement pattern is explained by their hyper vascular capillary network. Cystic change, calcification, and necrosis are common in large tumors, which are associated with a poorer prognosis and a higher prevalence of local and vascular invasion and metastases than are smaller tumors. However, there was no evidence of regional lymphadenopathy and liver metastasis in the current patient.

Pituitary adenomas may be the first clinical manifestation of the MEN1 syndrome in about 17%, presenting in 10% of familial cases and 25% of sporadic cases. References [3, 8] From anterior pituitary adenomas, functioning Prolactinomas represent about 20% of cases while others with different histology account for lesser percentages. [3] Prolactinoma manifests as sexual dysfunction and (more rarely) gynecomastia in males. The other possible pathologies of anterior pituitary adenomas includes tumors secreting GH (Growth Hormone), TSH (Thyroid Stimulating Hormone), ACTH (Adrenocorticotrophic Hormone), FSH (Follicle-Stimulating Hormone), and both GH & Prolactin. There was no clinical evidence in the current patient that suggested the hypersecretion of the aforementioned hormones. MEN1-associated tumors are significantly larger and more often invasive than sporadic pituitary tumors. References [3] Clinical signs of headache, pressure effect on optic chiasm and signs of hypopituitarism were all absent in the current patient.

Even though targeted biochemical hormone evaluation and nuclear medicine imaging are indicated, in the context of our setting, the diagnosis of MEN1 was reached using the available evidences of PHPT and pancreatic NET, specifically Gastrinoma. Respecting the autonomy of the patient to decide mode of intervention, he was conservatively followed with an eventful course.

#### 4. Conclusion

Neuro-endocrine tumors as differentials of pancreatic mass are underdiagnosed in Ethiopia. Their presence as a cause of with GOO should be considered if typical radiologic findings are indicative. And their co-occurrence with primary hyperparathyroidism should raise the index of suspicion for MEN type 1 syndrome.

#### References

- [1] Berhanu Kotisso. "Gastric Outlet Obstruction in Northwestern Ethiopia". *East and Central African Journal of Surgery*. 2000; 5:2: 25-29
- [2] Marini F, Falchetti A, Luzi E, et al. "Multiple Endocrine Neoplasia Type 1 (MEN1) Syndrome". 2008 Jul 18 [Updated 2008 Aug 9]. In: Riegert-Johnson DL, Boardman LA, Hefferon T, et al., editors. *Cancer Syndromes* [Internet]. Bethesda (MD): National Center for Biotechnology Information (US); 2009
- [3] Giusti F, Marini F, Brandi ML. "Multiple Endocrine Neoplasia Type 1". 2005 Aug 31 [Updated 2022 Mar 10]. In: Adam MP, Mirzaa GM, Pagon RA, et al., editors. *GeneReviews®* [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2023.
- [4] Erdheim J. "Zur normalem und pathologischen istologie der glandola thyroidea, parathyroidea, und hypophysis". *Beitr Pathol Anat*. 1903;33:158–236.
- [5] Cushing H, Davidoff LM. "The pathologic findings in four autopsied cases of acromegaly. With a discussion of their significance". *Monograph 22 1927; The Rockefeller Institute for Medical Research ed*. New York.
- [6] Wermer P. "Genetic aspect of adenomatosis of endocrine glands". *Am J Med*. 1954;16:363.
- [7] Brandi ML, Bordi C, Tonelli F et al. "Multiple endocrine neoplasia type1". In: Bilezikian JP, Raisz GA, Rodan LG, editors. *Principles of bone biology*, 3rd ed. San Diego, CA: Academic Press, 2008: 1345-1374. Chapter 62
- [8] Hilary R. Keller, Jessica L. Record, Neil U. Lall. "Multiple Endocrine Neoplasia Type 1: A Case Report With Review of Imaging Findings". *Ochsner Journal* 18:170–175, 2018
- [9] Gibril F, Schumann M, Pace A, Jensen RT. "Multiple endocrine neoplasia type 1 and Zollinger-Ellison syndrome: a prospective study of 107 cases and comparison with 1009 cases from the literature". *Medicine (Baltimore)*. 2004; 83:43–83.
- [10] Rachel BL, Grant EL, Edina P. "Pancreatic Endocrine Tumors: Radiologic-Clinicopathologic Correlation". *Radiographics* 2010 Oct; Vol.30 No.6
- [11] Tonelli F, Fratini G, Falchetti A, Nesi G, Brandi ML. "Surgery for gastroenteropancreatic tumours in multiple endocrine neoplasia type 1: review and personal experience". *J Intern Med*. 2005; 257:38–49.