Case Report

Diagnostic challenge in a rare case of neuroendocrine tumor of the pancreas

Hareesh Chandran[1], Kamala V V[2]

From [1]Assistant Professor, [2]Professor, Department of Pathology, Sree Narayana Institute of Medical Sciences, Kunnukara, Kerala, India

ABSTRACT

A pancreatic neuroendocrine tumor is a rare disease with varying behavior, clinical, and microscopic appearances. We present a case of neuroendocrine tumor of the pancreas in a 63-year-old female. Right from the beginning, our case was a diagnostic challenge from the clinical and radiological perspective. Radiological features can often be misleading and microscopic confirmation is all-important. This case report describes the approach to the diagnosis of such a case combining clinical, radiological, and pathological aspects to ensure proper management of the patient.

Key words: Gastrointestinal pathology, Neuroendocrine tumor, Pancreas

Neuroendocrine tumors were earlier called amine precursor uptake and decarboxylation-omas as they were thought to arise from the specialized cells called as Amine precursor uptake and decarboxylation cells [1]. However, neuroendocrine tumors are now known to arise from cells of neuroendocrine function, that is, cells with both neural and hormone secretory function. Neuroendocrine cells are frequently distributed throughout different tissues. Neuroendocrine tumors too can present throughout the body, most common sites being the gastrointestinal tract and the lung [2,3]. While neuroendocrine tumors arise from neuroendocrine cells, they may well retain their endocrine properties and remain functional or lose the property resulting in a non-functional tumor.

Gastrointestinal tumors involving multiple organs, including the stomach, pancreas, and also spleen, can be challenging to diagnose based on radiologic and clinical features. Details from the history of the patient will enable a list of differentials to be arrived at and may help decide the treatment modality. Biopsy could be technically difficult, especially when the tumor is retroperitoneal even when recent techniques such as endoscopic ultrasound-guided biopsies have made them possible. Stepwise approach and having a close look at gross and microscopic features can reveal subtle clues to finally reach the diagnosis.

CASE REPORT

A 63-year-old lady complained of vague abdominal pain for a month. There was no past medical history and family history. On general examination, the vitals were stable. On clinical examination, there was abdominal distension and mild tenderness.

A computed tomography abdomen showed a solid cystic mass lesion involving the wall of the stomach and tail of the pancreas. Radiological gross differentials included a gastrointestinal stromal tumor (GIST) and neuroendocrine tumor; however, a pancreatic neoplasm was to be excluded from the study.

The patient underwent distal pancreatectomy, splenectomy, and sleeve gastrectomy. On gross examination, a large 10.7 cm lesion involving both the stomach wall and the pancreas was present. The lesion was both solid and cystic and reached up to the muscularis propria of the stomach also involving the pancreas. Resection margins appeared free (Fig. 1).

Microscopic examination of the lesion showed a partly circumscribed solid-cystic tumor composed of small oval to plasmacytoid cells with salt-pepper chromatin. The tumor is arranged in rosettoid, nested, and solid pattern. There was extensive necrosis. Mitoses were present (4/10 hpf). Adjacent pancreas showed Islet cell hyperplasia (Figs. 2 and 3).

Based on the above features, microscopic differentials of a neuroendocrine tumor and solid pseudopapillary neoplasm were kept. On having a closer look, rosettes comprised both true rosettes with a lumen and pseudorosettes around the blood vessels (Fig. 3c). Solid pseudopapillary neoplasms show pseudopapillae which have no true lumen and arise because only the cells around the blood vessels remain due to the adequate blood supply, while rest undergo necrosis. Furthermore, the age of the patient favored the final diagnosis of the neuroendocrine tumor as solid pseudopapillary neoplasms are mostly seen in young women of the second decade. We reported the tumor as a "cystic well-differentiated pancreatic neuroendocrine tumor, grade 2"

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Correspondence to: Dr. Hareesh Chandran, Royal Meadows, KAU Post, Thrissur - 680 656, Kerala, India. E-mail: hareesh0300@gmail.com

arising from the tail of the pancreas involving the stomach wall. Lymphovascular invasion and necrosis were present. Adjacent pancreas showed islet cell metaplasia. Resection margins were free and two lymph nodes/tumor deposits were seen. These features correspond to the TNM stage of pT4N1Mx.

The patient was referred to another center for immunohistochemical study, that is, CD56, synaptophysin, chromogranin, CD10, Ki-67, and further treatment. Her markers were positive for synaptophysin, chromogranin, and cd56. Ki-67 was 3%. The patient underwent frequent follow-up. The patient is currently cured of the disease and doing well.

DISCUSSION

Neuroendocrine tumor of the pancreas is a rare tumor mostly seen after the fifth decade. The incidence does not vary with population and is around 1 in 100,000 population. The syndromic association is frequent and includes multiple endocrine neoplasia and Von Hippel–Lindau syndrome [3]. Our case was sporadic and showed no other site of the tumor.

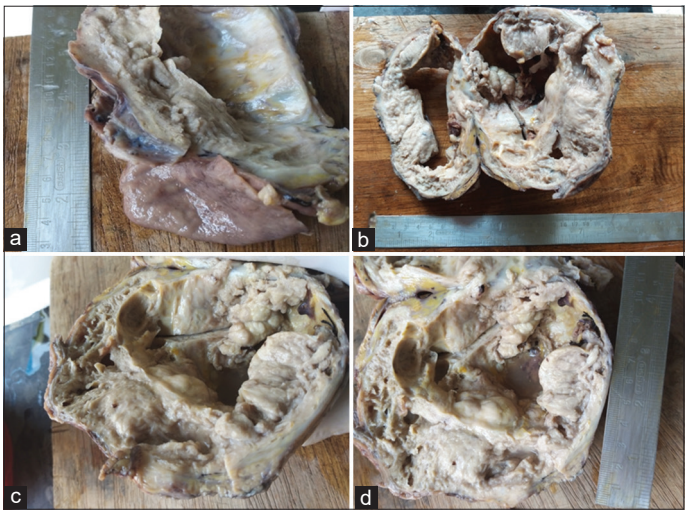

Figure 1: (a) Solid cystic tumor with overlying stomach mucosa; (b) tumor with pancreas and the stomach; (c) tumor with the pancreas and stomach involving adjacent fat; (d) pancreatic tumor

Neuroendocrine tumors of the pancreas are mostly non-functional (around 60%) and the rest being functional, which includes insulinoma, glucagonoma, somatostatinoma, or VIPomas. Of these, insulinomas show the frequent presence of amyloid while somatostatinomas show psammoma bodies. Our case was of a non-functional tumor. Clinical clues to diagnosis could be recurrent hypoglycemia episodes without known cause as a part of Whipple's triad for insulinomas. Glucagonomas are much rarer and present with the opposite, that is, hyperglycemia. Usually, the patient had no history of diabetes but rapidly developed over a period of a few months. Gastrinomas can present with peptic ulcers, while the vasoactive intestinal peptide secreting tumors (VIPomas) present with diarrhea and metabolic disturbances. Somatostatinomas can present with weight loss and diabetes. A much rarer tumor is a pancreatic polypeptide secreting tumor. While these tumors are commoner in the pancreas, neuroendocrine tumors at other sites can be adrenocorticotrophic hormone secreting or even renin secreting. Clinical clues such as these can be valuable pointers to the neuroendocrine nature of the tumor.

Other important features include the age of the patient, where neuroendocrine tumor predominates in the elderly. While neuroendocrine tumors are specific to diagnose, it is important to understand that the prognosis varies widely based on the pathological features, the most important being gross staging and microscopic grading [4-6].

Grossly, when we get a mass lesion involving multiple organs comprising stomach, pancreas, and spleen, while such spread indicates an aggressive tumor. Differential diagnosis is fairly broad encompassing that includes GISTs because of the

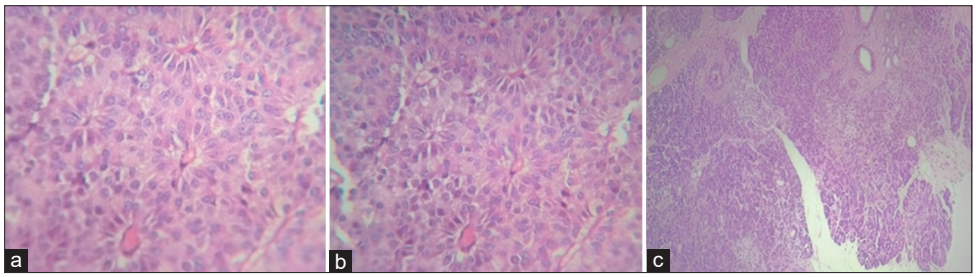

Figure 2: (a) Rosettes, monotonous cells with salt-pepper chromatin; (b) mitotic figures 4/10 hpf; (c) pancreas with islet cell hyperplasia

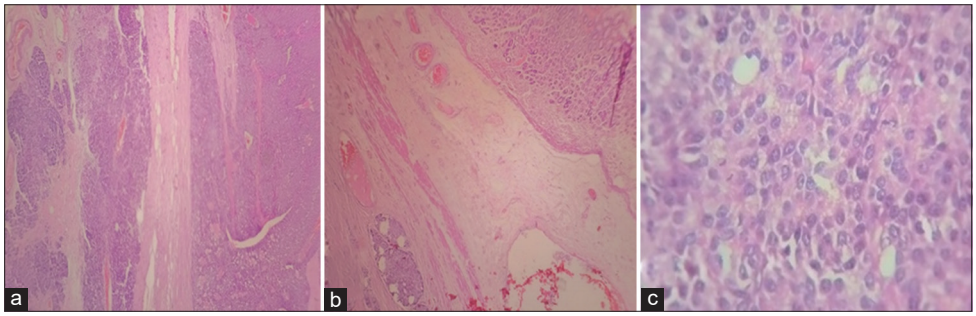

Figure 3: (a) Tumor with pancreas; (b) tumor involving the stomach wall; (c) true rosettes with central lumen

stomach wall involvement, while other entities being a pancreatic adenocarcinoma, which is the most common pancreatic malignancy. Tumor margins, necrosis, and lymph nodes should be carefully looked for. Also important is to look for secondary tumors or concurrent tumors. Insulinomas are known to arise as multiple small pancreatic tumors called microadenomas, size criteria being <0.5 cm.

Microscopic features of neuroendocrine tumors include cells with stopped or powdery fine chromatin and neuroendocrine patterns which include organoid, rosettoid, and nested form. One has to look for the presence of lymphovascular emboli. Our case had multiple emboli which usually indicate a higher incidence of recurrence. Features of a bad tumor include highly pleomorphic cells, increased mitosis, and necrosis. Ki-67 is used as a prognostic factor in addition. Hotspots are used to determine both mitosis and Ki-67 count.

Grading of neuroendocrine tumors includes well-differentiated, Grade 1 – <2 mitoses/10 Hpf or Ki 67 <3%, well-differentiated, Grade 2 – 2–20 mitoses/10 Hpf or Ki 67 -3 to 20%, well-differentiated, Grade 3 – >20 mitoses/10 Hpf or Ki 67 >20%, and poorly differentiated neuroendocrine carcinoma [6-9].

Thus, neuroendocrine tumors are diagnosed and prognosticated based on microscopy. Additional immunohistochemical stains include cd56 (also called neural cell adhesion molecule, synaptophysin, and chromogranin which serve as useful adjuncts to confirm the diagnosis, especially when morphology is confusing). The tumors we excluded include solid pseudopapillary tumor which is seen in young women (20s) and acinar cell carcinoma of the pancreas [10].

CONCLUSION

Neuroendocrine tumors are rare tumors with common morphology but arise in different sites**.** Functional symptoms, age of the patient, syndromic association, and site of the tumor can be helpful clues. Staging, pathological grading, tumor excision with clear margins, and lymphovascular invasion determine prognosis.

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