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Case Report

Duodenal Neuroendocrine Tumour: An Incidental Discovery of an Indolent Disease

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Abstract

Neuroendocrine neoplasms arise from the neuroendocrine cells distributed throughout the body. Duodenal neuroendocrine neoplasms are rare. Most of these are nonfunctional and therefore present with nonspecific symptoms or with clinico-pathological features unique to their location. The management of neuroendocrine tumours is dependent on its grade and stage. Classification of neuroendocrine tumours and hence its grading has been updated multiple times. Here we present a patient who complained of very non specific upper gastrointestinal symptoms and was found to have a duodenal polyp on endoscopy which was diagnosed by histology and immunohistochemistry as a grade three neuroendocrine tumour according to the latest WHO classification (2022).

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Introduction

Neuroendocrine neoplasms (NENs) are a heterogenous collection of tumours derived from neuroendocrine cells. These cells are widely distributed throughout the body and therefore can give rise to tumours in almost any organ. Some tumours may be functional and produce hormones that give rise to specific symptoms, whereas others may be non-functional and therefore do not produce hormones. Hence, these patients may be asymptomatic or present with symptoms due to the local effects of the tumour. Neuroendocrine neoplasms of the duodenum (dNENs), are rare [1]. Their reported incidence is 0.17 per 100,000 [1]. Here we present a rare case of a duodenal neuroendocrine tumour in a middle-aged man who presented with non-specific upper gastrointestinal symptoms.

Case Report

A 65-year-old man presented with dyspeptic symptoms and on-and-off melena of one year duration. He was otherwise well with no comorbidities. All parameters of his full blood count were within the normal range. Upper gastrointestinal endoscopy revealed antral gastritis and a polyp in the first part of the duodenum (Fig 1A). Histology of this patient's polyp showed nests of cells in the mucosa, muscularis mucosa and submucosa (Fig 1B). The constituent cells had round

to oval nuclei with stippled chromatin and moderate amounts of cytoplasm. There was no necrosis, apoptosis was minimal, and mitoses were 23 per 2 mm^2. Immunohistochemistry showed strong cytoplasmic positivity for chromogranin (Fig 1C) and strong membrane positivity for synaptophysin (Fig1 D). The Ki 67 index was 24% (Fig 1E). Therefore, this was diagnosed as a grade 3 neuroendocrine tumour. Contrast-enhanced Computed Tomography (CECT) of chest, abdomen and pelvis showed residual tumour within the duodenal wall and a small nodule in the left lobe of the lung, suspicious for metastasis. The pelvis showed no evidence of tumour deposits. A distal gastrectomy with gastrojejunostomy reconstruction was done. We received the distal part of the stomach and the duodenum for histopathology. Macroscopically, a tumour was not identified in the duodenum. Therefore, the entire duodenum was serially sectioned and processed. No lymph nodes were retrieved. Microscopy showed residual grade 3 neuroendocrine tumour in three of the sections. The tumour extended into the superficial muscularis propria and was staged as pT2. The patient recovered from the surgery but unfortunately died 11 days post op due to a cerebrovascular accident.

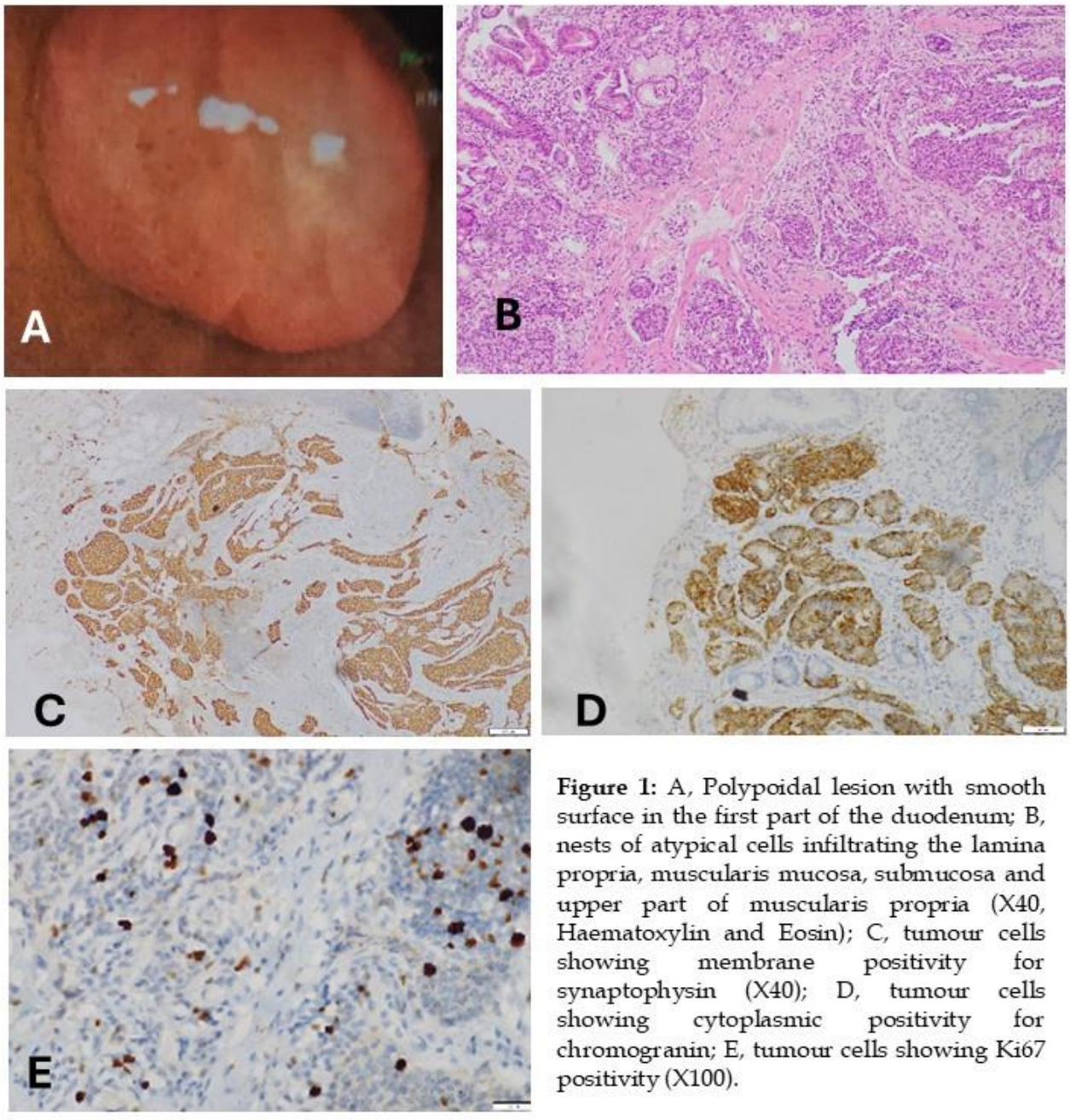

Figure 1: A, Polypoidal lesion with smooth surface in the first part of the duodenum; B, nests of atypical cells infiltrating the lamina propria, muscularis mucosa, submucosa and upper part of muscularis propria (X40, Haematoxylin and Eosin); C, tumour cells showing membrane positivity for synaptophysin (X40); D, tumour cells showing cytoplasmic positivity for chromogranin; E, tumour cells showing Ki67 positivity (X100).

Discussion

This 65-year-old man presented with dyspeptic symptoms and the endoscopy revealed a duodenal polyp which was diagnosed as a Grade 3 neuroendocrine tumour (NET) according to the current WHO classification. CECT showed residual tumour in the duodenal wall and a small nodule suspicious for metastasis in the left lung. A distal gastrectomy with gastrojejunostomy reconstruction was done, and the tumour was staged as pT2.

Neuroendocrine neoplasms (NENs) are a heterogenous collection of tumours derived from neuroendocrine cells that are distributed widely throughout the body. They are epithelial neoplasms showing predominant neuroendocrine differentiation. They can occur in most organs. While some clinico-pathological features of these tumors are unique to the site of origin, other characteristics are shared regardless of the site.

Our patient showed a duodenal polyp on endoscopy. Most duodenal polyps are of the non neoplastic type and include inflammatory polyps, hyperplastic polyps, Brunner gland adenomas and hamartomas. The commonest neoplastic polyp is an adenoma. Neuroendocrine neoplasms of the duodenum (dNENs) are rare tumours that account for 2.7% of all NENs [1]. These tumours can be of the non functioning or functioning type. In the last 20 years the proportion of detected non-functioning dNENs have increased and is currently the most prevalent type [1]. This is mainly due to increased incidental detection of these tumours at endoscopy [1]. Non functioning dNENs may be asymptomatic or present with symptoms related to bleeding or mass effect such as obstruction and jaundice [2,3]. Functioning NENs cause symptoms related to the hormone it secretes e.g. Gastrinomas cause Zollinger-Ellison syndrome Somatostatinomas rarely cause somatostatinoma syndrome and carcinoids can cause carcinoid syndrome, if liver metastasis is present.

The classification of NEN has been updated multiple times. The latest update was in 2022 being the WHO Classification of Endocrine and NEN. Accordingly, tumor cells that retain the morphological features of neuroendocrine cells and are well differentiated are termed neuroendocrine tumours (NETs) [3]. Neuroendocrine carcinomas (NECs) are poorly differentiated and can be either of the large cell or small cell type [3,4]. Molecular data are not available for sporadic duodenal NENs as of yet [2].

Duodenal NENs are usually small in size and limited to the mucosa and submucosa. However, 40–60% of cases show metastasis to the regional lymph nodes [3]. Most dNENs are low-grade and well differentiated (50–70%), whereas a minority of these tumours (<3%) can be high-grade–poorly differentiated [3].

Neuroendocrine tumours can also occur in the context of genetic conditions. Duodenal gastrinomas occurring in multiple endocrine neoplasia 1 (MEN 1) and duodenal somatostatinomas associated with neurofibromatosis 1 are such examples [3].

Diagnosis is made using a combination of clinical features, tumour markers, imaging and histology with immunohistochemistry.

Biomarkers in blood and urine can be used for diagnostic purposes as well as for following up patients with established disease. Serum levels of Chromogranin A (CgA) is the most important serum biomarker [5]. CgA is present in the dense secretory granules of neuroendocrine cells. It is a moderately sensitive marker, the specificity of which relies on the tumour burden [5]. Significantly elevated CgA levels are unlikely to be due to other tumours. However false positive CgA elevations are seen in patients taking proton pump inhibitors, renal disease, uncontrolled hypertension and pregnancy. 5-hydroxyindolacetic acid (5HIAA) is the urinary metabolite of 5-hydroxytryptamine. Urinary levels of 5 HIAA is a biomarker that has proven great value in the diagnosis and follow up of patients with carcinoid syndrome. For functional tumours, the related specific hormones can be measured e.g. glucogen in glucogonoma and gastrin in gastrinoma.

Imaging modalities used include Computed Tomography (CT), MRI and ultrasound. Cross sectional imaging is essential for diagnosis [5]. Contrast enhanced CT (CECT) of the chest abdomen and pelvis is the conner stone in diagnosis, staging and follow up of NENs [5]. MRI is superior to CT in assessing bone, brain and abdominal disease [5]. 68Ga-Dotatate PET/CT scan is the current investigation of choice for well differentiated NENs [5]. 68Ga-Dotatate which is injected as a tracer, is subsequently taken up by the somatostatin receptors in the body including those in neuroendocrine tumours. The scan shows where the tracer has accumulated in the body, thereby enabling visualisation of the primary tumour as well as the metastatic deposits. 68Ga-Dotatate scan is not available in Sri Lanka at the moment.

Histopathology is the gold standard for diagnosis of NENs. In addition to the conventional H&E analysis, immunohistochemistry with synaptophysin, and chromogranin A (CgA) is also required. Well differentiated NETs are graded depending on the number of mitotic figures per 2mm^2 and the Ki 67 index into grade 1 or low grade (< 2 mitoses/2 mm^2, Ki67 index: < 3%), grade 2 or intermediate grade (2 - 20 mitoses/2 mm^2, Ki67 index: 3 - 20%) and grade 3 or high grade, (> 20 mitoses/2 mm^2, Ki67 index: > 20%) [2,3]. NECs show brisk mitoses and necrosis [4]. The Ki 67 value of a NEC is >20% and may even be >70%. NECs are further classified as small and large cell types.

The prognosis of dNENs depend on a number of factors such as tumour size, histological type, depth of invasion, mitotic activity, presence of lymph node metastasis and liver metastasis. Though this patients duodenal polyp was less than 10mm in maximum dimension, The fact that it was a grade 3 neuroendocrine tumour that extended into the muscularis propria (pT2) were adverse prognostic features.

Management of duodenal neuroendocrine tumours is not standardized [6]. The management depends on the tumour size, depth of invasion and the presence or absence of nodal and distant metastasis. The mainstay of treatment has been surgery. This includes endoscopic resection for lesions less than 1-2cm and surgical resection for larger lesions [6]. Adjuvant systemic chemotherapy is used in high grade tumours as well as tumours with metastasis [7]. As this patient had a grade 3 tumour and as there was residual tumour following polypectomy, a distal gastrectomy with gastrojejunostomy reconstruction was done. It was planned to follow up the patient on discharge in order to further investigate the suspicious lesion seen on CECT in the lung. However, unfortunately the patient died 11 days post op due to a cerebrovascular accident.

Conclusion

Duodenal neuroendocrine neoplasms are rare tumours that can present with non-specific symptoms. The criteria for histological diagnosis have been updated on multiple occasions, making it challenging for pathologists to give a diagnosis that is durable and reliable over time. The lack of standardized management protocols makes it challenging for the clinician to offer the best treatment. Therefore, establishment of clear, evidence based guidelines are urgently needed to enhance and facilitate diagnosis and patient management thereby reducing morbidity and mortality associated with this disease.

Consent

As the patient was deceased, informed written consent was obtained from the patient's next of kin (son) for publishing this case report.

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