Case Report

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Duodenal Neuroendocrine Tumour: A Report of Two Cases with Rare Presentations

Surgery Section

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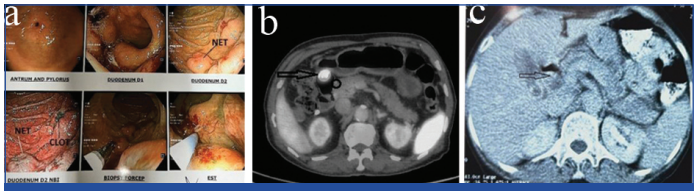
ABSTRACT

Duodenal Neuroendocrine Tumours (D-NETs) are extremely rare tumours with a propensity to be solitary and limited to the first and second parts of the duodenum, the periampullary area contributing to only about 20% of such cases. They can be discovered incidentally at imaging or at Upper Gastrointestinal Endoscopy (UGIE) for vague Gastrointestinal (GI) symptoms. The authors encountered two successive cases (55-year-old female; 50-year-old male) of D-NETs within a couple of months in which one presented with acute upper GI bleeding and another with vague upper GI symptoms. The first case was located at the second part of the duodenum with nodal metastasis, whilst the second case had multiple D-NETs at the second and third parts of the duodenum. Sub-centimetric growths may be treated by endoscopic mucosal resections but larger ones require surgery. Both cases were more than 20 mm in size and were successfully managed by classical Whipple's procedure. Diagnoses were confirmed and graded with histopathology and Immunohistochemistry (IHC) using chromogranin, synaptophysin, and Kiel 67 (Ki67). Normally these are mucosal and submucosal lesions, however, in the first case, the tumour invaded muscularis propria and extended upto subserosa. The authors present these two cases because of their rarity, singular presentations, and successful management in a rural set-up with logistical constraints.

Keywords: Histopathology, Immunohistochemistry, Whipple's procedure

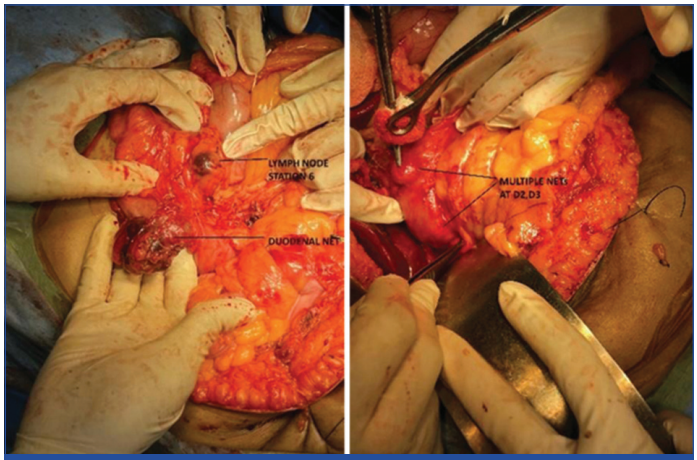
Case 1

A 55-year-old female presented to the Emergency Department with a bout of upper Gastrointestinal (GI) bleeding for one day. There was pallor with a haemoglobin of 7 g/dL. There was no pain in the abdomen or vomiting. Physical examination revealed slight tachycardia with a pulse rate of 100/minute, though the systolic blood pressure was 100 mmHg. Two units of packed red blood cell transfusion stabilised her clinically. Then she underwent Upper Gastrointestinal Endoscopy (UGIE) that revealed a D2 growth that was biopsied followed by endoscopic sclerotherapy [Table/Fig-1a-c]. Liver function tests were normal. Contrast-enhanced Computed Tomography (CECT) revealed a D2 mass (3.3 cm×1.8 cm) with an enlarged infrapyloric (station 6) lymph node [Table/Fig-1b]. She underwent classical Whipple's procedure that confirmed the above findings [Table/Fig-2a]. At the outset of the surgery, the authors excluded metastasis to the 16B1 lymph node on the frozen section. Then the authors performed the superior mesenteric artery first approach to confirm on-table resectability in place of the presence of lymphadenopathy. However, postoperatively she developed diarrhoea which responded to octreotide, though there were no metastases to the liver. Serum markers chromogranin A, 5-hydroxyindoleacetic acid (5-HIAA), and gastrin were normal. She recovered and was discharged on day 28. She was doing well even after six months. The Histopathological Examination (HPE) showed tumour mass composed of cells arranged in nests, sheets, trabecular, and organoid patterns. Cells showed small round to oval nuclei, stippled chromatin, inconspicuous to prominent nucleoli in some cells along with scant to moderate cytoplasm.

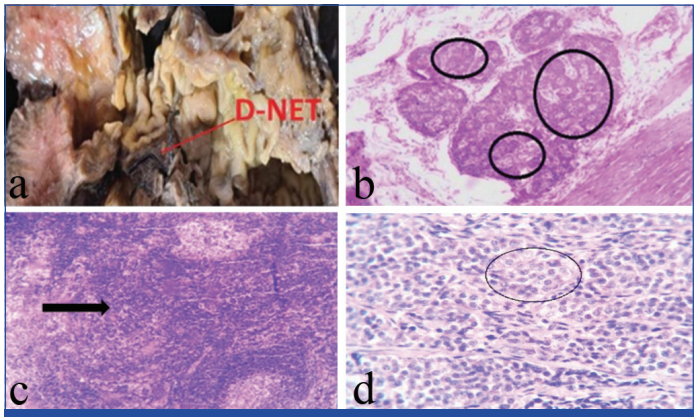


[Table/Fig-1]: a) Case 1: Endoscopy, biopsy, injection sclerotherapy, and Endoscopic Sclerotherapy (EST); b) CT (Case 1): Arrow showing D-NET, circle showing lymph node; c) CT (Case 2): D-NET compressing duodenal lumen.

One infra-pyloric node showed a metastatic deposit [Table/Fig-3a-c]. Immunohistochemistry (IHC) showed positive staining for

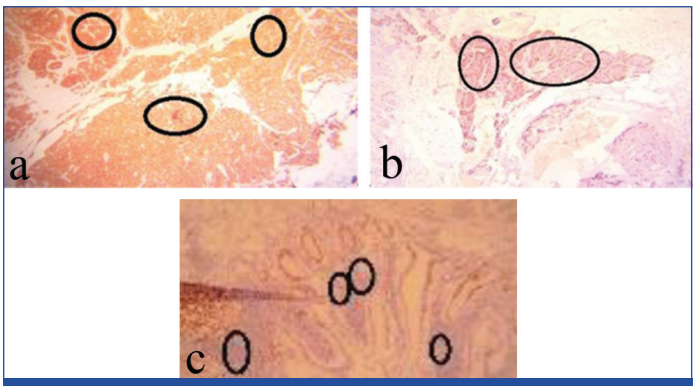


[Table/Fig-2]: Intraoperative findings: a) Case 1: D-NET at D2; metastatic infra-pyloric node; b) Case 2: Multiple D-NETs. (Images from left to right)



[Table/Fig-3]: a) Gross appearance; b) Case 1: Microscopic examination of D-NET (10x). Encircled areas showing trabecular and nesting pattern of neoplastic cells; c) Case 1: Microscopic examination of deposits of D-NET in lymph node. Arrow depicts nodal tumour infiltrate; d) Case 2: Microscopic examination of D-NET (40x). Encircled areas depict insular patterns with stippled nuclear chromatin in neoplastic cells.

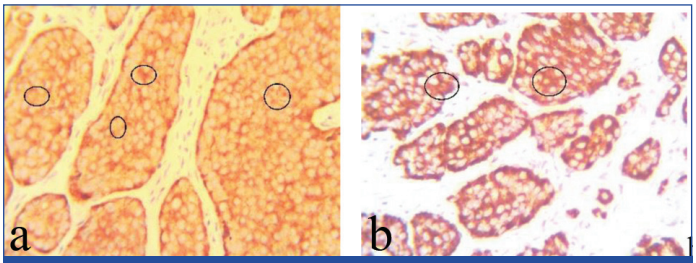
synaptophysin and chromogranin A and Ki67 (<2%) in neoplastic cells [Table/Fig-4]. The final diagnosis was Duodenal Neuroendocrine Tumour (D-NET) grade 1 in D2 (Gr1 pT3N1Mx).



[Table/Fig-4]: Case 1: IHC (10x); a) Synaptophysin: Encircled areas depict synaptophysin cytoplasmic positivity in neoplastic cells; b) Chromogranin A: Encircled areas depict chromogranin A cytoplasmic granular positivity in neoplastic cells; c) Ki67: Encircled areas depict low mitotic activity in neoplastic cells (<2%). IHC: Immunohistochemistry

Case 2

A 50-year-old male presented with epigastric pain of two weeks duration to the surgery Outpatient Department (OPD). The pain was not associated with any exacerbating or relieving factor, nor was it associated with vomiting. There was no similar past history of pain or any other illness. All the members of the family were healthy. He had a history of recent weight loss. The left mid-arm circumference was 22 cm. Examination of the abdomen revealed mild hepatomegaly. There was hypoalbuminemia (serum albumin 2.8 g/dL) with a slight increase in serum alkaline phosphatase, though there was no history of jaundice. Serum markers were normal. CECT revealed a 2.2 cm×1.2 cm growth in D2 and two smaller growths at the junction of D2 and D3 [Table/Fig-1c] and that was confirmed at surgery [Table/Fig-2b]. Classical Whipple's procedure was performed here too that was largely uneventful in the postoperative phase. However, he received hyperalimentation and albumin infusion on postoperative days 2 and 3 and was discharged on day 21. There was no recurrence six months post-discharge. Laboratory reports were normal at discharge. HPE [Table/Fig-3d] and IHC [Table/Fig-5 a,b] were similar to case one except for the absence of nodal metastases (Gr1 pT2N0Mx).



[Table/Fig-5]: Case 2: IHC (40x). a) Synaptophysin: Insular patterned neoplastic cells with cytoplasmic positivity, highlighted by the circles; b) Chromogranin A: Neoplastic cells depicting cytoplasmic granular positivity, highlighted by the circles. IHC: Immunohistochemistry

DISCUSSION

The D-NETs are rare neoplasms that are occasionally noticed while performing UGIE. The incidence of D-NETs is 0.19/100,000 in the United States [1]. England and Japan have a lower prevalence with only 0.04 per 100,000 and 0.17 per 100,000, respectively [2,3]. In a multicentre study from a web-based registry, patients were divided into three cohorts-those diagnosed from 2001 to 2005, from 2006 to 2010, and from 2011 to 2016. Of the 407 cases registered, 37 were in Cohort I, 136 in Cohort II, and 234 in Cohort III. So it appears that D-NETs are on the rise in India [4].

They are commonly seen in the 6th decade of life and male predominance is observed (1.5:1) [1]. Both the cases in the present study were in the sixth decade, one female and one male. Kaliounji A et al., encountered a female patient in the 7th decade [5], whereas Malladi UD et al., found five cases of D-NETs, age ranging from 35-57 years all of whom were males and Wang X et al., found a male in the sixth decade [6,7]. Of all GI D-NETs, the ileum is the commonest site of occurrence and duodenum is the least common amounting to 2-3% [8]. First and second portions of the duodenum (D1, D2), are commonly involved and periampullary region is involved in 20% of the cases [9-12]. They are at times discovered incidentally in about 15% to 33% of cases [10,11,13]. Hoffmann KM et al., stated that if the tumour is under 1 cm it can be resected endoscopically, while the larger ones require surgical resection [8]. Irrespective of this evaluation, there is no agreement about the perfect treatment approach for D-NETs [8].

The present cases were however distributed to the D2, D3. The patient of Kaliounji A et al., had a D-NET at D2, whereas the patient of Wang X et al., had a tumour at the ascending portion of D2 extending into the jejunum [5,7]. All the patients of Malladi UD et al., had their tumours at D1, except one which was located in D2 [6].

They are usually small and solitary tumours, with around 75% of them smaller than 20 mm in size [9,10]. Both of the present cases had D-NETs whose sizes were >20 mm and the second case had multiple D-NETs. Kaliounji A et al., found the size > 30 mm, and Malladi UD et al., found that all were sub-centimetric, except one which was large [5,6]. Wang X et al., found a large tumour of about 6 cm [7]. CECT can be used to determine the primary site, but only histopathology can determine the specific type. Most of them are localised to mucosa and submucosa of the gut [9,10]. But in the first case, the tumour had invaded through the muscularis propria up to the sub-serosa of duodenum. Kloppel G et al., and Norton JA et al., declared that there is an incidence of about 40-60% of nodal information at the detection of D-NETs [14,15]. However, liver secondaries at diagnosis were recorded as <10% by Hoffman KM et al., [8]. The current World Health Organisation (WHO) classification includes three grades, based on the number of mitotic figures in the tumour cells/ Ki67 index: Grade 1 (G1), the number of mitotic figures is <2/2 mm^2 or Ki67 index is <3%; Grade 2 (G2), the number of mitotic figures is 2 to 20/2 mm^2 or Ki67 index is 3% to 20%; and Grade 3 (G3), the number of mitotic figures is >20/2 mm^2 or Ki67 index is >20% [6].

Neuroendocrine Carcinomas (NECs) are poorly differentiated tumours and are now separately grouped as small and large-cell types [6]. The five-year survival rate is 80%-85% in individuals with a well-differentiated D-NET [9]. Both the patients in the present study were discharged albeit after a prolonged recovery and were doing well till the last follow-up at six months post-discharge from the hospital.

CONCLUSION(S)

Mostly asymptomatic, their clinical presentation is varied. So it is important to consider it in the differential diagnoses of vague GI symptoms. An increase in UGIEs has led to improved rates of discovery, which are later confirmed by HPE and IHC. Even then, it is such a rare entity that its diagnosis may be overlooked. The authors have presented these two cases because of their rarity and successful management. Singularities observed were that both cases had tumours >20 mm with distribution in the second and third parts of the duodenum.

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REFERENCES

[1] Yao JC, Hassan MM, Phan AT, Dagohoy CG, Leary CC, Mares JE, et al. One hundred years after "Carcinoid": Epidemiology of and prognostic factors for neuroendocrine tumors in 35,825 cases in the United States. J Clin Oncol. 2008;26:3063-72.

[2] Ellis L, Shale MJ, Coleman MP. Carcinoid tumors of the gastrointestinal tract: Trends in incidence in England since 1971. Am J Gastroenterol. 2010;105(12):2563-69.
[3] Ito T, Sasano H, Tanaka M, Osamura RY, Sasaki I, Kimura W, et al. Epidemiological study of gastroenteropancreatic neuroendocrine tumors in Japan. J Gastroenterol. 2010;45(2):234-43.
[4] Palepu J, Shrikhande SV, Bhaduri D, Shah RC, Sirohi B, Chhabra V, et al. Trends in diagnosis of gastroenteropancreatic neuroendocrine tumors (GEP-NETs) in India: A report of multicenter data from a web-based registry. Indian J Gastroenterol. 2017;36(6):445-51. Doi: 10.1007/s12664-017-0808-7. Epub 2018 Feb 19. PMID: 29457213.
[5] Kaliounji A, Alkoutami S, Farraj M, Kaliounji H, Farraj KL. A rare presentation of a duodenal neuroendocrine tumor. Cureus. 2023;15(1):e33747. Doi: 10.7759/cureus.33747. PMID: 36788876; PMCID: PMC9922524.
[6] Malladi UD, Chimata SK, Bhashyakarla RK, Lingampally SR, Venkannagari VR, Mohammed ZA, et al. Duodenal neuroendocrine tumor-tertiary care centre experience: A case report. World J Transl Med. 2023;11(1):01-08. Doi: 10.5528/wjtm.v11.i1.1.
[7] Wang X, Wu Y, Cao X, Zhang X, Cheng Y, Kong L. Duodenal neuroendocrine tumor: A rare case report. Medicine (Baltimore). 2021;100(6):e24635. Doi: 10.1097/MD.0000000000024635. PMID: 33578581; PMCID: PMC7886419.
[8] Hoffmann KM, Furukawa M, Jensen RT. Duodenal neuroendocrine tumors: Classification, functional syndromes, diagnosis and medical treatment. Best Pract Res Clin Gastroenterol. 2005;19(5):675-97.
[9] Soga J. Endocrinocarcinomas (carcinoids and their variants) of the duodenum. An evaluation of 927 cases. J Exp Clin Cancer Res. 2003;22(3):349-63. Available from: https://pubmed.ncbi.nlm.nih.gov/14582691/.
[10] Witzigmann H, Loracher C, Geissler F, Wagner T, Tannapfel A, Uhlmann D, et al. Neuroendocrine tumours of the duodenum. Clinical aspects, pathomorphology and therapy. Langenbecks Arch Surg. 2002;386:525-33.
[11] Zyromski N, Kendrick ML, Nagorney DM, Grant CS, Donohue JH, Farnell MB, et al. Duodenal carcinoid tumors: How aggressive should we be? J Gastrointest Surg. 2001;5(6):588-93.
[12] Rossi RE, Rausa E, Cavalcoli F, Conte D, Massironi S. Duodenal neuroendocrine neoplasms: A still poorly recognized clinical entity. Scand J Gastroenterol. 2018;53(7):835-42.
[13] Margonis GA, Samaha M, Kim Y, Postlewait LM, Kunz P, Maithel S, et al. A multi-institutional analysis of duodenal neuroendocrine tumors: Tumor biology rather than extent of resection dictates prognosis. J Gastrointest Surg. 2016;20(6):1098-105.
[14] Klöppel G, Perren A, Heitz PU. The gastroenteropancreatic neuroendocrine cell system and its tumors: The WHO Classification. Ann NY Acad Sci. 2004;1014:13-27.
[15] Norton JA, Alexander HR, Fraker DL, Venzon DJ, Gibril F, Jensen RT. Does the use of routine Duodenotomy (DUODX) affect rate of cure, development of liver metastases, or survival in patients with Zollinger-Ellison Syndrome? Ann Surg. 2004;239:617-26.

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