Rectal MiNEN: A rare case series

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ABSTRACT

Rectal mixed neuroendocrine non-neuroendocrine neoplasms (MiNEN) are rare tumors with two components, neuroendocrine and non-neuroendocrine, each comprising 30% of all tumors. There have been limited studies on the epidemiology, clinical and prognostic characteristics of these tumors. Here, we report a case series of two cases of rectal MiNEN from a tertiary care center in North East India. These tumors are known to be aggressive and often with poor prognosis.

Key words: Histopathology, Immunohistochemistry, Mixed neuroendocrine non-neuroendocrine neoplasms, Rectal

Mixed neuroendocrine non-neuroendocrine neoplasms (MiNEN) of the gastrointestinal tract are rare, and until now, only few case reports and small case series are available in the literature. MiNENs represent a rare category of neoplasms that account for an incidence of 0.01/100,000 population per year [1]. The current terminology was given by the World Health Organization classification of digestive tract (2019), where each component must constitute at least 30% [2]. The use of immunohistochemistry has allowed the diagnosis of such cases. The non-neuroendocrine component can be squamous cell carcinoma or more often adenocarcinoma. The neuroendocrine component can be a neuroendocrine tumor or neuroendocrine carcinoma based on the mitotic count and Ki-67 index. The two components can be closely intermingled (composite tumors) or are present as separate components within the tumor (collision tumor) [3]. Colorectal MiNENs seem to have a prevalence of only 3.2% and are diagnosed generally in late stages [4]. Knowledge about the epidemiological and clinical properties of these tumors has been described in very few studies to date [5,6].

CASE SERIES

Case 1

A 78-year-old lady presented with complaints of loose stools along with blood and mucus for 6 months. She went to the local physician and was advised of some medications for the same but as her symptoms were not relieved, she visited our center.

At our center, after a general examination, she was advised contrast-enhanced computed tomography (CECT) scan of the abdomen. CECT scan showed asymmetrical circumferential polypoidal-nodular wall thickening of 16 mm involving the distal rectum and causing significant luminal narrowing with perirectal infiltration. Regional lymph nodal was enlarged. A colonoscopic biopsy was done and was reported as a neoplasm with neuroendocrine features. Immunohistochemistry was done and synaptophysin was positive along with Ki-67 of 97%.

The patient was given neoadjuvant chemoradiation. Magnetic resonance imaging pelvis was done, and circumferential thickening involving the proximal and middle one-third of the rectum was noted with minimal infiltration of peri-rectal fat planes and subserosal rectal tissue along with a few enlarged regional lymph nodes. The patient was prepared for surgery and abdominoperineal resection was done.

A gross examination showed a specimen of APR measuring 22 cm in length. On cut open, an ulceroproliferative tumor was noted measuring 4×2×2 cm in the rectum involving the bowel wall. The cut surface was solid and whitish. The tumor was 13.5 cm from the proximal and 4.5 cm from the distal resection margins. Total mesorectal excision was complete. Twelve lymph nodes were isolated, the largest measuring 0.7×0.5×0.3 cm.

Histopathological examination (HPE) of the tumor showed a mixture of two components, one was non-neuroendocrine (50%) and the other was neuroendocrine (50%). The non-neuroendocrine component was well-differentiated adenocarcinoma and the neuroendocrine component was

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large-cell neuroendocrine carcinoma. The mitotic rate was 60/10 HPF. Scanty foci of necrosis were seen. The tumor was infiltrated up to the perimuscular connective tissue. The morphology was consistent with MiNEN (Fig. 1). Lymphovascular invasion was seen and perineural invasion was not seen. Both resection margins were free of tumors. Isolated 12 lymph nodes were free of tumors.

Case 2

A 27-year-old male presented with complaints of on-and-off loose stools with blood for 3 months.

On general examination, the patient was pale and cachectic. A digital rectal examination was done and a mass was identified. A true cut biopsy was sent for HPE.

Gross examination showed three grey-white linear cores, the longest measuring 1 cm in length. All tissues were processed. HPE showed a high-grade biphasic malignant neoplasm with epithelial and neuroendocrine features (Fig. 2). IHC showed synaptophysin, cytokeratin, and CD117 positivity and vimentin negativity (Fig. 3). HPE and IHC suggested mixed neuroendocrine and non-neuroendocrine neoplasm.

DISCUSSION

Neuroendocrine neoplasms are a rare and heterogenous group of tumors arising from multiple anatomic sites with characteristic histology and immunohistochemistry. MiNEN express a wide spectrum of biomarkers of neuroendocrine differentiation (Chromogranin A, CD56, and synaptophysin) on the neuroendocrine compartment, as well as, site-specific markers such as CK20 and caudal type homeobox 2 on adenocarcinoma compartment.

Due to non-specific colonoscopic and macroscopic findings, histopathology and immunohistochemistry are crucial from a diagnostic point of view. Endoscopic findings are often as semicircular tumors with deep ulceration or a mass occupying the lumen [7]. Due to the rarity of this diagnosis, the limited published data, and the use of inconsistent terminology, the epidemiology, prognosis, and best therapeutic management of patients with MiNEN remain unknown. However, these tumors are generally associated with aggressiveness and poor prognosis [5,8].

According to a multicentric meta-analysis across five European centers done by Frizziero *et al*., the site of origin of the primary tumor was as follows; appendix 60.3%, colon–rectum 14.5%, colon 11.2%, rectum 1.9%, either colon or rectum 1.4%, stomach 6.7%, esophagus/esophagogastric junction 5.9%, pancreas 3.7%, biliary tract 1.6% (n=39), small bowel <1%, anus <1%, and unknown primary <1%. The majority of the participants were males. Reporting the grade of differentiation of the neuroendocrine component, a large proportion of MiNENs had a grade 3 neuroendocrine component, whereas 4.3% and 3.1% had a grade 1 and a grade 2 neuroendocrine components, respectively. Among MiNENs with a grade 3 neuroendocrine component, the morphological subtype (large cell or small cell), the majority was a large cell. The histology of the non-neuroendocrine component was consistent with adenocarcinoma in the majority of cases. This review also suggested that the biological behavior of MiNENs is mostly driven by the

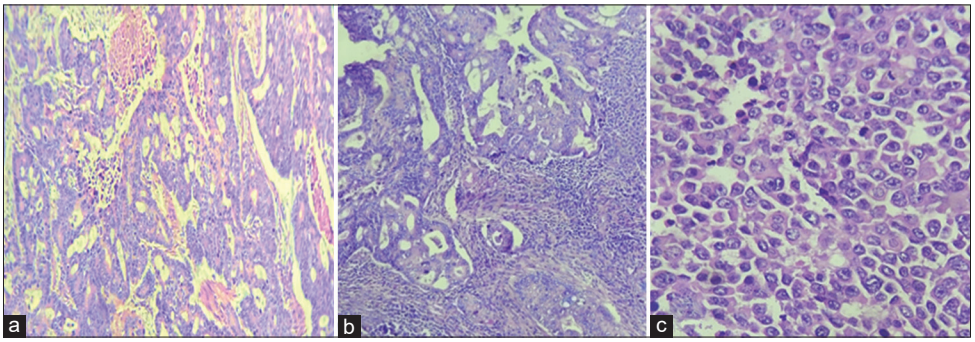

Figure 1: (a) Adenocarcinoma component and neuroendocrine components; (b) mixture of adenocarcinoma and neuroendocrine components; (c) high power view of neuroendocrine component (case 1)

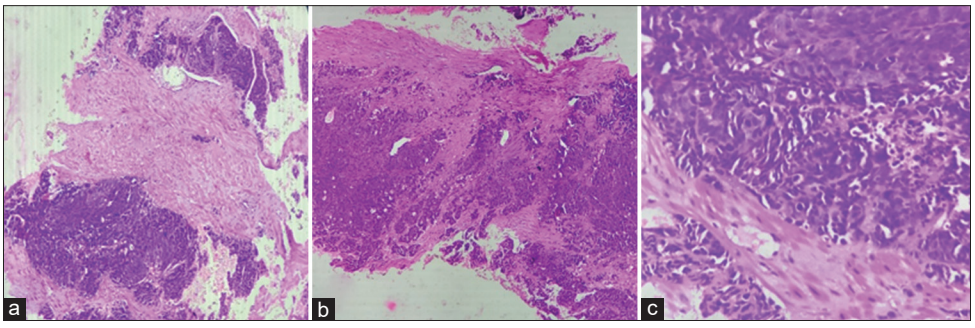

Figure 2: (a) Histopathological examination (b) low power view of both components; (c) high power view of neuroendocrine component (case 2)

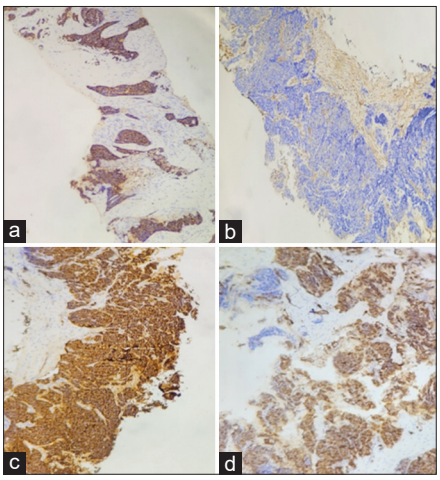

Figure 3: Immunohistochemistry showing (a) CK positivity; (b) vimentin negativity; (c) synaptophysin positivity (d) CD117 positivity (Case 2)

neuroendocrine component, which is poorly differentiated in approximately 90% of cases, and also the same morphology noted in distant metastatic sites [3]. Similar data were also seen in studies done by Zhang *et al*. [9] and La Rosa *et al*. [10].

CONCLUSION

MiNEN are most likely an underestimated entity due to its rarity. Awareness of this entity is key to analyzing histopathology meticulously along with judicious immunohistochemistry. Management of these tumors is challenging and concomitant neoadjuvant and surgery remain the mainstay of treatment. The number of such cases is likely to enrich our knowledge regarding the epidemiology of this rare entity.

REFERENCES

1. Laffi A, Fazio N, Rubino M, Spada F. Mixed Neuroendocrine and Non-Neuroendocrine Neoplasms (Mi NEN). Germany: Springer; 2021.
2. Nagtegaal ID, Odze RD, Klimstra D, Paradis V, Rugge M, Schirmacher P, *et al*. The 2019 WHO classification of tumours of the digestive system. Histopathology 2020;76:182-8.
3. Frizziero M, Wang X, Chakrabarty B, Childs A, Luong TV, Walter T, *et al.* Retrospective study on mixed neuroendocrine non-neuroendocrine neoplasms from five European centres. World J Gastroenterol 2019;25:5991-6005.
4. Silva DJ, Dos Santos J, Vaz AP, Mesquita A. Rectal mixed adenoneuroendocrine carcinoma: Case report. Medicine (Baltimore) 2021;100:e27348.
5. Paspala A, Machairas N, Prodromidou A, Spartalis E, Ioannidis A, Kostakis ID, *et al.* Management of MANEC of the colon and rectum: A comprehensive review of the literature. Mol Clin Oncol 2018;9:219-22.
6. Wang J, He A, Feng Q, Hou P, Wu J, Huang Z, *et al.* Gastrointestinal mixed adenoneuroendocrine carcinoma: A population level analysis of epidemiological trends. J Transl Med 2020;18:128.
7. Tanaka T, Kaneko M, Nozawa H, Emoto S, Murono K, Otani K, *et al.* Diagnosis, assessment, and therapeutic strategy for colorectal mixed adenoneuroendocrine carcinoma. Neuroendocrinology 2017;105:426-34.
8. Khudiakov A, Al-sadawi M, Qin J, Haddadin M, Soroka S, Hartt A, *et al*. Rare case of rectal mixed adeno-neuroendocrine carcinoma. Am J Med Case Rep 2019;207:117-20.
9. Zhang Y, Shang L, Zhang PP, Chen LH, Wang W, Fang C, *et al.* Clinicopathological features and prognostic validity of the European neuroendocrine tumor society (ENETS) and American joint committee on cancer (AJCC) 8th staging systems in colonic neuroendocrine neoplasms. Cancer Med 2019;8:5000-11.
10. La Rosa S, Marando A, Sessa F, Capella C. Mixed adenoneuroendocrine carcinomas (MANECs) of the gastrointestinal tract: An Update. Cancers (Basel) 2012;4:11-30.

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