Doi: 10.32677/IJCR.2017.v03.i02.003 Case Report

A rare case of composite type of gastric mixed adenoneuroendocrine carcinoma

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Received: 16 Jan 2017 *Initial Review: 13 Feb 2017* *Accepted: 01 Apr 2017* *Published Online: 17 Apr 2017*

ABSTRACT

Cancers exhibiting a combination of epithelial and neuroendocrine features can occur in various organs. In the WHO classification of neoplasms of the gastrointestinal tract, such tumors are called “mixed adenoneuroendocrine carcinomas”. They may be composite, combined or amphicrine type. We present here a rare case of composite adenocarcinoma and neuroendocrine carcinoma of stomach.

Keywords: MANEC, Composite tumour, Stomach.

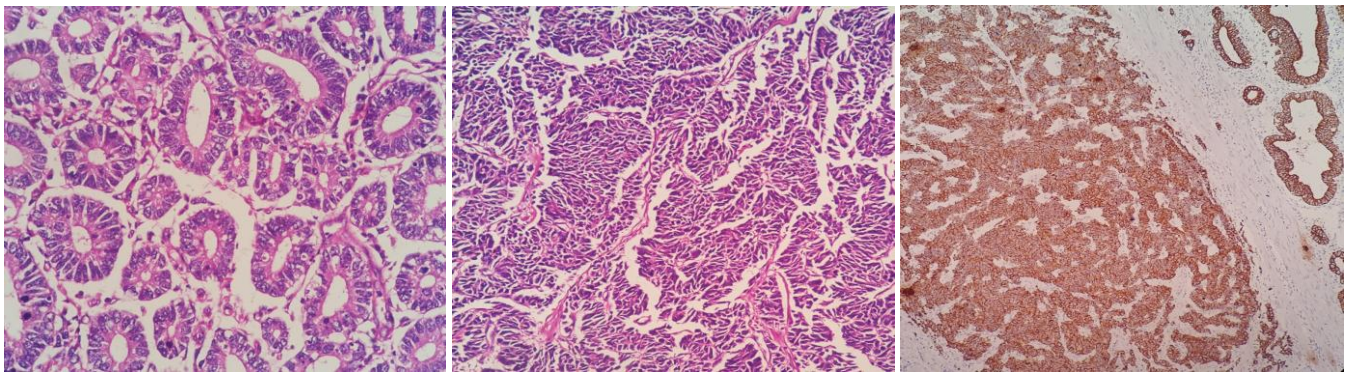
Cancers showing epithelial and neuroendocrine components are seen in gastrointestinal tract, but they are rare in stomach and till 2015, less than 40 such gastric carcinomas have been reported [1]. These are referred to in the WHO classification of tumors of gastrointestinal tract as mixed adenoneuroendocrine carcinomas (MANEC) [2]. It is important to identify this condition and to grade the neuroendocrine component to choose the correct treatment modality. Neuroendocrine carcinoma (NEC) and adenocarcinomatous components are difficult to identify separately by gastroscopy or ultrasound. Hence, histopathology along with immunohistochemistry (IHC) is of paramount importance.

According to the morphological and immuno-histochemical features, they are divided into composite, combined or amphicrine types. In composite or collision tumors, the two components are separate and in combined tumors, the two components are mixed. In amphicrine tumors the same tumor cell shows both exocrine and endocrine features by IHC [2]. While carcinoma with interspersed endocrine cells is the most frequent, the remaining tumors have rarely been reported in the stomach [1]. We report a case of composite type of MANEC.

CASE REPORT

A 56 year old lady presented with pain in the abdomen of more than five months duration. She was a known psychiatric patient on treatment. On general examination, pallor was present. No jaundice or lymphadenopathy noted. Abdominal examination showed a tender mass in the epigastrium. Other systems on examination were within normal limits. A neoplastic lesion was suspected and oesophago-gastroscopy was done. This revealed an ulcer in the antrum with everted edges.

Biopsy was taken which showed adenocarcinoma. CT scan was done and showed focal eccentric wall thickening in antro-pyloric region of stomach implying a malignant lesion. Small perigastric nodes were also noted. Distal radical gastrectomy was done. Macroscopic examination of the specimen showed an ulcero-proliferative neoplasm measuring 3x1.5x1 cm located towards the distal end.



Figures: Fig. 1 - Carcinoma cells arranged in glandular pattern, Fig. 2 - cells with scanty cytoplasm and nucleus showing powdery chromatin arranged in nests, Fig. 3 - carcinoma cells positive for CK

Cut surface was grey white with hemorrhagic areas. Microscopy of the H&E stained sections revealed an invasive adenocarcinoma in the mucosal aspect (**Fig. 1**). Deeper portions showed smaller cells arranged in nests, trabeculae and solid patterns suggesting NEC (**Fig. 2**). Brisk mitotic activity was noted but no necrosis was seen. No lymphovascular emboli or perineural invasion were seen. The neoplasm involved the sub mucosa.

Four out of ten dissected lymph nodes showed neuroendocrine tumour metastasis without adenocarcinoma component. On IHC, both components were positive for cytokeratin (**Fig. 3**). Synaptophysin and chromogranin (**Fig. 4**) were positive in the neuroendocrine component while the adenocarcinoma component was negative. Final diagnosis of MANEC composite type was made on the basis of above mentioned findings.

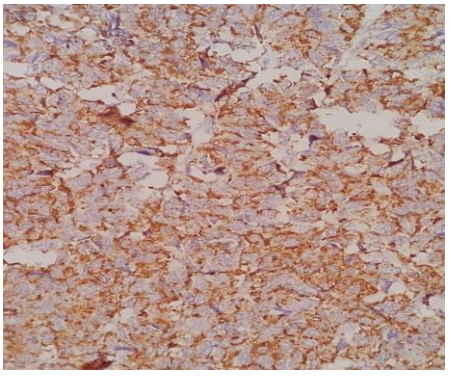


Figure 4 - Neuroendocrine component showing positivity for chromochromogranin

Patient was put on chemotherapy regimen VI B cycle chemo with FOLFOX protocol comprising of injection Oxaliplatin, Inj 5 Flourouracil and Leucovorin. Following this, patient was given adjuvant radiotherapy. Total dose given was 50.Gy/28# to the tumour bed and 45Gy/245# to the subclinical disease areas. Patient is currently on follow up and is doing well.

DISCUSSION

MANECs are of three types. They may be composite or collision neoplasms where the neuroendocrine and exocrine components occur in separate areas of the same lesion or combined neoplasms where they are intimately and diffusely admixed. The third one is the amphicrine type where exocrine and neuroendocrine features are present in the same neoplastic cell and which shows a divergent immunophenotype. There are various hypotheses regarding the histogenesis of MANECs. It may either be the simultaneous proliferation of multiple cell lineages or the proliferation of stem cells capable of differentiating along multiple cell lines [3,4].

The presence of amphicrine type of MANEC supports the hypothesis of common precursor stem cell which can give rise to NEC, squamous cell carcinoma and adenocarcinoma. Chromosomal abnormalities are more in NEC than adenocarcinoma. The risk factors for NEC and adenocarcinoma are said to be the same. This includes hereditary, dietary and environmental factors [3]. The clinical behavior of composite carcinomas depends on the adenocarcinomatous component if the associated endocrine component is well differentiated, and upon the neuroendocrine component if it is poorly differentiated [2].

Our case was MANEC, composite type with the superficial portions showing adenocarcinomatous component and deeper portions showing NEC component.

Nodal metastasis showed NEC component. NEC and adenocarcinomatous components are difficult to identify separately by gastroscopy or ultrasound. So, histopathology along with IHC is confirmatory. Chromogranin and synaptophysin are neuroendocrine markers with high specificity for NEC. MEN1 gene detection and positron emission tomography (PET) scanning have been reported as advanced methods for the diagnosis of NEC and adenocarcinomatous components.

Prognosis is not good for these cases unless they are detected very early. Gastrectomy is the treatment of choice in such cases. In advanced stage, disease platinum based chemotherapy should be considered.

CONCLUSION

We report this case because of its rarity. Multimodal treatment should be the aim for these patients because of the neuroendocrine component of the tumor.

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How to cite this article: Surendran D, Moothiringode S, Kumar A. A rare case of composite type of gastric mixed adenoneuroendocrine carcinoma. Indian J Case Reports. 2017; 3(2): 58-60.

Conflict of interest: None stated, Funding: Nil