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Collision Tumor of the Stomach: Co-Existing Adenocarcinoma And Neuroendocrine Carcinoma: Managed Surgically

[1]Rajesh Dogra, [2]Nina Furia, [3]Harshad Jariwala, [4]Pratik Jariwala, [5]Leena Salunkhe, [6]Kaushik Joshi

Department of Gastroenterology And Dr Jariwal Laboratories , Wockhardt hospitals , The Umrao Institute Of Medical Sciences And Research, Asmita Enclave ,Mira Road (E) , Dist Thane, Mumbai , Maharashtra, P.O. Box 401107, India

Abstract: **Collision tumors are gastrointestinal tumors displaying both exocrine and Neuroendocrine (NE) differentiation. True collision tumors are defined as those in which NETs and conventional carcinomas are closely juxtaposed, but not admixed. These are well recognized, but very uncommon. Recently world health organization has renamed these as mixed Adenocarcinoma Neuroendocrine (MANECs). Gastric MANECs are rare and usually described to be composed of an exocrine component represented by an Adenocarcinoma with a variable grade of differentiation and a neuroendocrine component usually represented by a NEC. We present here a case which presented with dyspeptic symptoms and weight loss. The Esophagogastroduodenoscopy (EGD) revealed a mass at the cardiac end of stomach and at lesser curvature. Also a nodule was identified at the gastric antrum and in 1st part of duodenum. Endoscopic biopsy from cardiac end of stomach and lesser curvature showed features of Adenocarcinoma, while biopsy from nodule in gastric antrum and duodenum was diagnosed as Neuroendocrine carcinoma after confirmation with Immunohistochemistry (Synaptophysin and Chromogranin A.). Subtotal Gastrectomy showed multiple tumors in fundus, body and antrum of the stomach. Microscopy revealed poorly differentiated Adenocarcinoma – Stage: T2bNxMx and Neuroendocrine carcinoma G1. Two hypotheses have arisen to describe the histological origin. One is that are derived from a common multipotential epithelial stem cell, the NEC component resulting from differentiation from the Adenocarcinoma. The second is that Adenocarcinoma and NEC carcinoma arise from a multipotential epithelial stem cell and a primitive NEC, respectively. The clinical behavior of composite carcinomas depends on the poorly differentiated components. Treatment consists of excision of operable / curable tumors.**

Keywords: **mixed tumors of stomach; collision tumors; double tumors; Adenocarcinoma; Neuroendocrine carcinoma; MANEC tumors.**

1. INTRODUCTION

Gastrointestinal tumors displaying both exocrine and neuroendocrine differentiation are well recognized, although uncommon. . Morphologically, such lesions are classified into two subgroups: composite-type tumors, in which both components are mixed haphazardly and collision-type tumors, which are considered as double tumors with a “side by side” pattern. Two hypotheses have arisen regarding the mechanism for the association of Adenocarcinoma and NEC carcinoma. One is that both are derived from a common multipotential epithelial stem cell, the NEC component resulting from differentiation from the adenocarcinoma. The second hypothesis is that adenocarcinoma and NEC carcinoma arise from a multipotential epithelial stem cell and a primitive NEC, respectively.

2. CASE PRESENTATION

A 58 Year female presented with pain in the upper abdomen, vomiting, weight loss and malena. Physical examination revealed –pallor and a vague fullness in epigastrium.

A. *Esophagogastroduodenoscopy (EGD):*

It revealed a huge, fungating , mass at the cardiac end of stomach and lesser curvature. Also a nodule was identified at the gastric antrum and duodenum.

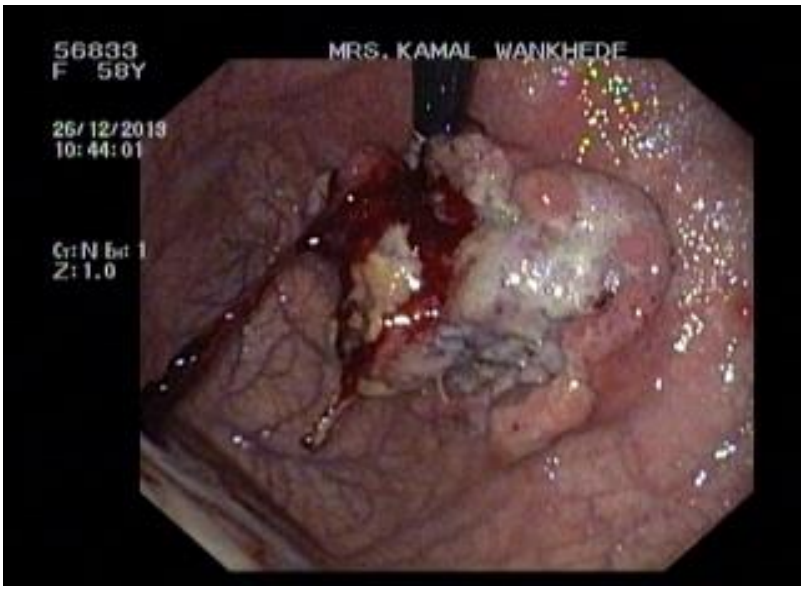

Fig. 1: A huge fungating mass seen along the lesser curvature and fundus with central ulceration and hemorrhage.

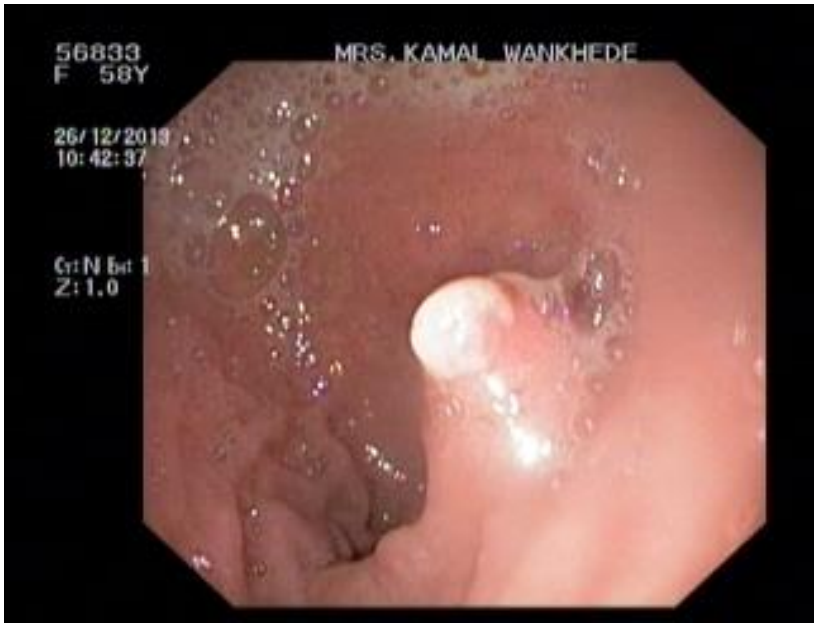

Fig. 2: EGD – one of the polypoid nodules seen along the lesser curvature in body and antrum of stomach

B. Endoscopic biopsy:

It was done from different sites. Biopsy from cardiac end of stomach and lesser curvature showed features of Adenocarcinoma, while biopsy from nodule in gastric antrum and duodenum was diagnosed as Neuroendocrine carcinome after confirmation with Immunohistochemistry (Synaptophysin and Chromogranin A)\

C. Surgery:

Subtotal Gastrectomy was done subsequently. On gross examination, the mucosal surface showed a large fungating mass measuring 9.0x5.0x2.0cm. Cut surface was mucoid, friable, and hemorrhagic and showed variegated appearance, Another tumor measuring 2.5x2.0x1.0 was identified at the pyloric end. Multiple yellowish submucosal nodules were also identified at gastric antrum and body of stomach. Largest measures 1.0 x 1.0 cm. Cut surface is yellowish.

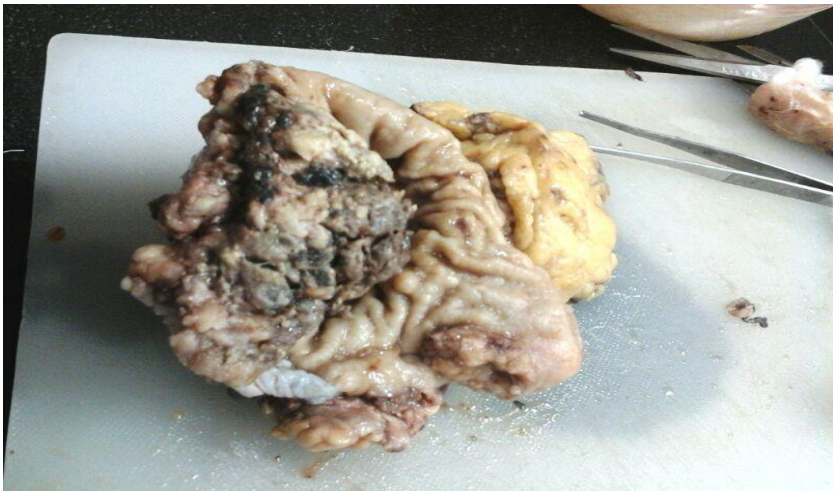

Fig 3: Subtotal Gastrectomy specimen showing a large fungating mass at the cardia.

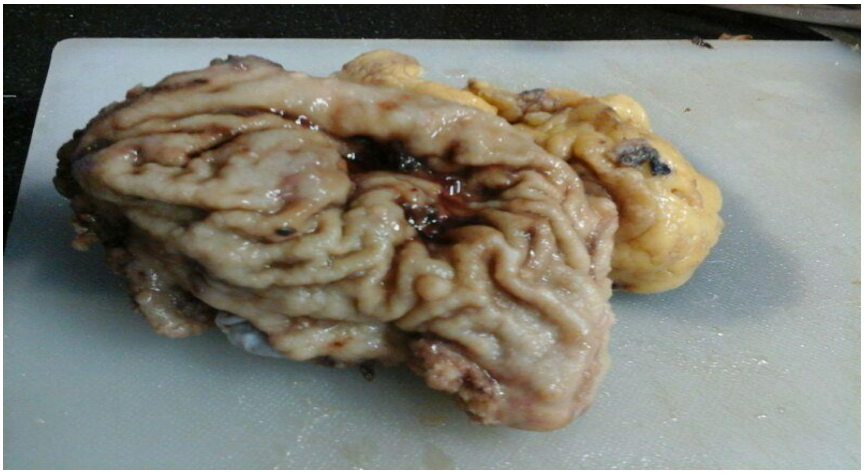

Fig 4: Gross photograph of submucosal nodule at the body of stomach

D. Histopathology:

On microscopic examination, multiple section studied from tumor at cardiac and pyloric end of stomach showed sheets of tumor cells with gland formation and focal mucin secretion. Section from nodules at gastric antrum and body show tumor cells arranged in sheets and rosettes,

Immunohistochemistry showed tumor cells from cardiac end of stomach were positive for Cytokeratin (CK)and negative for Synaptophysin and Chromogranin A, while tumor cells from gastric antrum were positive for Synaptophysin and Chromogranin A and negative for Cytokeratin.

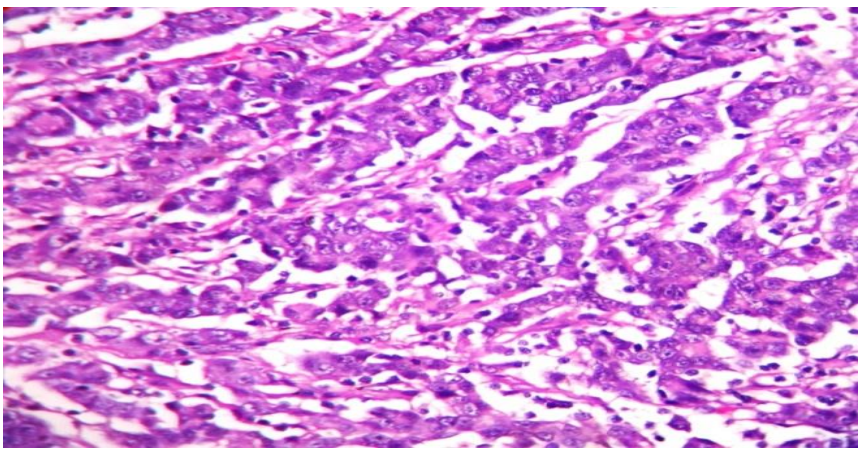

Fig. 5: H&E stained sction shows high power view of poorly differentiated adenocarcinoma.

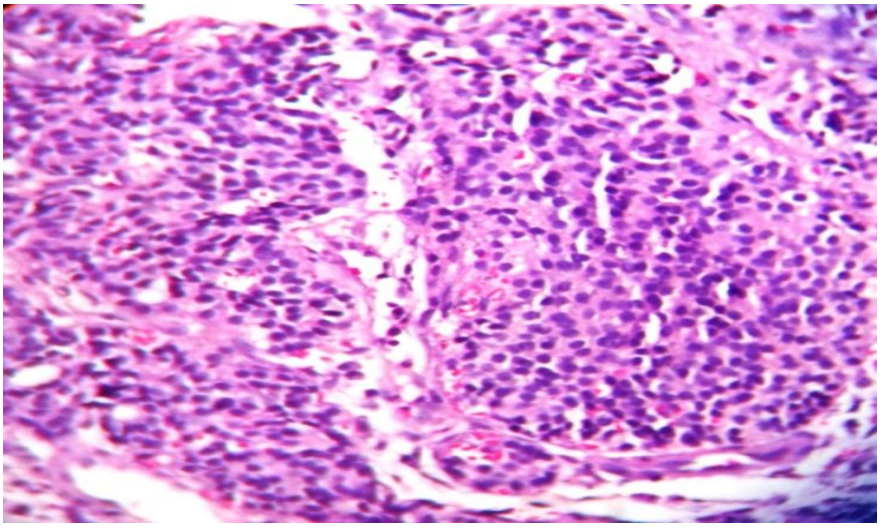

Fig 6: H&E stained section from biopsy shows low power view of Neuroendocrine carcinoma (Inset shows high power view)

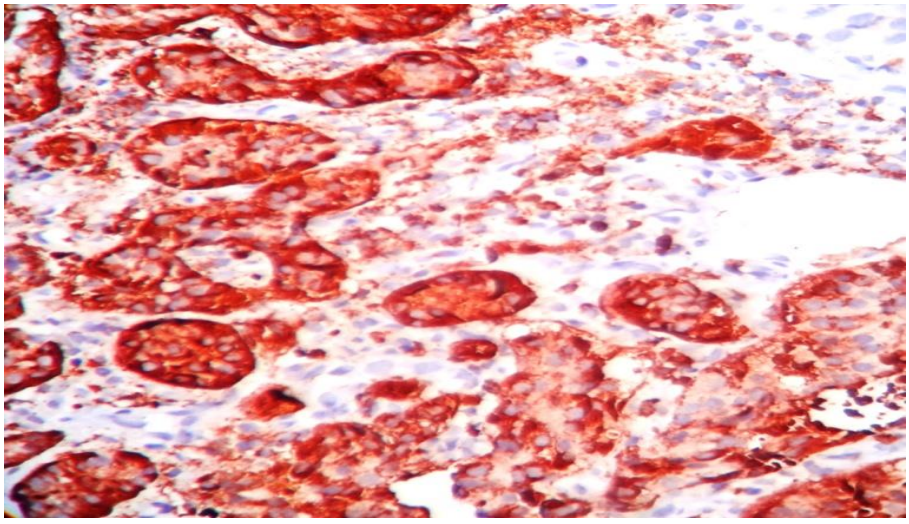

Fig 7: tumor cells are immunopositive for Cytokeratin.

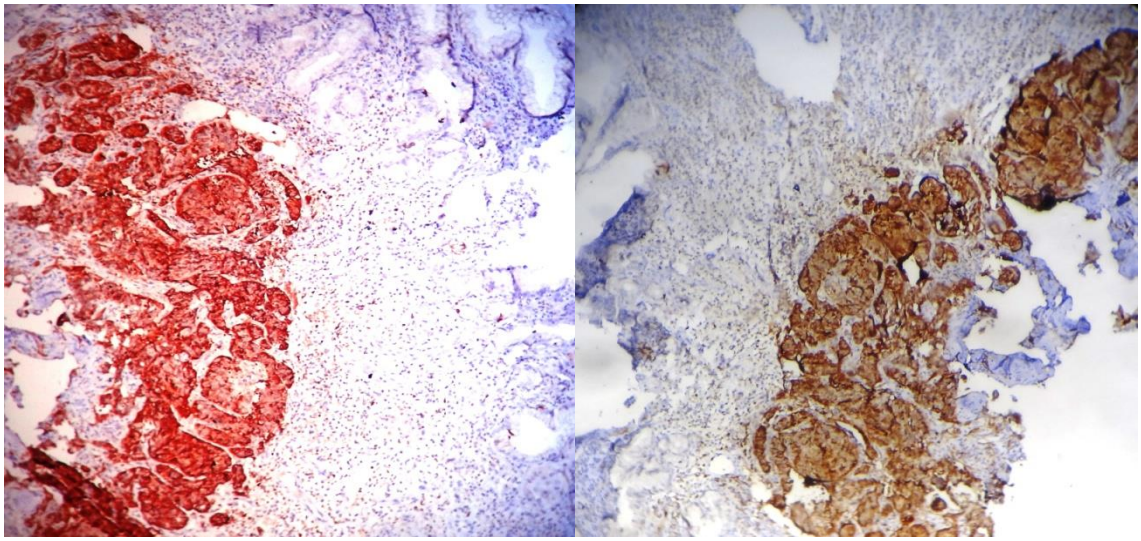

Fig 8 & 9: The tumor cells are immunopositive for Synaptophysin and Chromogranin A (The glands show negative staining)

E. The diagnosis:

The diagnosis was given as poorly differentiated Adenocarcinoma-Stage: T2bNxMx, And Neuroendocrine carcinoma: G1.

3. DISCUSSION

Gastrointestinal tumors displaying both exocrine and neuroendocrine differentiation are well recognized, although uncommon. Most of them arise in the appendix, but they also occur in the colon, stomach, esophagus, duodenum and gallbladder [1]. Most of the collision tumors of stomach described in literature include Adenocarcinoma with lymphomas, carcinoid and GIST or neuroendocrine tumors [2] our case is a mix of poorly differentiated adenocarcinoma and neuroendocrine carcinoma .While carcinoid are generally more indolent in nature, they may demonstrate a greater degree of malignant potential if there is a concomitant gastric Adenocarcinoma. [2]. mixed endocrine and non-endocrine epithelial tumors have been classified into six categories: 1) neuroendocrine cells interspersed within carcinomas; 2) carcinoids (neuroendocrine tumors [NETs]) with interspersed non-endocrine cells; 3) composite glandular-neuroendocrine cell carcinomas containing areas of carcinoid and conventional carcinomas; 4) collision tumors in which NETs and conventional carcinomas are closely juxtaposed, but not admixed; 5) amphicrine tumors predominantly composed of cells exhibiting concurrent neuroendocrine and non-endocrine differentiation; and 6) combinations of the previous types. [3,4]. According to this classification, our case could be classified as Collision tumor.

Morphologically, such lesions are classified into two subgroups: composite-type tumors, in which both components appear to be mixed haphazardly and collision-type tumors, which are considered as double tumors with a "side by side" or "one upon another" pattern(4).

According to the World Health Organization classification of tumors of the digestive system, tumors can be classified as truly mixed only if both components are present in significant proportions – at least 30% of either component should be identified to qualify for this definition. In 2010, mixed exocrine-NECs have been renamed as MANECs by the World Health Organisation. Gastric MANECs are rare and usually described to be composed of an exocrine component represented by an adenocarcinoma with a variable grade of differentiation and a neuroendocrine component usually represented by a NEC [1]. Herein we present similar case.

The histologic origin of composite tumors is unclear [2]. Two hypotheses have proposed. One is that both are derived from a common multipotential epithelial stem cell, the NEC carcinoma component resulting from differentiation from the adenocarcinoma to the NEC phenotype during tumor progression. The second hypothesis is that adenocarcinoma and NEC carcinoma arise from a multipotential epithelial stem cell and a primitive NEC, respectively, and that they exist next to each other coincidentally [4].

The treatment consists of surgical excision of operable / curable lesions and endoscopic removal of small non-malignant endocrine tumors.

4. CONCLUSION

Collision tumors should be considered as one of the differential diagnosis when multiple tumors are visualized on Esophagogastroduodenoscopy. A high index of suspicion is often rewarding. Ultrasonography and computed tomography in such cases may be unremarkable with non-visualization of smaller lesions. Multiple biopsies from all the tumors should be taken so that proper therapy /surgery can be planned.

Conflict of interests: The authors have no conflict of interests to disclose.

The preliminary report was presented at MAPCON (Maharastra Asso of path chapter conference and APPI – association of practicing pathologist)

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