CASE REPORT

Mixed Neuroendocrine – Nonneuroendocrine Neoplasm Arising in Barrett's Esophagus

Soon Liang Lee[1], Chiun Yann Ng[2], Lai Teck Gew[3], Jasminder Sidhu[4], Zuliatul F Baharom[5]

Abstract

Barrett's esophagus, which results from chronic gastroesophageal reflux disease, is a known precursor to dysplasia and ultimately esophageal adenocarcinoma. Mixed neuroendocrine – nonneuroendocrine neoplasm (MiNEN) is a rare and heterogenous group of neoplasm with aggressive clinical behavior in general. There have been rare reports of MiNEN arising in Barrett's esophagus, and its pathogenesis remains unclear. Surgical resection with lymph node dissection remains the most effective treatment of MiNEN of the esophagus to date, although the evidence on its optimal treatment is scant.

Keywords: Barrett's esophagus, Esophageal adenocarcinoma, Neuroendocrine neoplasm.

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Introduction

Mixed neuroendocrine – nonneuroendocrine neoplasm (MiNEN) is a rare and heterogeneous group of neoplasm with aggressive clinical behavior in general. According to World Health Organization (WHO) 2017 classification, MiNEN comprises a neuroendocrine component and a nonneuroendocrine component, with both accounting for at least 30% of the neoplasm.[1] There are rare reports of MiNEN in Barrett's esophagus, but its exact pathogenesis and prognosis remain unclear.[2] We hereby present a rare case of MiNEN arising in Barrett's esophagus in a patient with iron deficiency anemia.

Case Description

A 74-year-old man with severe aortic stenosis and chronic kidney disease was admitted to the cardiac unit for acute heart failure. He was noted to have persistent iron deficiency anemia. There were no constitutional symptoms or symptoms suggestive of gastrointestinal bleeding. An esophagogastroduodenoscopy (EGD) found a 1.5-cm friable Paris 0–1s lesion (Fig. 1A) arising in one of Barrett's segments of C2M4 on Prague classification (Fig. 1B). Narrow band imaging of the lesion showed amorphous surface pattern (Fig. 1C). Histopathological examination of the tissue biopsies from the lesion revealed the presence of moderately differentiated adenocarcinomatous glands and well-differentiated neuroendocrine tumor (Fig. 2A, H&E, Orig. mag. × 40). The neuroendocrine tumor component was positive for synaptophysin (Fig. 2B, Orig. mag. × 100) and chromogranin stain. Ki-67 proliferative index was above 20%, while the mitotic index was more than 20/2 mm^2 confirming high-grade NET, G3. Computer tomography scan did not show any adjacent esophageal invasion or distant metastases. However, a Gallium-68 dotatate scan revealed focal uptake in a subcentimeter mediastinal node. He was referred for systemic chemotherapy and radiotherapy as he was a poor surgical candidate. He, however, declined the proposed treatment after discussion and was referred for hospice care.

[1–4]Department of Medicine, Gastroenterology and Hepatology Unit, Kuala Lumpur General Hospital, Kuala Lumpur, Wilayah Persekutuan, Malaysia

[5]Department of Pathology, Kuala Lumpur General Hospital, Kuala Lumpur, Wilayah Persekutuan, Malaysia

Corresponding Author: Soon Liang Lee, Department of Medicine, Gastroenterology and Hepatology Unit, Kuala Lumpur General Hospital, Kuala Lumpur, Wilayah Persekutuan, Malaysia, e-mail: soonliang13@gmail.com

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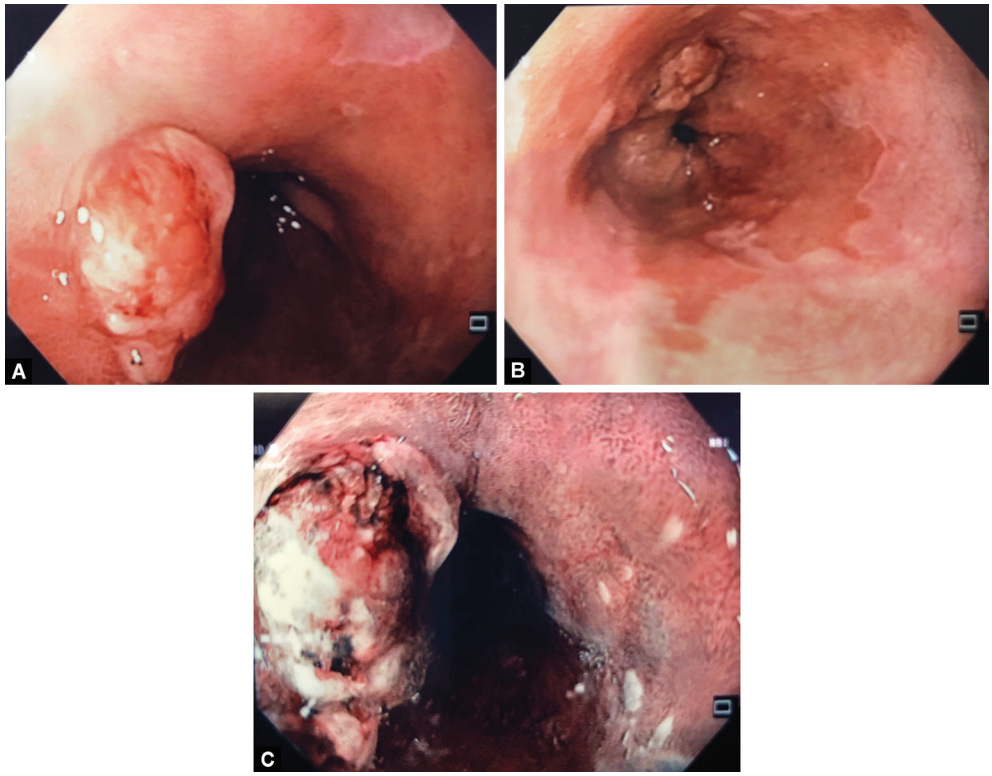
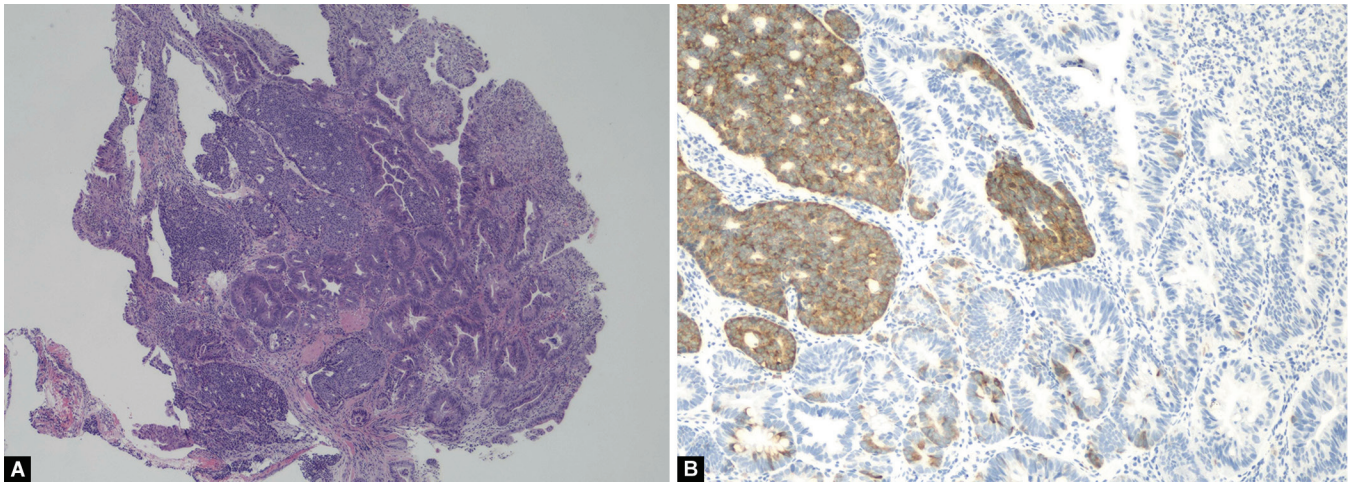
Discussion

Barrett's esophagus, which results from chronic gastroesophageal reflux disease, is a known precursor to esophageal adenocarcinoma. However, pathogenesis and prognostic features of neoplasm with neuroendocrine differentiation arising in Barrett's esophagus remain unclear with scant literature reported.[2] Mixed neuroendocrine – nonneuroendocrine neoplasm (MiNEN) was defined by World Health Organization (WHO) in 2017 as having at least 30% of the neuroendocrine and nonneuroendocrine components within the neoplasm. Although this cutoff value applies to the resection sample and needs to be cautiously interpreted in the biopsy sample, as in this case, there was a clear presence of neuroendocrine morphology with positive stains along with malignant glands in the biopsy sample.[2] MiNEN in esophagus is exceedingly rare, with its prognosis driven mainly by the neuroendocrine component and its Ki-67 proliferation index.[3]

Classification of MiNEN into high grade, intermediate grade, and low grade, proposed by La Rosa et al., helps determine the most suitable therapeutic strategy as targeting the most



Figs 1A to C: (A) An EGD showing a 1.5-cm friable Paris 0–1s lesion; (B) Arising in one of the Barrett's segment of C2M4 on Prague classification; (C) Narrow band imaging of the lesion revealed amorphous surface pattern



Figs 2A and B: Histopathological examination revealing moderately differentiated adenocarcinomatous glands and well-differentiated neuroendocrine tumor (A, H&E, orig. mag. × 40) that was positive for synaptophysin (B, orig. mag. × 100)

aggressive component remains the core principle of treatment. The high-grade MiNEN comprises a poorly differentiated neuroendocrine carcinoma with a nonneuroendocrine tumor. As illustrated in this case, the intermediate grade combines a well-differentiated NET G1, G2, and G3 with a nonneuroendocrine carcinoma. A combination of a well-differentiated NET and an adenoma is categorized as low-grade MiNEN.[4] Apart from low-grade MiNEN, MiNEN generally has aggressive clinical behavior with a poor prognosis.[1,3,4]

To date, surgical resection with lymph node dissections is considered the best treatment option for MiNEN in the esophagus. However, due to the rarity and heterogeneity of MiNEN of esophagus, evidence on its optimal treatment is still lacking, and more studies are needed to establish the best-recommended treatment for this condition.[5]

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Orcid

Soon Liang Lee https://orcid.org/0000-0003-0341-5394

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