Diagnostic Pathology: Open Access

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Commentary on Clinicopathologic and Genetic Characteristics of Gastric Neuroendocrine Tumor (Net) G3 and Comparisons with Neuroendocrine Carcinoma and Net G2

Yan Sun* **and Lin Sun**

Department of Pathology, Tianjin Key Laboratory of Digestive Cancer, Tianjin, China

***Corresponding author:** Dr. Yan Sun, Department of Pathology, Tianjin Key Laboratory of Digestive Cancer, Tianjin, China, E-mail: sunyan@tjmuch.com

Received: 14-Dec-2023, Manuscript No. DPO-23-122925; **Editor assigned:** 18-Dec-2023, PreQC No. DPO-23-122925 (PQ); **Reviewed:** 01-Jan-2024, QC No. DPO-23-122925; **Revised:** 08-Jan-2024, Manuscript No. DPO-23-122925 (R); **Published:** 15-Jan-2024, DOI: 10.4172/2476-2024.9.1.228

Citation: Sun Y and Sun L (2024) Commentary on Clinicopathologic and Genetic Characteristics of Gastric Neuroendocrine Tumor (Net) G3 and Comparisons with Neuroendocrine Carcinoma and Net G2. Diagnos Pathol Open 9: 228.

Description

We are honor to be invited by editorial team to comment on the article we published in Histopathology 2023. In this article, we aimed to characterize the clinicopathologic and genetic characteristics of gastric neuroendocrine tumor G3 (gNET G3) and compare with gastric neuroendocrine carcinoma (gNEC) and gNET G2 [1]. One hundred and fifteen cases of gastric neuroendocrine neoplasms (gNENs) were reviewed and reclassified according to the 5th WHO classification of digestive system tumors, and the clinicopathological and survival analyses were performed. Then, we conducted genome-wide Copy Number Variation (CNV) and Whole Exome Sequencing (WES) analyses for 7 cases of gNET G3, 8 gNEC and 5 gNET G2 to examine the common and different genetic alterations. We confirmed that gNET G3 was a unique type of gNENs and different from gNEC and gNET G2, demonstrated for the first time that DLL3 gain/overexpression was frequent in gNET G3, and indicated that DLL3-targeted drugs might be used for gastric high-grade NENs with high DLL3 levels. Although TP53 mutation indicated NEC rather than NET G3, we detected a nonsense mutation of TP53 and negative expression for p53 in one NET G3.

NET G3 was separated from NEC in the 5th WHO classification of digestive system tumors in 2019 [2]. Due to the rarity of incidence and difficulty in diagnosis, the clinical and genetic characteristics of NET G3 remain unclear, especially for gastric NET G3 (gNET G3). Although this article offered insight into the decision that gNET G3 is a distinct entity with unique genetic characteristics and provided some molecular alterations that might contribute to the development and progression of gNET G3 and serve as potential therapeutic targets, the conclusion is restricted. First, we only analyzed a small number of gNET G3 and gNET G2 samples due to the limited number of cases in our tumor cancer center. While even in the literature, gNET G3 was very few [3,4]. Although, there some studies performed on gastroenteropancreatic neuroendocrine neoplasms, most of them focused on pancreatic or small intestinal NENs. However, site specificity of NETs is universal consensus. Thus, more multiple-center studies with large-scale samples are needed to clarify its clinicopathological features and biological behaviors of gNET G3. Second, no *in vitro* or *in vivo* experiments were performed for the key molecular alterations. Considering the rarity of gNET G3 and diagnostic difficulties in distinguishing from large cell gNEC, the gNET G3 cell lines were not easy to establish and there existed difficulty in achieving basic research to clinical practice effectively. Third, as previously study, NETs G3 was proposed to originate from NETs G1/2 as carrying similar genetic alterations, while obviously different from those of NECs, in which TP53 mutations was more frequent [5,6]. Thus, TP53 mutations was often used to distinguish NET G3 from NEC [7]. In this study, we found abnormal TP53/p53 in one gNET G3 which was diagnosed basing on the well-differentiation morphology. However, the degree of differentiation is a relatively subjective feeling of pathologists. In fact, there was no objectively decisive evidence to supporting this case as gNET or not. In addition, there was inconsistency of TP53 mutation and p53 expression in some gNET G3 and gNEC samples. Therefore, the further studies are needed to reveal the molecular mechanism underlying the development and progression of NET and NEC and supply the potential biomarkers to distinguish them.

References

1. Chen S, Sun L, Chen HC (2023) Clinicopathological and genetic characteristics of gastric neuroendocrine tumour (NET) G3 and comparisons with neuroendocrine carcinoma and NET G2. Histopathology 83:700-711.
2. Klimstra DS, Klöppel G, La Rosa S, Rindi GW (2019) Classification of neuroendocrine neoplasms of the digestive system. In WHO Classification of tumours, 5th Edition, IARC Press, pp:16-19.
3. Mafficini A, Scarpa A (2019) Genetics and epigenetics of gastroenteropancreatic neuroendocrine neoplasms. Endocr Rev 40:506-536.
4. Samsom KG, Levy S, van Veenendaal LM (2021) Driver mutations occur frequently in metastases of well-differentiated small intestine neuroendocrine tumours. Histopathology 78:556-566.
5. Rindi G, Klimstra DS, Abedi-Ardekani B (2018) A common classification framework for neuroendocrine neoplasms: an International Agency for Research on Cancer (IARC) and World Health Organization (WHO) expert consensus proposal. Mod Pathol 31:1770-1786.
6. Uccella S, La Rosa S, Metovic J (2021) Genomics of high-grade neuroendocrine neoplasms: Well-differentiated Neuroendocrine Tumor with high-grade features (G3 NET) and Neuroendocrine Carcinomas (NEC) of various anatomic sites. Endocr Pathol 32:192-210.
7. Asa SL, La Rosa S, Basturk O (2021) Molecular pathology of well-differentiated gastro-entero-pancreatic neuroendocrine tumors. Endocr Pathol 32:169-191.