Virchows Archiv (2023) 482:931–932
https://doi.org/10.1007/s00428-023-03494-w

LETTER TO THE EDITOR

Reply to: Neuroendocrine neoplasms of the breast: diagnostic confusion and future perspectives

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Received: 19 December 2022 / Revised: 19 December 2022 / Accepted: 13 January 2023 / Published online: 20 January 2023

In Reply:

We are grateful to Dr. Kawasaki and colleagues for their comments on our paper [1] where we showed an overall diagnostic agreement among experts regarding breast neuroendocrine carcinoma (NEC) and neuroendocrine tumor (NET) diagnosis.

Dr. Kawasaki et al. agreed with the diagnosis of high-grade NEC presented in Fig. 1c [1], a tumor which showed small cells with hyperchromatic nuclei and high mitotic index. Five years after the initial treatment with hormone therapy, the patient underwent local recurrence which was treated surgically. The patient was then lost at follow-up.

The precise distinction between solid papillary carcinoma (SPC), a special-type breast carcinoma, and NET represents a challenge in the routine diagnostic practice, as well as in the case-revision process of our study. This challenge was in particular recognized when differential diagnosis between SPC and NET was rendered by endocrine pathologists. However, the main differences between the two entities are visible at low magnification because the tumor contour of SPC is well circumscribed and delicate fibrovascular cores are interspersed within the tumor nests, while in NET the borders are irregular, as in infiltrative lesions, and the cell clusters are separated by thick desmoplastic collagen [2]. Similar issues may regard mucinous carcinomas, although characterized by distinctive morphological features, such as presence of mucus, as another neuroendocrine-marker-expressing type of tumor. Currently, it represents a separate category from that of NET/NEC, generating confusion in the classification system and in routine diagnostic process.

No special type (NST) carcinoma showing NE differentiation, unlike SPC, should represent a less challenging entity in terms of distinction from NET/NEC. If conventional NE histological features and NE marker expression are not distinct or uniform enough to classify a neoplasm as NET or NEC, invasive carcinoma NST with NE differentiation should be diagnosed. We acknowledge that in our study, NET and NST carcinomas with NE differentiation had a similar outcome, which is better than that of NEC. This result may support at least the distinction between NET and NEC in the breast.

In conclusion, the classification of breast NENs is still a matter of debate. The numerous modifications of the diagnostic criteria over the years puzzled pathologists and created a certain confusion regarding clinical management of these patients. Investigation of a larger series is required to understand their evolutionary profile and potential impact on the clinical outcome.

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Author contribution Conceptualization: IC, AS, JM. Writing—original draft preparation: JM, IC, AS. Writing—review and editing: all authors.

Declarations

Conflict of interest The authors declare no competing interests.

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