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Brain Pathology

LETTER TO THE EDITOR

Reply to letter by Melmed et al.

Dear Editor(s),

We would like to thank Professor Melmed and colleagues for commenting on our review recently published in Brain Pathology and highlighting areas for improvement.

This invited review is part of a Mini Symposium on the WHO Classification of Pituitary Tumors, covering an overview of the 5th Edition with comparison between CNS5 and ENDO5, a review on practical approaches of diagnosing PitNET/adenomas according to cell lineage, our review on grading and staging, an update on aggressive and metastatic PitNETs and a review on posterior pituitary and rare pituitary tumors. These manuscripts are available online [1–4] before the publication in a special format, which will include an introduction to the issue covering also the PANOMEN consensus. In this respect, the letter to the Editor does not take into consideration the other manuscripts and is premature. The Editor and authors of the four reviews have taken great care in ensuring that content was accurate and that no overlap and repetitions occurred.

Our review on grading and staging of pituitary tumors included 112 references and priorities original studies providing new insights or proof of concept on well-characterized cohorts as well as systematic reviews. This approach was adopted to cite studies relevant to the focus of the manuscript and avoid unnecessary repetition and self-citation.

The clinical classification of pituitary neoplasms proposed by the PANOMEN workshop [5] represents a promising and innovative approach that has the potential to be adopted widely once validated by independent prospective studies. We hope that the IARC-WHO working group will consider an integrated multidisciplinary classification that acknowledges the recently proposed workflows once thoroughly validated.

Currently, the only viable alternative to the WHO classification for a staging and/or classification system is the five-tiered prognostic classification [6] that has already been tested by several independent cohorts on more than 3000 patients.

The low rate of histologically confirmed pituitary tumors as indicated in the Central Brain Tumor Registry of the United States (CBTRUS) statistical report [7] does not account for the large number of pituitary tumors that are followed up and/or medically treated and therefore lack histopathologic confirmation. Indeed, as stated in the report and in the CBTRUS website: "The Central Brain Tumor Registry of the United States (CBTRUS) is a not-for-profit research corporation, recognized by the international research community as the premier resource for annual histology-specific statistical information for all primary brain and other CNS tumors in the United States."

The change of nomenclature from adenoma to PitNET will favor the registration of adenohypophyseal tumors in NET/NEN Cancer Registries, allowing for the collection of more accurate epidemiological and follow-up data.

As discussed in our previous review in Endocrine-Related Cancer [8] and in the review by Casar-Borota et al. included in the Mini Symposium [5], we agree with Melmed et al. that given the predominant incidence of indolent lesions, the unpredictable behavior of some PitNETs, and the lack of agreement on their prognostic stratification it remains unclear why the ENDO5 consensus panel decided to adopt the ICD-O/3 "malignant" code rather than/1, which classifies neoplasms of "uncertain malignant potential" and reflects ICD11 in CNS5.

Our proposed clinical–histological–molecular workflow for adenohypophyseal tumors with aggressive potential provides a framework for the same multidisciplinary approach advocated by Melmed and colleagues, build on the integration of clinical, pathological, and molecular features.

It is reassuring that we all aim to identify tumors at high risk of recurrence and care about patients' outcome, despite the divergent opinions on how to achieve this goal.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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