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Letter to the Editor

Response to Adomas Bunevicius

Dear Dr. Bunevicius,

Thank you for your interest on our article on hypopituitarism in patients with high grade gliomas. We are glad to answer the questions you raised.

Question 1: Temporal proximity of serum sampling to brain tumor surgery: all samples given as baseline samples are in fact preoperative samples, collected within the week before brain tumor surgery. Thyroid hormones are part of the requested laboratory values before general anesthesia in our hospital. The rate of patients presenting with low fT3 is with 27% much lower than in your cohort of patients described in Oncotarget 2016, where 49/230 patients suffered from high grade glioma [1–3].

The early postoperative changes of thyroid hormones that you cited in your question probably have to be interpreted as part of the "acute, nonthyroidal illness syndrome" which we found lasting to the second blood sample, around three months later.

Question 2: Proportion of patients with repeated surgery: around 30% at very variable time points.

Question 3: Lack of individual follow up of hormonal values: For each of the time intervals listed in the Tables 2–5, only one patient sample was chosen, regardless of the number of samples taken during each period. Patients had 3–35 samples with hormone levels; no patient with less than 3 samples was included in this study. We addressed the missing data as one of the major limitations of this study and agree with Dr. Bunevicius that a complete follow up of all patients would have been preferable. However, we focused in our work on late samples after 3 and 4 years of follow up, which is a rather ambitious goal in patients with GBM and can present data relying on more than 4000 hormonal levels measured in this patient cohort. Our aim was to document that pituitary deficiencies develop over years also in adult patients that have undergone the actual standard treatment for high grade gliomas – similarly as in childhood brain tumor patients.

In fact, we tried to present the data as graphs with individual follow up, but discarded this form of presentation as we thought that the chosen form of presentation within tables was more informative. We apologize for the inconvenience, but the proportion of hormonal deficiency for pituitary, thyroid and sex hormones for each time point is given in Tables 2–5 – and this was the aim of our study.

Question 4: Association of hormonal levels with patient outcome: we fully agree with Dr. Bunevicius that this is an eminently interesting question. We also agree with him that hypothyroidism severely impacts the quality of life as stated in the discussion, as well as deficiencies in sexual hormones do – as also discussed.

So far we did not correlate hormonal levels with survival duration but agree that this is an interesting question. We are willing to do the analyses, but unfortunately, due to health issues of several persons in the author team, we cannot provide this analysis together with the response to this letter, but we will try keeping you and the journal informed, as soon as we will have done this analysis.

References

[1] Bunevicius A, Deltuva VP, Tamasauskas S, et al. Preoperative low triiodothyronine concentration is associated with worse health status and shorter five year survival of primary brain tumor patients. Oncotarget 2016;5:8648–56.

[2] Bunevicius A, Laws ER, Deltuva V, Tamasauskas A. Association of thyroid hormone concentrations with quality of life of primary brain tumor patients: a pilot study. J Neurooncol 2017;2:385–91. https://doi.org/10.1007/s11060-016-2311-x. PMID:27830477.

[3] Bunevicius A, Smith T, Laws ER. Low tri-iodothyronine syndrome in neurosurgical patients: a systematic review of literature. World Neurosurg 2016;95:197–207. https://doi.org/10.1016/j.wneu.2016.07.035. PMID:27450974.

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