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Letter to the Editor

Are hypothyroidism and hypogonadism clinically relevant in patients with malignant gliomas? A longitudinal trial in patients with glioma

Handisurya and colleagues undertook longitudinal analysis of thyroid hormone, sex steroid and prolactin serum concentrations in large sample of high-grade glioma patients [1]. Their findings suggested that hormonal deficiencies are common in high-grade glioma patients and hormone concentrations fluctuate throughout the disease course.

It was previously documented that thyroid hormone concentration can change after the brain tumor surgery. Specifically, a study in 90 patients who underwent surgery for different brain tumors, including 17 patients with high-grade gliomas, showed that free tri-iodothyronine and thyroid stimulating hormone concentrations decreased, while free thyroxin concentrations increased within two days after the surgery [2]. Thus, it would be interesting to know temporal proximity of serum sampling for thyroid hormone assessment with brain tumor surgery, and what proportion of patients underwent repeated tumor resection surgery during follow-up.

Furthermore, it was not specified what was the overlap between patient samples across the study visits, thus making it challenging to interpreted fluctuations of hormone levels. For example, patient sample sizes ranged from 77 to 266 patients for free tri-iodothyronine concentration assessment and from 123 to 336 patients for thyroid stimulating hormone concentration assessment across the study visits. These findings suggest that only a proportion of the total sample of 436 patients were subjected to two or more assessments of hormone levels. Therefore, it remains unclear in what proportion of patients hormone concentrations remained stable or changed (decreased or increased) across the study course. Longitudinal information about hormone concentrations at individual patient level and in relation to treatment could provide with valuable information above and beyond the existing knowledge, helping to better understand sensitivity of various endocrine axes for brain tumor treatment(s) and possible prognostic value of the observed endocrine changes. This information would be extremely valuable for clinicians caring of high-grade glioma patients to better define time windows of greatest vulnerability to neuroendocrine abnormalities and for researchers planning neuroendocrine intervention trials in high-grade glioma patients.

Finally, the association of hormone levels with patient outcomes (survival, functional status and/or progression free survival) was not reported, thus it remains unclear if the observed neuroendocrine fluctuations have clinical significance in high-grade glioma patients or represent normal variation/adaptive changes. Given large and mostly homogenous (with regards to tumor diagnosis) patient sample, it would be interesting to see if the studied neuro-endocrine biomarkers carried any clinical significance. For example, there is some evidence to suggest that reduced tri-iodothyronine concentrations can be associated with worse functional status and shorter survival of glioma patients [3]. Pre-clinical studies suggested that sex steroids [4] and prolactin [5] can play a role in glioma biology; however, to the best of my knowledge, there are no studies directly investigating possible prognostic value of the association of sex steroids and prolactin levels with prognosis of high-grade glioma patients. This information would be important to advice as to whether the diagnosed neuro-endocrine abnormalities should be addressed is in high-grade glioma in order to improve patient prognosis and quality life.

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