Understanding treatment options in craniopharyngioma better

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As the most extensive review on Craniopharyngioma in recent years, I was pleased to see a description of the clinical and research work on this important disease (Müller, H. L., Merchant, T. E., Warmuth-Metz, M., Martinez-Barbera, J. P. & Puget, S. Craniopharyngioma. *Nat. Rev. Dis. Primers* 5, 75 (2019))¹. However, the research community is increasingly optimistic about treatment outcomes in craniopharyngioma despite it having been described as an incurable and irresectable, albeit benign, tumour². Accordingly, it is necessary and meaningful to comment on some of the controversies underlying these different views.

The essential characteristic of the benign cellular behaviour of craniopharyngioma³ is the relationship between the tumour and the adjacent nervous tissue, especially the hypothalamus but also the neurohypophysis and pituitary stalk^{4,5}. The tumour displaces the hypothalamus through invagination^{6,7} rather than infiltration, leading to an inflammatory reaction and gliosis mediated by microglial proliferation. Three patterns regarding the relationship between tumour and the third ventricular floor were identified based on our research: mantle-like, moat-like and mortise-like. To ensure safe surgical resection and avoid severe hypothalamic injury³, understanding the pattern of gliosis is essential. Müller et al.¹ proposed preoperative grading of the hypothalamic involvement using preoperative images, which can mistakenly reflect the interplane of tumour to nervous tissue. For example, different tumours might appear similar on imaging, but their underlying relationship with the hypothalamus

may be different³; accordingly, understanding this relationship is essential to protect the hypothalamus during surgery. Conservative surgical therapy with adjuvant radiotherapy is supported widely by the field generally. This conservative approach contrasts with reports from a few clinical centres, in which gross total resection of tumour was associated with significantly improved quality of life⁸.

The authors of the Primer did not adequately discuss the issue of recurrent disease in patients who undergo subtotal tumour resection and radiotherapy. Conservative surgery with adjuvant radiotherapy will eventually result in tumour recurrence, and even malignant transformation⁹, compromising long-term survival. Importantly, postoperative radiotherapy typically results in tumour regrowth that is ‘thorny’, precluding subsequent definitive surgical treatment. Indeed, severe hypothalamic injury should be avoided as indicated by conservative treatment, but further damage by irradiation to visual acuity, as well as endocrinological and hypothalamic function, should not be underestimated¹⁰. These issues are particularly relevant for childhood patients who may require repeated adjuvant radiotherapy to control the tumour.

Further molecular research should focus on identifying strategies to decrease the inflammatory reaction along the infundibulum and floor of the third ventricle. Such an approach may enable curative treatment of this benign tumour.

There is a reply to this letter by Müller, H. L. *Nat. Rev. Dis. Primers* <https://doi.org/10.1038/s41572-020-0174-0> (2020).

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1. Müller, H. L., Merchant, T. E., Warmuth-Metz, M., Martinez-Barbera, J. P. & Puget, S. Craniopharyngioma. *Nat. Rev. Dis. Primers* 5, 75 (2019).
2. Akinduro, O. O. et al. Endocrine and visual outcomes following gross total resection and subtotal resection of adult craniopharyngioma: systematic review and meta-analysis. *World Neurosurg.* 127, e656–e668 (2019).
3. Liu, Y. et al. Pathological relationship between adamantinomatous craniopharyngioma and adjacent structures based on QST classification. *J. Neuropathol. Exp. Neurol.* 77, 1017–1023 (2018).
4. Songtao, Q., Yuntao, L., Jun, P., Chuanping, H. & Xiaofeng, S. Membranous layers of the pituitary gland: histological anatomic study and related clinical issues. *Neurosurgery* 64 (Suppl. 3), ons1–9 (2009).
5. Lu, Y. T., Qi, S. T., Xu, J. M., Pan, J. & Shi, J. A membranous structure separating the adenohypophysis and neurohypophysis: an anatomical study and its clinical application for craniopharyngioma. *J. Neurosurg. Pediatr.* 15, 630–637 (2015).
6. Prieto, R. & Pascual, J. M. Letter to the Editor. The craniopharyngioma-hypothalamus relationship. *J. Neurosurg.* <https://doi.org/10.3171/2019.7.JNS191780> (2019).
7. Prieto, R. et al. Craniopharyngioma adherence: a reappraisal of the evidence. *Neurosurg. Rev.* <https://doi.org/10.1007/s10143-018-1010-9> (2018).
8. Hidalgo, E. T. et al. Quality of life, hypothalamic obesity, and sexual function in adulthood two decades after primary gross-total resection for childhood craniopharyngioma. *Childs Nerv. Syst.* 36, 281–289 (2020).
9. Lu, Y., Qi, S., Peng, J., Pan, J. & Zhang, X. Malignant transformation of craniopharyngioma in an infradiaphragmatic case. *Chin. Med. J. (Engl.)* 127, 3187–3188 (2014).
10. Willard, V. W., Berlin, K. S., Conklin, H. M. & Merchant, T. E. Trajectories of psychosocial and cognitive functioning in pediatric patients with brain tumors treated with radiation therapy. *Neuro. Oncol.* 21, 678–685 (2019).

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Competing interests

The author declares no competing interests.