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EDITORIAL (BY INVITATION)

Why we need new classification models in meningioma management

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Itbecomes more and more apparent that many questions remain unanswered when it comes to assessing the extent of resection in meningioma surgery, mainly because intracranial meningiomas are far more than arachnoidal warts and that complex histological and biomolecular mechanisms play a role in their genesis and recurrence.

In a recent article entitled: "Proposal of a new grading system for meningioma resection: the Copenhagen Protocol", Haslund-Vinding et al. suggest an objective and straightforward grading system based on microscopic analyses of resection margins along with DOTATOC PET scanning [4]. Hopefully, this is the promise for better days in understanding and prognostication of intra-cranial meningiomas, in line with other emerging techniques involving DNA-methylation analysis [12, 14, 15], which are at the basis of new classifications systems [15]. For sure, times (and paradigms!) are changing in the field of assessment and prognostication if intracranial meningiomas.

The current management of intra-cranial meningiomas is based on data brought to the field by Simpson in the late 1950s. At that time, Simpson would retrieve the estimated extent of resection of meningiomas based on operative reports [18]. Major advances have been made since: the implementation of the surgical microscope and the advent of accurate and dedicated imaging modalities [10]. Surprisingly, none of these were sufficiently powerful to let emerge new surgical classifications and, by extension, improve prognostication in terms of tumor recurrence and histological transformation.

In a recent publication "The Simpson grade: abandon the scale but preserve the message", Schwartz and McDermott discuss the concept of Simpson grade 0 resection, that is the existence of satellite dural tumoral clusters [16]. The presence of clusters, their identification by new imaging modalities, and their consideration in the surgical planning shows how the extent of resection is the golden rule, when it comes to meningioma surgery.

While histologically benign meningiomas may behave clinically aggressively due to their location, gross total resection is achieved in most of WHO grade I lesions [5, 8]. The problem arises when masked borderline WHO grade I tumors may escape our vigilance [2]. In these cases, biomarkers associated with tumor grading (Ki-67/MIB-1, SMARCE1, BAP1, KLF4/TRAF7) as well as methylome profiling must be considered [3, 9, 11, 12, 14, 15, 17], illustrating how surgery does not solve the whole equation by itself.

The "issue" with most meningiomas is their benign profile, forgiving (temporarily) the surgeon whenever incomplete resection is performed and sometimes (up to 20%) resulting in mid-to-long-term recurrences [1, 20]. These delayed recurrences made neurosurgeons believe that no matter the extent of resection, the meningiomas have the potential to recur [7]. Still, we have shown that in a very large cohort, whenever radiologically documented high extent of resection was achieved, recurrence rates are reduced and age remains only predictive factor for tumor reappearance [7]. The problem is more complex with intermediate-to-high grade lesions, where recurrence is the result of a complex process involving tumor biology and location, surgical extent of resection and patients' characteristics. Recently, Soni et al. [19] yet again confirmed and demonstrated how the extent of resection was paramount when it comes to increase the post-operative overall survival in patients with intermediate grade meningiomas. In the same vein, Rydzewski et al. [13] were able to show that gross total resection with adjuvant radiotherapy were associated

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with improved survival in patients with atypical meningiomas and were found to be independent predictors of overall survival. They also showed that gross total resection was associated to a lower probability of receiving radiotherapy.

Achieving a maximal extent of resection remains part of the armamentarium of meningioma management [5, 10]. The challenge will forever be the same: reducing tumor load to safely reduce the risk of recurrence or malignant degeneration as much as possible [6, 10], but it should never prevent implementation of new imaging modalities or treatments.

In a short communication commenting Haslund-Vindings' publication, our esteemed colleague Atul Goël affirms that "the rate of recurrence of a meningioma is independent of the extent of tumor resection" [4]. This affirmation is questionable, especially in the light of the emerging grading and classification tools discussed above.

Atul Goël's comment, implying that a meningioma remains a meningioma and that surgery is and will remain the only valid treatment, without being able to be more precise in the identification and stratification of patients at risk, seems therefore one-dimensional. Staying simplistic and binary is the guarantee of the stagnation in the meningioma management and the depressing promise of a perpetual debate between conservatives and progressists.

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