Clinical case

The importance of measuring the velocity of diameter expansion on MRI in upfront management of suspected WHO grade II glioma – Case report

L’importance de mesurer quantitativement la vitesse d’expansion diamétrique devant une suspicion de gliome de grade II de l’OMS – Cas clinique

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ABSTRACT

A right insular lesion was incidentally discovered in a 48-year-old male. Morphological and metabolic radiological characteristics on magnetic resonance imaging (MRI) were in favor of a World Health Organization (WHO) grade II glioma. Despite being advised that surgery was appropriate, the patient elected for conservative management. A second MRI was performed 5 months after, and interpreted as unchanged. A third MRI 4 months later demonstrated a significant increase in tumor size and enhancement in a new distant tumor focus. The patient was referred to our center and underwent surgical resection. Histopathology revealed a grade III astrocytoma. A retrospective quantitative measurement of the radiological growth between the two first MRIs yielded a growth rate of 12 mm/year. This value, highly suggestive of a malignant glioma, should have triggered surgery at the time of the second MRI. We conclude that, whenever surgical treatment of a suspected WHO grade II gliomas is postponed, assessing tumor kinetics quantitatively is important to identify patients whose tumor is indeed a WHO grade III glioma. The tumor should be indeed followed by serial MRIs with quantitative measurement of tumor growth, not just “eyeball” qualitative examination. Immediate treatment is indicated in patients with radiological tumor expansion of greater than 8 mm/year.

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RÉSUMÉ

Une lésion insulaire droite a été découverte fortuitement chez un homme de 48 ans. Les caractéristiques radiologiques morphologiques et métaboliques sur l’IRM étaient en faveur d’un gliome de grade II de l’OMS. Bien que la chirurgie lui fut recommandée, le patient choisit une attitude de surveillance proposée dans un autre centre. Une deuxième IRM réalisée cinq mois après fut interprétée comme stable. Une troisième IRM quatre mois plus tard mit en évidence une augmentation de la taille de la lésion et l’apparition d’un nodule de prise de contraste. Le patient fut alors pris en charge et opéré, l’histologie concluant à un astrocytome de grade III. Rétrospectivement, la mesure quantitative de l’évolution entre les deux premières IRM montre un taux de croissance de 12 mm/an. Cette valeur, tout à fait évocatrice d’un gliome de haut grade, aurait dû alerter et inciter à débuter le traitement sans plus de délai. Nous concluons, à partir de ce cas, qu’il est important de suivre l’évolution radiologique d’un probable gliome diffus de bas grade par des mesures quantitatives, et pas seulement une comparaison «de visu». Le traitement ne devrait être en aucun cas retardé devant un taux de croissance supérieur à 8 mm/an.

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1. Introduction

There is a growing body of literature suggesting that surgery is the best option for a radiologically suspected WHO grade II glioma. Surgery provides a definitive histopathological diagnosis, improves
survival [1,2], and controls symptoms such as seizures [3] with a limited functional risk [4,5], even within eloquent areas such as the insula [6–10]. However, due to a lack of class I evidence, there remains no consensus. Some centers recommend immediate surgery to delay anaplastic transformation. Other institutions advocate a conservative follow-up until the occurrence of malignant transformation on the basis that despite surgical advances, the functional risk of the resection still outweighs survival benefit [11,12]. The situation is less clear when the tumor is diagnosed incidentally.

When conservative management is chosen, sequential MRIs are performed to detect changes suggestive of malignant transformation. However, there is no consensus about the best way to monitor this radiological evolution. Here, we report a failure of qualitative monitoring to detect the transformation of a grade II to grade III glioma and argue that quantitative monitoring should be performed.

2. Clinical history

A right-handed 48-year-old male presented with tinnitus. MRI showed a non-enhancing lesion of the right insula. Perfusion MRI and FDG-PET were suggestive of a WHO grade II glioma (Fig. 1). Although the senior author (CT) recommended surgical excision, conservative management was advocated for this lesion by another neurosurgeon at a separate institution. The patient elected observation, and a second MRI was performed 5 months later. This second examination was interpreted as stable (Fig. 1), both on standard morphological sequences and on perfusion sequences. A third MRI was done 4 months later. This third MRI showed significant increase in the insular tumor (still without contrast enhancement), but there was now a second contrast-enhancing focus in the right cerebral peduncle (Fig. 2). The insular tumor remained hypometabolic on FDG-PET. Based on these changes, the patient now accepted surgery. Uncomplicated, gross-total resection was achieved via a trans-sylvian approach. The patient remained intact and his tinnitus decreased in intensity. Histopathological diagnosis was made of grade III astrocytoma. Adjuvant radiation therapy and chemotherapy (temozolomide) were subsequently administered (Fig. 3).

Fig. 1. Axial FLAIR imaging of the presenting MRI.

IRM initiale, coupe axiale FLAIR.

3. Technique and results

Tumor volumes on the three pre-operative MRIs were retrospectively computed by 3D segmentation (Osirix® software, v3.3.2; http://www.osirix-viewer.com), on axial slices of FLAIR sequences. Segmentation were performed by two independent neurosurgeons, who were blinded to the dates of MRI examinations. Volumes were converted into mean tumor diameters (MTD = 2 x V1/3). Annual growth rate of the MTD was then computed [13]. Results are presented in Table 1. Annual growth rates were 12 mm/year between the first and second MRI, and 14 mm/year between the second and third MR.

4. Discussion

While it is now well-established that tumor growth rates, as measured on MRI during the pretreatment follow-up period, are predictive of both anaplastic transformation and overall survival [11,12,14,15], their use in clinical practice remains limited. This report highlights the importance of quantitative estimation of tumor growth, as it may have avoided this patient’s avoidable and potentially catastrophic delay in treatment.

4.1. Quantitative versus “de visu” estimation of growth

The tumor, manually visualized on the second MRI, was thought to be stable. Because of the three dimensional growth pattern, failure to cause mass effect, and non-enhancing nature of these tumors, determining growth between serial scans is often difficult and readily missed. In review, a careful 3D segmentation of the tumor yielded an increase of tumor volume from 3.1 cc to 6.15 cc over 5 months, or, after converting volumes to diameters, a 5 mm increase.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Quantitative tumor measurements and growth rates of the three MRI scans. Mesure quantitative (volumes et diamètres) de l’évolution de la tumeur et taux de croissance calculé d’après les trois IRM préopératoires.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volumes (cc)</td>
<td>Diameters (mm)</td>
</tr>
<tr>
<td>Initial MRI</td>
<td>3.1</td>
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<tr>
<td>5 months MRI</td>
<td>6.15</td>
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<tr>
<td>9 months MRI</td>
<td>10.66</td>
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increase in 5 months. The corresponding annual growth rate of 12 mm/year would indicate a high-grade tumor [15], correcting the misdiagnosis made by qualitative interpretation. Thus, a precise quantitative volumetric estimation of radiological changes should be made systematically in radiological follow-up of a suspected grade II glioma.

4.2. Monitoring tumor size and growth by assessing volumes versus diameters

There is some controversy whether tumor growth rates should be evaluated by assessing volumes [12,14] or diameters [15]. As detailed in a previous work [13], this question is complex: depending on the chosen method, differing conclusions can be made when inferring the biological aggressiveness of tumors from their radiological assessment. In the present case, the volume increasing (3 cc in 5 months) would have ranged this patient in the low risk group according to the study of Brasil Caseiras et al. [14], whereas following the study of Pallud et al. [15], diameter based measurements (5 mm in 5 months) would have properly stratified this patient into a higher risk group. This case provides support to the hypothesis that assessing diameters rather than volumes gives a better estimation of the tumor’s biological properties [16].

4.3. Optimal timing of the second follow-up MRI

Even in the absence of radiographic characteristics of high-grade glioma, any suspected grade II lesion with an annual growth rate greater than 3 mm/year should be considered a high-grade glioma [15]. In this situation there is no rational to delay the histological diagnosis and active oncological treatment. In our experience a 2 mm diameter increase can be reliably measured with careful segmentation of the MRI. We propose a three months interval as being the optimal timing for the second MRI when choosing a non-surgical treatment algorithm of a suspected grade II glioma.

5. Conclusion

Conservative management of suspected grade II gliomas is losing support in the literature [17]. However, should observation, rather than surgery, be chosen, MRIs should be performed each three months as they may detect subtle but important volumetric progression indicative of malignant transformation The validity of the aforementioned conclusions may be equally applicable to post-operative follow-up.

Disclosure of interest

The authors have not supplied their declaration of conflict of interest.

References


