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Short Communication

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Intrinsic Brainstem Tumours - The Importance of an Accurate Diagnosis

Marcos Dellaretti[1]* and Breno Bezerra Arruda Câmara[2]

[1]Department of Neurosurgery, Santa Casa de Belo Horizonte Hospital, Belo Horizonte, Minas Gerais, Brazil
[2]Department of Surgery, Federal University of Minas Gerais (UFMG), Belo Horizonte, Minas Gerais, Brazil

Correspondence to: Marcos Antonio Dellaretti Filho, Department of Neurosurgery, Santa Casa de Belo Horizonte Hospital, Federal University of Minas Gerais, 1111 Francisco Sales Avenue, 4th Floor, Belo Horizonte, MG, Brazil CEP 30150-220, Brazil; E-mail: mdellaretti@mac.com

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Intrinsic brainstem lesions are rare tumors comprising approximately 1.6% of intracranial tumors [1]. Despite affecting all age groups, these tumors have greater epidemiological relevance in children and adolescents, corresponding to 10.7% of brain tumors in this population [2,3,4].

Since the papers by Albright [5] and Epstein [6], intrinsic diffuse lesions have been treated with radiotherapy without the need for histological confirmation. However, more recent studies show that approximately 15.6% of these lesions may not correspond to diffuse gliomas, and the range of differential diagnoses includes other tumors, such as pilocytic astrocytomas, ependymomas, haemangioblastomas, lymphomas, and infectious, immunological and ischaemic lesions [7,8,9].This finding is even more relevant in brainstem lesions that affect adults, where up to 30% of cases do not constitute diffuse gliomas, and the differentiation of the histological grade directly affects the prognosis, unlike pediatric cases [2,10].

The reason for "empirical" radiotherapy treatment is that the surgical procedures needed to obtain histopathological samples would carry unjustifiable risks for new deficits and even death. However, with the advancement of technology, we now have access to high-precision equipment, and the latest data bring the risk of new deficits to the order of 7.8%, with 1.7% being definitive, and the risk of death related to the procedure being only 0.9%. The diagnostic accuracy rate is approximately 96.2% [2,11].

Another basis for treatment without histopathological confirmation is that the disease has a severe, rapidly progressing, and fatal course without therapy to dramatically change the prognosis. However, due to this practice, there has been a lapse in recent years in obtaining histopathological material that could improve the development of new therapies [7].

It is worth mentioning that the rate of agreement among radiologists in the interpretation of MRIs suggestive of diffuse brainstem glioma is approximately 43.8% [12], the treatment of a differential diagnosis of a diffuse brainstem glioma can be completely distinct from that of diffuse pontine gliomas, and radiotherapy carries risks and complications [13].

Research centers work on identifying the genetic profile and molecular targets that can bring about an oncological treatment that truly changes outcomes. Diffuse pontine gliomas are related to changes in tyrosine-kinase receptors PDGFR-alpha, MET, and IGF1R [14,15] and are classified into 3 distinct molecular subgroups: H3-K27 M, silent and MYCN [16,17]. To keep expanding these boundaries, tumor tissue samples are fundamentally needed [10,11,18].

A pontine diffuse glioma is characterized by a central lesion that occupies more than 50% of the pons' diameter in axial sections, has imprecise margins, has either hypointensity on T1-weighted images with varying levels of contrast uptake or hyperintensity on T2-weighted images, is classically not restricted to diffusion, and has no exophytic or cystic components [3,18]. This tumor is associated with a compatible clinical presentation and characterized by a progressive motor deficit, gait ataxia, and variable impairment of cranial nerves; thus, we would assume that radiotherapy treatment is indicated despite a lack of histopathological samples.

Dellaretti [19,20] systematized brainstem lesions based on MRI findings into 4 groups: type 1: diffuse non-enhancing; type 2: diffuse enhancing; type 3: focal and non-enhancing; and type 4: focal and enhancing.

In a publication involving only children [19], type 1 lesions corresponded to 20.4% of brainstem lesions, type 2 to 45.4%, type 3 to 11.36%, and type 4 to 22.7%. Among the 41 cases confirmed by stereotactic biopsy, 37 (90.2%) corresponded to diffuse gliomas. The other diagnoses were pilocytic astrocytoma (4.9%), ependymoma (2.4%), and ganglioglioma (2.4%).

Among the type 1 lesions, 100% were diffuse gliomas (8 low-grade tumors and 1 high-grade tumor). Among the type 2 lesions, 90% were diffuse gliomas (4 low-grade tumors and 14 high-grade tumors), 5% were ependymoma, and 5% were ganglioglioma. For type 3, 80% were diffuse low-grade gliomas, and 20% were inconclusive. For type

4, 60% were diagnosed as diffuse glioma (2 low-grade tumors and 4 high-grade tumors), 20% were pilocytic astrocytomas, and 20% were inconclusive. In this way, considering contrast-enhanced lesions, the biopsy was impactful in the treatment of 13.3% of the cases, reaching 20% among the cases of focal lesions [19].

Regarding survival, children with low-grade gliomas had an average survival of 56 months, compared to only 12 months for those with diffuse high-grade gliomas. The 1-year disease-free survival rate was 80.4% for low-grade gliomas and 48.6% for high-grade gliomas. These data show the clinical importance of histological confirmation[10,12].

Of the series involving adults [20], 33.3% had type 1 lesions, 32.2% had type 2, 10.4% had type 3 and 24% had type 4. Among the histologically confirmed cases, diffuse gliomas corresponded to 68.47%, with lymphomas (7.6%), metastases (6.5%), pilocytic astrocytomas (4.34%), craniopharyngioma (1%), and ganglioglioma (1%) being the other identified tumors. Also, 10.8% of the conditions were nontumoral, including inflammatory diseases (5.4%), ischaemic injuries (2.17%), fungal abscesses (2.17%), and gliosis (1%).

Among the 32 type 1 tumors, 89.3% were diffuse gliomas (18 low-grade tumors and 7 high-grade tumors), 6.3% were lesions due to inflammatory diseases, 3.1% lymphoma and 12.5% were inconclusive. The type 2 tumors comprised 67.8% diffuse gliomas (3 low-grade tumors and 18 high-grade tumors), 12.9% lymphomas, 9.7% metastases, 3.2% pilocytic astrocytoma, 3.2% ganglioglioma and 3.2% inflammatory diseases. Among the 10 tumors in group 3, 90% were low-grade gliomas and 10% were ischaemic injuries. The type 4 tumors accounted for 23 lesions and had the widest range of differential diagnoses: 30.4% high-grade gliomas, 4.3% low-grade gliomas, 13% pilocytic astrocytomas, 13% metastases, 8.7% lymphomas, 8.7% fungal abscesses, 8.7% lesions due to inflammatory diseases, 1 case of craniopharyngioma (4.3%), 1 case of gliosis and 1 case of ischaemic injury [20].

The group of focal enhancing lesions (type 4) presented 65.3% of the different etiologies of diffuse gliomas, with significant differences from the other tumor types. Focal lesions were also significantly related to a nontumoral etiology [18,20].

When facing lesions whose natural history and prognosis are different from those of pontine diffuse gliomas, the patient needs to be informed precisely about the pathology and the risks of treatment. An inaccurate clinical diagnosis and inadequate treatment may lead to drastic consequences for the patient and legal implications. Thus, it is accepted that stereotactic biopsies are indicated for children with focal enhancing or contrast-enhanced lesions, for diffuse non-enhancing lesions with an atypical clinical progression, or as part of research protocols. For adult patients, biopsies should always be performed because the range of differential diagnoses is much wider with an impact on treatment and prognosis.

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Conflict of Interests Statement

The authors have no conflicts of interest to declare.

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