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ARS Medica Tomitana - 2020; 4(26): pag. 154 - 158
doi: 10.2478/arsm-2020-0031

RECURRENCE OF AN OLIGODENDROGLIOMA IN AN ANAPLASTIC FORM – CASE REPORT AND SHORT LITERATURE REVIEW

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ABSTRACT

Oligodendrogliomas are a rare diffuse astrocytic tumor, usually present in young adults, which depending on the pathogenic alterations can lead to major disabilities or even death. We present a case of a male patient in the fifth decade of life, who initially presented with an oligodendroglioma, and approximately one year after the first therapeutic intervention the condition recurred in the form of an anaplastic oligodendroglioma. We made a complete histopathological and immunohistochemical panel in order to have a final diagnosis with the greatest accuracy, thus making a comparison with the literature in order to assess the diagnosis and subsequent therapeutic conduct.

Keywords: Anaplastic oligodendroglioma, Brain tumor, diffuse astrocytoma, Immunohistochemestry, Oligodendroglioma

Introduction

Oligodendrogliomas come from oligodendrocytes located predominantly in the white matter of the central nervous system (1, 2). According to the 2016 WHO classification, oligodendroglial tumors are analyzed both histologically and molecularly (3). Oligodendroglioma (grade II) accounts for 5-6% of gliomas and anaplastic oligodendroglioma (grade III) is rare and accounts for 1.2% of primary brain tumors; over two-thirds of them have the 1p/19q codeletia (4). This cytogenetic aspect divides this category into oligodendroglioma/ anaplastic oligodendroglioma IDH mutant and 1p/19q codeleted and oligodendroglioma/ anaplastic oligodendroglioma NOS (3).

Histologically, both tumor entities are characterized by a diffuse, oligodendrocyte infiltrative cell proliferation with perinuclear halo, with variable mitotic activity and nuclear pleomorphism - low in oligodendroglioma and marked in anaplastic oligodendroglioma (5). The presumptive diagnosis of oligodendrocyte glial tumor can be based on imaging examination (computed tomography/magnetic resonance imaging), but the final diagnosis will be given only after histopathological examination, because sometimes it is difficult to differentiate

imaging between them and other diffuse astrocytoma, ganglioglioma, a dysembryoplastic neuroepithelial tumor or a pleomorphic xanthoastrocytoma (3).

This study aims to present a patient diagnosed with oligodendroglioma who has an evolution to an anaplastic oligodendroglioma despite an appropriate treatment, but also a brief review of the literature.

Case Report

A 44 years old male patient presented with generalized epileptic seizures that begin in the last week. Magnetic resonance imaging (MRI) revealed an intranevraxial expansive-infiltrative lesion, with discrete gadophilia, with a maximum diameter of 75 mm, left fronto-parietal lobes with a suggestive character for oligodendroglioma. The patient did not show up for control imaging. After surgery, the tissue fragments were processed and examined histopathologically with the diagnosis of NOS oligodendroglioma (Figure 1A).

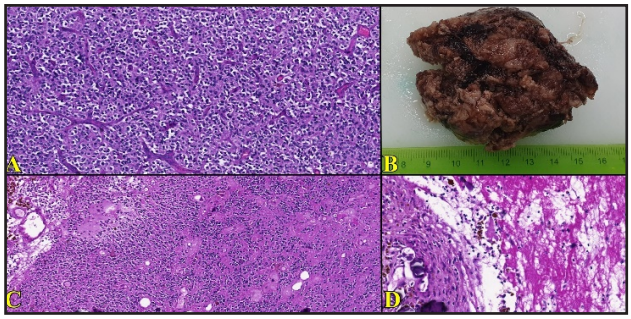

Figure 1 A. Oligodendroglioma (hematoxylin-eosin staining, x100): cell proliferation with the appearance of "fried eggs" with vascular network "chicken wire". B. Piece of brain tumorectomy (after fixation) with areas of hemorrhage and calcifications. C, D. Anaplastic oligodendroglioma (hematoxylin-eosin staining, x100): cell proliferation with moderate pleomorphism, with areas of calcification, with hemosiderin accumulations and areas of necrosis.

At eleven months the patient returned for grand mal seizures with increased frequency. The computed tomography (CT) examination identified a replacement of space, supratentorial, intranevraxial, left fronto-parieto-temporal lobes, with a maximum axial diameter of 63 mm, with inhomogeneous structure with calcareous inclusions, without contrast and surrounded by digitiform edema. MRI revealed a left frontal lobe and right frontal-parieto-basal infiltrative tumor mass with calcification areas, with dimensions of 73/61/60 mm, suggestive characters for an anaplastic oligodendroglioma or a calcified glial malignancy. The surgical resection piece received the anatomopathological diagnosis of anaplastic oligodendroglioma NOS (Figure 1C, D).

Immunohistochemical tests were performed that showed intense positivity for GFAP, IDH R132H, S100 and Synaptophysin (Figure 2). Immunomarkers SOX10, ATRX and Vimentin were negative. The p53 protein had a nuclear expression of 15%, oligodendrocyte transcription factor (Olig2) was positive in over 50% of the nuclei and and the cell proliferation marker Ki-67 showed a nuclear positivity of approximately 25% (Figure 3). Following these, the final diagnosis was anaplastic oligodendroglioma mutant IDH with 1p/19q codeletia.

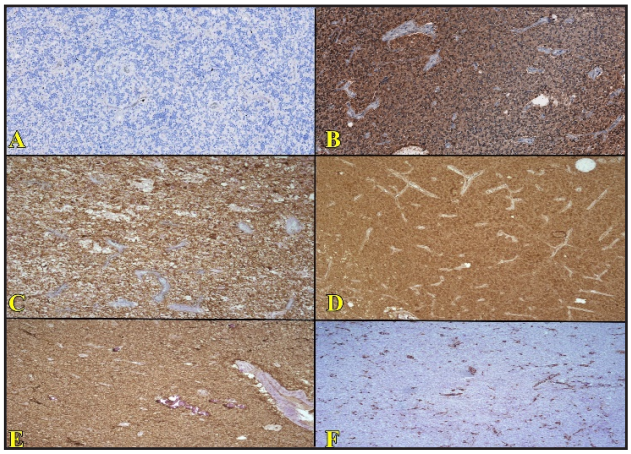

Figure 2 Anaplastic oligodendroglioma (x100): A. ATRX staining – negative. B. IDH1 R132H staining – intensely positive cytoplasmic. C. GFAP staining – intensely positive cytoplasmic. D. S100 staining – intensely positive cytoplasmic and nuclear. E. Synaptophysin staining – membrane strongly positive. F. Vimentin staining - vascular positive, tumor negative.The computed tomography imaging examination performed one month postoperatively revealed a tumor residue with axial diameters of 40/20 mm, with calcareous inclusions, without contrast enhancement and with small perilesional edema.

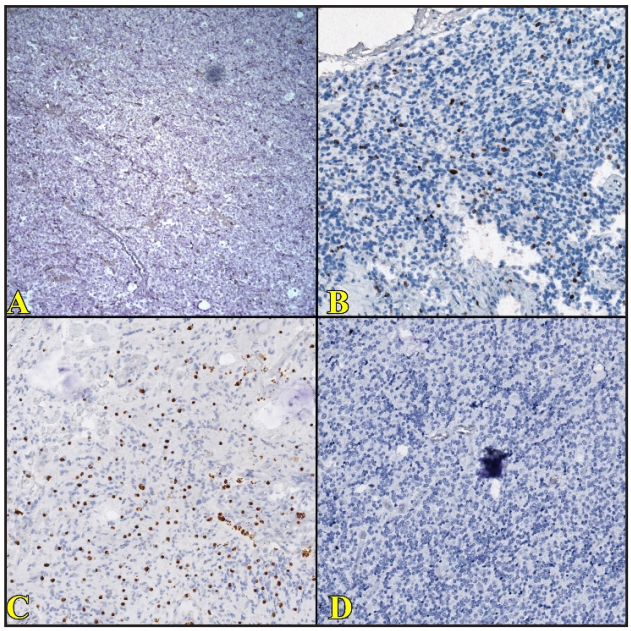

Figure 3 Anaplastic oligodendrolioma (x100): A. p53 staining – 15% of the nuclei are weakly positive. B. Ki-67 staining – positive in 25% of the nuclei. C. Olig2 staining – positive in over 50% of the nuclei. D. SOX10 staining – negative.

Discussions

Oligodendrogliomas have a slow growth rate, with clinical manifestations usually beginning five years after their development (2). In our case, being asymptomatic for a long time, it was allowed to grow the tumor to enormous dimensions of 75 mm. The only manifestation was epileptic seizures. Seizures are common, up to 85% of cases, and represent the first manifestations of oligodendrocyte tumors (6).

Imaging examination can guide the diagnosis, MRI having an increased accuracy in detecting and demarcating the tumor (7). Thus, on MRI examination they appear heterogeneous in T1 and T2, due to calcifications or cystic spaces and in a third of cases may be accompanied by perilesional edema (8). After administration of the contrast substance can be observed in a proportion of up to 50% minimum to moderate enhancement (7). CT examination characterizes oligodendrogliomas by their cortico-subcortical presence, by calcifications and by the variability of the contrast enhancement (3). Contrast enhancement is lower in children and more pronounced in adults and in high-grade tumors (III - anaplastic form) (3, 8). In our case the imaging aspects suggested the diagnosis of anaplastic oligodendroglioma both by the infiltrative aspect and by the presence of microcalcifications.

Histologically, they are characterized by increased cellularity composed of small cells with optically empty perinuclear cytoplasm and small nucleus – fried eggs appearance. The anaplastic variant also has a moderate-marked nuclear pleomorphism, an increased mitotic rate and the possibility of developing tumor necrosis (9). Also, there is a dense network of capillaries with chicken wire pattern, microcalcifications and areas of hemorrhage (5). In adults, intratumoral calcifications are associated in most cases (72.3%) with 1p/19q codeletia (10).

Immunophenotyping helps establish the diagnosis and together with cytogenetic tests give the diagnosis with certainty. While GFAP and IDH1 attest to the cerebral origin of proliferation, the positivity of the immunohistochemical markers S100, Olig-2 and synaptophysin indicates the diagnosis of oligodendroglioma (11, 12). The difference between the two subtypes is made by SOX10 (positive in grade II oligodendroglioma) and Ki-67 (12). A Ki-67 <5% is specific for grade II, while a Ki-67> 5% suggests a grade III (5). In our case, this differentiation protocol confirmed the final diagnosis of anaplastic oligodendroglioma, showing increased mitotic activity (Ki-67 25%) and immunonegativity for SOX10. In the case of mutant IDH anaplastic oligodendroglioma, as in our case, Ki-67 overexpression correlates with a poor prognosis of survival (13). ATRX immunonegativity is found in 47-73% of cases and indicates the presence of 1p/19q codelection. Also, a p53 >10% represents the most accurate reaction that suggests both the IDH mutation and the 1p/19q codeletion (14). Adding these aspects, stated in the literature to the IDH immunopositivity of our case and to the fact that p53 is about 15% we can conclude that our case has 1p/19q codeletia. The 5-year survival rate after treatment is between 49.38% and 53.8% (15).

The treatment consists of complete surgical resection with radio-chemotherapy. Radiotherapy is applied with doses of 54-60 Gy, fractionated 1.8-2 Gy per session, and chemotherapy may consist of Procarbazine, Vincristine and Lomustine (PCV) or second-line Temozolomide

or Nitrosureas (3, 16).

Conclusions

Our study focused on presenting a case of mutant IDH anaplastic oligodendroglioma with 1p/19q codelection (indicated indirectly by immunohistological tests) from an oligodendroglioma and on completing the morphological picture of these two entities.

Anaplastic oligodendrogliomas are rare tumor entities with a good prognosis compared to glioblastomas, as long as the treatment is effective. Its progression from an oligodendroglioma occurs based on the pathogenetic process such as ATRX alterations and p53, which will potentiate the proliferation rate quantified by Ki-67.

Acknowledgements

For this article all the authors have equal contributions. No funding or sponsorship was received for this study or publication of this article.

Conflict of interest

The authors declare that there is no conflict of interest.

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