CASE REPORT

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Multifocal and multicentric low-grade oligoastrocytoma in a young patient

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Abstract

Multiple primary central nervous system tumors are rarely seen in clinical practice and reported in the literature. The pathogenesis of multicentricity of primary tumors of the central nervous system still remains a debate, this pathology being found in almost two percent of reported tumor cases. Multifocal tumors are often described within the same hemisphere and supposed to be disseminated along the white matter tracts. On the opposite, multicentric tumors are found in the other hemisphere in subtentorial structures and are considered synchronous. We illustrate here the case of a young man admitted for symptoms of intracranial hypertension, diagnosed with multifocal and multicentric low-grade oligoastrocytoma with particular evolution and imagistic appearance.

Keywords: low-grade glioma, multicentric, multifocal.

Introduction

Multicentric gliomas are rarely reported in the literature and are more prone to localize supratentorial representing separate synchronous tumors. On the other side, multifocal gliomas are characterized by dissemination along white matter tracts, on the same hemisphere [1]. Here we present the case of a young male who was diagnosed with multifocal and multicentric low-grade oligoastrocytoma with particular magnetic resonance imaging (MRI) findings.

Case presentation

History and imaging

A 30-year-old man was admitted in the Department of Neurology for chronic headache with gradual onset. Several days prior to the admission, he started vomiting and complaining of blurring vision. After the admission, the neurological examination revealed a mild right hemiparesis with hypoesthesia, reduced visual acuity with bilateral papiledema, bilateral pyramidal syndrome and bradypsychia.

The cerebral MRI discovered four non-enhancing infiltrative lesions in both hemispheres (three on the left, one on the right side) with compression of the midline structures (Figure 1, white arrows). The most prominent lesions involved the left temporal lobe with extension towards the frontal lobe with compression on the mesecephalon (Figure 1, A, C, E, G and I), embedding the middle cerebral artery (Figure 1G, black arrow). On spectroscopy, a very high peak of choline was remarked (Figure 1J). The MRI appearance suggested for a low-grade glioma. The symptoms ameliorated after intravenous methylprednisolone therapy. Two lesion biopsies taken from different lesions showed a high cellularity without atypical cells. Gradually, the patient developed myoclonic jerks of the face and upper limb poorly controlled with anticonvulsive therapy. Suddenly, the patient entered in coma, probably because of compression of the brain stem and afterwards was declared brain dead.

Pathology

After autopsy, brain tissue was available for pathology and immunohistochemistry (IHC), after obtaining the written informed consent from the relatives of the patient. On microscopy, on Hematoxylin–Eosin (HE)-stained slides, the tumor presented as a diffusely infiltrating mass composed of mostly monomorphic cells with small and round nuclei, sometimes with distinct small nucleoli, and most of the time with a clear cytoplasm giving a honeycomb-like appearance. Gemistocyte-like cells with eccentric nuclei and eosinophilic cytoplasm were also abundant and present either as separate fields or intermixed with the cells with clear cytoplasms (Figure 2). Sometimes, arborizing thin capillaries were present in the tumor areas or at the periphery. Next, on consecutive seriate sections following the histopathological diagnosis, immunodetection was performed for the astrocytes cyto-

skeleton [glial fibrillary acidic protein (GFAP), 1:30 000 dilution, Z0334, Dako, Glostrup, Denmark], isocitrate dehydrogenase 1 (IDH-1, 1:500 dilution, HPA035248, Atlas Antibodies, Bromma, Sweden), oligodendrocyte specific transcription factor Olig-2 (1:400 dilution, HPA003254, Sigma Aldrich), blood vessel endothelia (CD34, 1:100 dilution, M7165, Dako), and the Ki-67 proliferation marker (1:50 dilution, M7240, Dako). Briefly, after antigen retrieval by microwaving in citrate buffer pH 6, endogenous peroxidase was blocked in 1% oxygenated water (30 minutes), unspecific immune sites were blocked by incubation in 3% skimmed milk, and finally the slides were incubated overnight with the primary antibodies in the specified dilution. Next day, after thorough washing in phosphate-buffered saline (PBS), the slides were incubated with a species-specific peroxidase-labeled secondary polymeric system (Nikirei Histofine, Tokyo, Japan) for one hour. In the end, enzymatic detection was finalized utilizing 3,3'-Diaminobenzidine (DAB) chromogen, the sections were counterstained with Hematoxylin and coverslipped in a xylene-based mounting medium. Immunohistochemistry for IDH-1 showed nuclear positivity in neoplastic astrocytes differentiating them from reactive astrocytosis. After a staining for the oligodendrocyte-specific transcription factor Olig-2, a variable percentage of all tumor cells (30–70%) were deemed positive. Anti-GFAP staining showed a strong delineation of the astrocytic elements inside the tumor, again with a variable percentage in different tumor areas, but on the average, with Olig-2 positive cells being predominant. Anti-CD34 staining confirmed a well-vascularized tumor with occasional branching vessels. The tumor showed inexistent mitotic figures, with a very low Ki-67 index (<1%). Altogether, the histopathological and immunohistochemical profile suggests a well-differentiated low-grade oligoastrocytoma [World Health Organization (WHO) grade II] (Figure 2). No involvement of the meninges was observed.

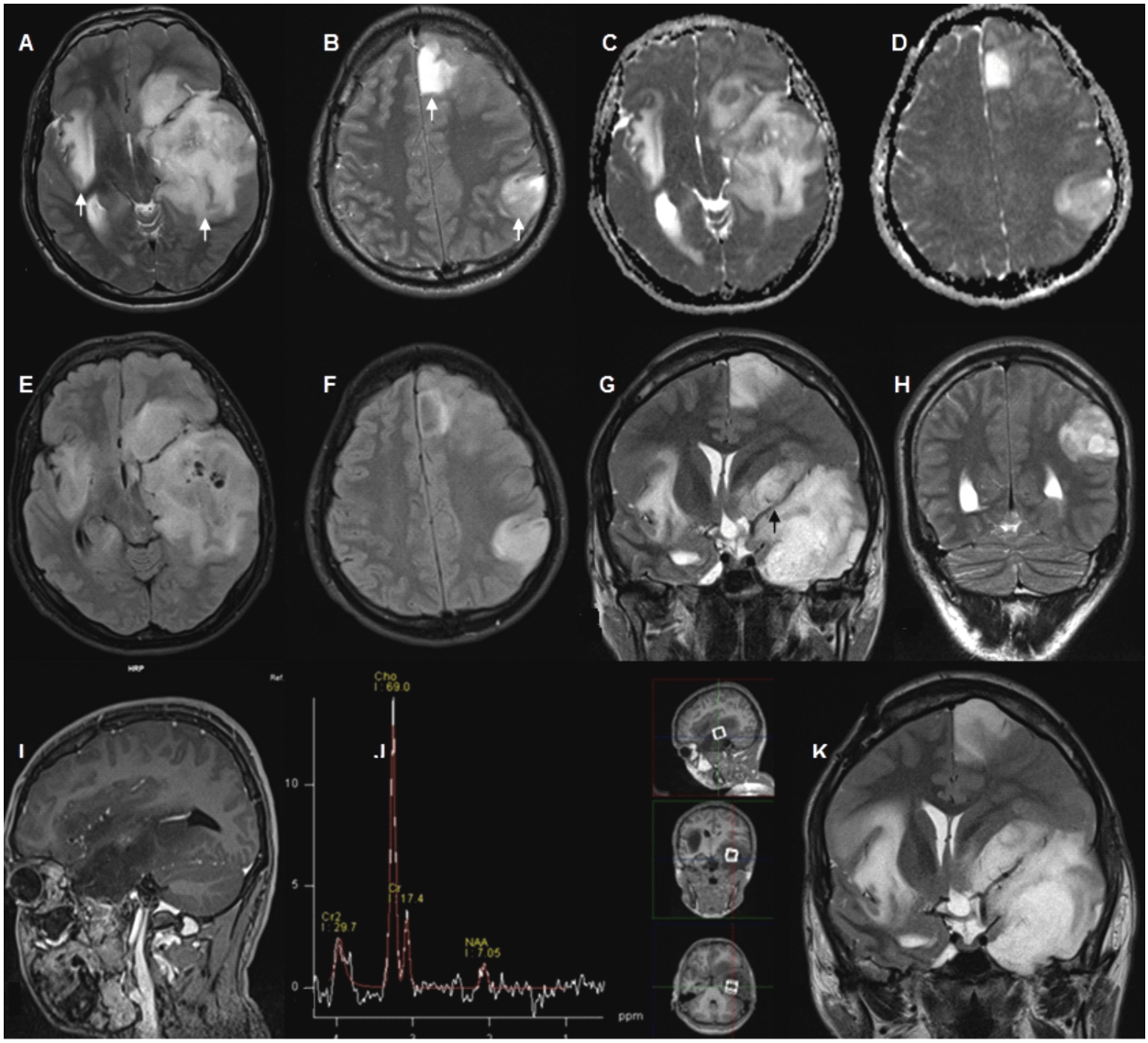

Figure 1 – ***(A) T2 bilateral temporal lesions (white arrows); (B) Left frontal and parietal T2 lesions (white arrows); (C and D) High apparent diffusion coefficient (ADC) map; (E and F) Fluid-attenuated inversion recovery (FLAIR) sequences showing tumoral lesions; (G and H) T2 coronal view. Left temporo-frontal lesion embed blood vessels (black arrows); (I) Sagital view of non-enhancing T1 temporo-frontal lesions; (J) MRI spectroscopy with high choline peak and decreased N-acetylaspartate (NAA) peak; (K) Reevaluation at six months showing stationary lesions in T2 coronal view.***

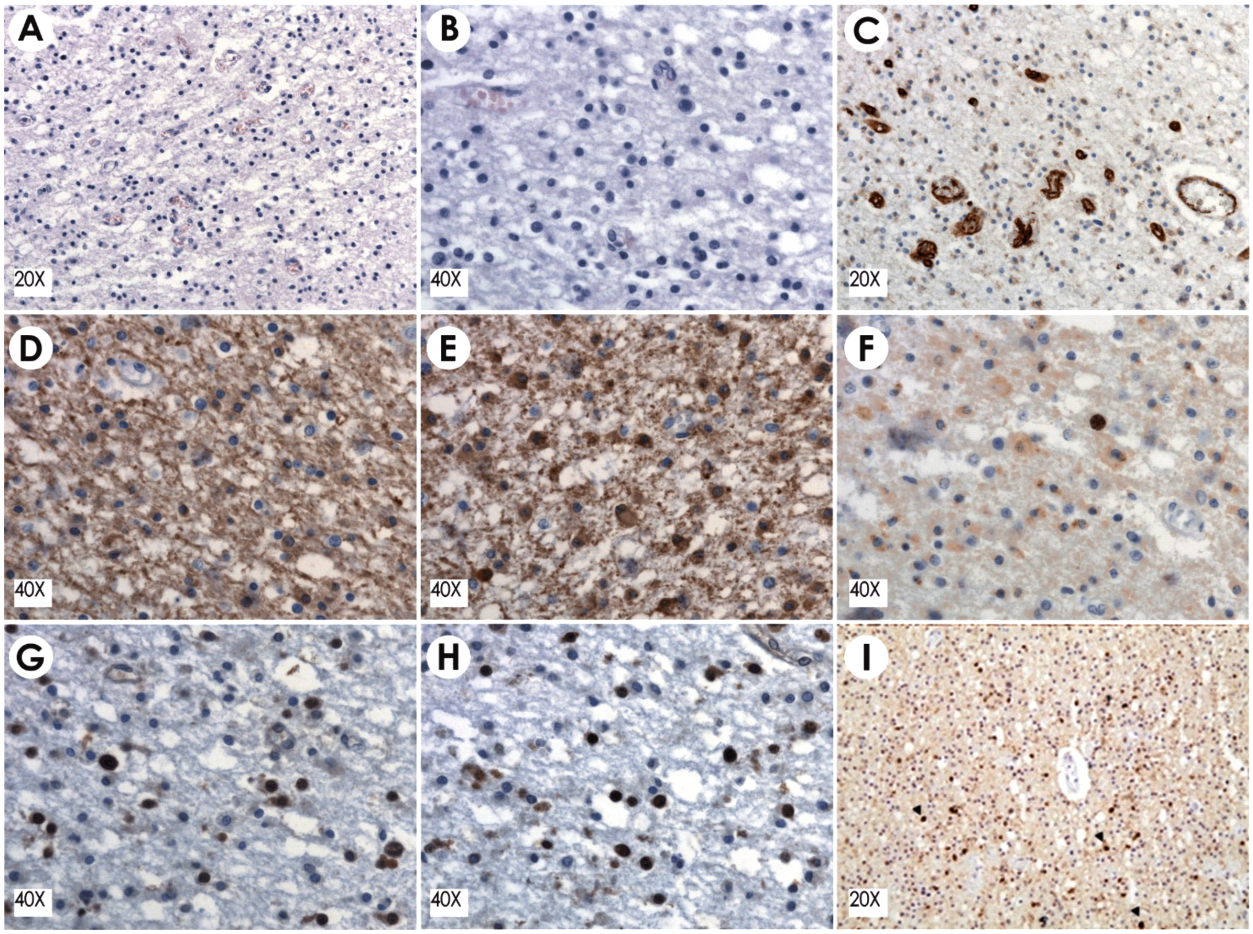

Figure 2 – ***(A and B) HE staining with slightly increased cellularity, poor nuclear atypia, no mitoses, and absence of necrosis; (C) Vascular proliferations, IHC for CD34; (D and E) GFAP variable density in the tumor, with gemistocytic cells in (E); (F) Very low Ki-67 index; (G and H) Variable immunopositivity for Olig-2; (I) IDH-1 nuclear positivity in neoplastic astrocytic cells.***

Discussion

For the present patient, the diagnosis was suggested by the MRI and spectroscopy, but other pathologies were also excluded, namely, multiple hemorrhages, encephalitis, abscesses, toxoplasmosis, metastatic disease and gliomatosis cerebri. The absence of enhancement, lack of surrounding edema, infiltrative pattern sparring great vessels and the spectroscopy ratio raised the suspicion of a multicentric low-grade glioma. Grade II gliomas are considered malignant tumors because of their capacity to infiltrate the surrounding tissue. Gradually, some can transform to anaplastic astrocytomas. Before establishing their filiation, the most important diagnostic challenge in these low grade tumors is to differentiate them from reactive gliosis, and to this extent immunohistochemistry for isocitrate dehydrogenase 1 (IDH1) using an antibody specific to the frequently found mutation (R132H) has been showed to be an ideal marker, even more sensitive than DNA sequencing to detect IDH1 mutations [2, 3]. Current WHO recommendations include, besides immunohistochemistry for R132H mutant IDH1, genetic testing for 1p/19q codeletion, and IDH1 complete gene sequencing for tumors that are negative for the IDH1 immunohistochemistry. Tumors which combine IDH mutation with 1p/19q codeletion are referred to as IDH mutant with 1p/q19 codeleted oligodendroglioma, while those carrying the IDH mutation but without 1p or 19q codeletion are encoded as IDH mutant diffuse astrocytoma [4]. In both cases, a mixed oligo-astroglial histopathology is not considered anymore. However, the present case is of particular interest first for its multicentricity and multifocal presentation of the tumor lesions, and second because this manifestation is usually observed in glioblastoma multiforme. Multicentric gliomas are characterized by separate synchronous tumors, usually in the opposite hemisphere or much more rarely separated by the tentorium [5]. Multifocal tumors are represented by multiple foci of lesion, connected by T2/FLAIR (fluid-attenuated inversion recovery) high signal on MRI along white matter tracts [6]. This MRI characteristic lacks in multicentric gliomas. Some case reports found different histotypes within multifocal or multicentric lesions [7]. Most of the published data are represented by case reports or small case series. A recent study showed that multicentricity can be found in 2% of the cases with gliomas [8]. Another analysis found that 17% from a total of 117 patients with glioblastoma is represented by multifocal disease [9]. The only effective treatment seems to be lesion excision, but this is limited by the grade of extension and the anatomy of the lesions [10]. In the case of 1p/19q codeletion, recent therapeutic trials proved that these oligodendroglial tumors seem to be responsive to chemotherapeutic agents like temozolomide, and when

the patients' status allows it, it could be an acceptable alternative to radiotherapy in cases with inoperable gliomas with oligodendroglial histopathology [11].

Conclusions

Multicentric oligodendroglioma is a very rare pathology with a variety of clinical and imaging patterns. Our paper presented a new case of oligodendroglial tumor at a young age and with rapid evolution towards exitus. A clear-cut panel of primary antibodies helped to identify the correct tumor pattern, and this might be of help for future cases when personalized therapeutic strategies will be available based on both the immunohistochemical and genetic profiles.

Conflict of interests

The authors declare that they have no conflict of interests.

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