A rare case of oligoastrocytoma with atypical symptoms initially diagnosed as multiple sclerosis: A case report

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Abstract. Oligoastrocytoma (OA) is an extremely rare tumor that may be difficult to diagnose, as it mimics multiple sclerosis (MS) clinically and radiologically. OA and MS are both space-occupying lesions. The symptoms of OA are complex and depend on tumor location and size. The clinical symptoms of OA are frequently not typical of glioma; therefore, OA is associated with a high misdiagnosis rate. We herein share our experience with diagnosing a rare OA case with atypical symptoms, which was initially diagnosed as MS, while stereotactic biopsy provided the final diagnosis. Due to the rarity and high misdiagnosis rate of OAs, it is suggested that clinical physicians update their knowledge regarding brain tumor classification and increase their awareness of rare tumor occurrence.

Introduction

Oligoastrocytoma (OA) is a type of brain tumor derived from neuroepithelial tissue that contains a variety of different neoplastic glial cells. OAs may be referred to as mixed gliomas, whereas OA cells originate from oligodendrocytes, ependymal cells and astrocytes. The most common types of mixed OA encountered in clinical practice include OA/OA2 [World Health Organisation (WHO) grade II] and anaplastic OA (AOA)/OA3 (WHO grade III) (1,2) OAs may originate anywhere within the cerebral hemispheres, although the frontal and temporal lobes are the most common locations. OAs comprise 5-10% of gliomas and 1% of all brain tumors and they typically develop in young and middle-aged adults (aged 30-50 years), whereas very few children are diagnosed with OA (3). The typical symptoms include seizures, headaches and personality changes, but the clinical manifestations and imaging characteristics of OAs are highly variable, which may further increase the difficulty of clinical diagnosis. In this report, we present the case of a patient with OA that was initially misdiagnosed as multiple sclerosis (MS).

Case report

A 46-year-old man was admitted to the Neurology Department of the China-Japan Union Hospital (Changchun, China). After recovering from a cold, the patient experienced dizziness and unsteadiness when walking. These symptoms continued for 5 days. The patient's medical history revealed that he had previously suffered from optic neuritis, but his vision improved following corticosteroid injections. A magnetic resonance imaging (MRI) scan of the head revealed abnormal, flaky, hypointense T1 and hyperintense T2 signals near the right basal ganglia and in the posterior horn of the right lateral ventricle. The visually evoked potentials (VEPs) were abnormal. The cerebrospinal fluid (CSF) oligoclonal bands (OCBs) were positive and, therefore, the patient was diagnosed with MS. Following this diagnosis, methylprednisolone was administered and the patient was discharged from the hospital after his symptoms improved. However, 1 week later the patient returned to the hospital with more severe dizziness and unsteadiness when walking and was admitted to the Neurology Department of The First Affiliated Hospital of Jilin University (Changchun, China) on January 17, 2014. Magnetic resonance spectroscopy (MRS) and an enhancement scan of the head revealed multiple abnormal signals, including a significant decrease in N-acetyl aspartate (NAA), a mild decrease in creatine (Cr), a significant increase in choline-containing compounds (Cho) and a mild increase in lactate (Lac). The MRS analysis indicated that a tumorigenic lesion could not be excluded; however, the results of the CSF analysis on January 20, 2014 were normal. The patient was diagnosed with multiple intracranial lesions and a biopsy was suggested, but was rejected by the patient's family. On February 6, 2014, the dizziness and unsteadiness became

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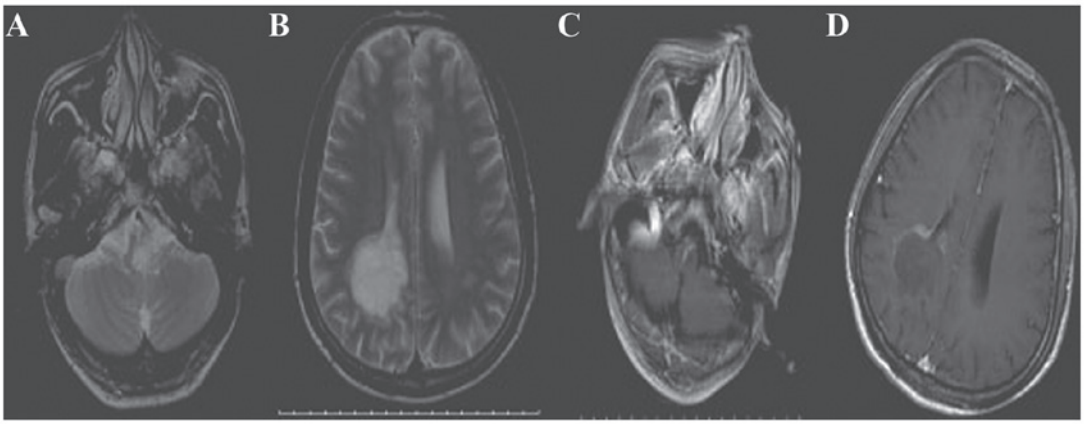

Figure 1. (A) Head magnetic resonance imaging (MRI) showing a flaky hyperintense T2 signal with unclear edges in the medulla oblongata. (B) The signal was strengthened after an enhancement scan. (C) Head MRI showing a flaky hyperintense T2 signal in the white matter around the posterior horn of the right lateral ventricle. (D) The lesion in the posterior horn of the right lateral ventricle appears as a low-intensity flaky signal that was only marginally strengthened after the enhancement scan.

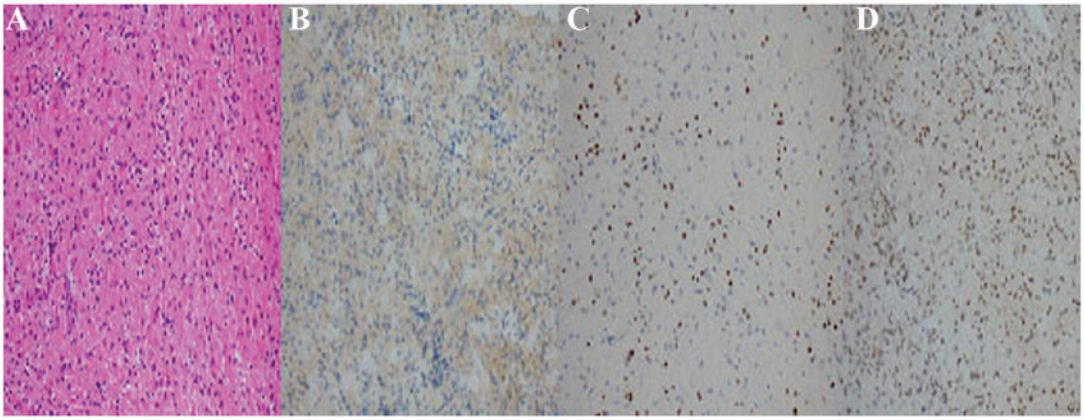

Figure 2. Immunohistochemistry-based neuropathological examination of the patient's biopsy material leading to the diagnosis of World Health Organisation grade II oligoastrocytoma. Magnification, x400. (A) Control hematoxylin and eosin staining; (B) weak epithelial growth factor receptor staining; (C) positive oligodendrocyte lineage transcription factor 2 staining; and (D) O^6-methylguanine DNA methyltransferase staining in ~75% of the tumor cells.

more pronounced, whereas additional symptoms appeared, including dysarthria, dysphagia, blurred vision and numbness of the right-sided limbs. Due to the worsening of the symptoms, the patient returned to our hospital for treatment. A head MRI on February 18, 2014 revealed flaky, hypointense T1-weighted and hyperintense T2-weighted signals and a fluid-attenuated inversion recovery (FLAIR) signal with unclear edges in the medulla oblongata. These signals were strengthened after an enhancement scan (Fig. 1A and B). The head MRI also revealed flaky, hypointense T1, hyperintense T2 and FLAIR signals in the right basal ganglia region and in the white matter around the anterior and posterior horn of the right lateral ventricle. The posterior horn lesion appeared flaky, with low-signal intensity that was marginally strengthened after the enhancement scan, particularly close to the edges (Fig. 1C and D). A biopsy below the trigone of the right parieto-occipital cortex was performed, and differential immunohistochemistry-based neuropathological examination using a set of diagnostic glioma markers led to the diagnosis of OA (WHO grade II). Immunohistochemistry yielded the following results: Ki-67 (~1%); p53 (-); glial fibrillary acidic protein (GFAP) (+); IDH1-R132H (-); oligodendrocyte lineage transcription factor 2 (Olig2) (+); O^6-methylguanine DNA methyltransferase (MGMT) (+ in >75% of the tumor cells); epidermal growth factor receptor (EGFR) (±); CD68 (-); myelin basic protein (partially +); and neurofilament (+) (Fig. 2). The biopsied tissue displayed weak staining for the astrocytoma marker EGFR, but was positive for the oligodendrocyte marker Olig2 and the OA marker MGMT in ~75% of tumor cells. These results combined were indicative of WHO grade II OA. The patient underwent craniotomy, while the symptoms persisted and were gradually exacerbated. The patient succumbed 1 month later in a local hospital due to a pulmonary infection.

Discussion

The etiology of OA has not yet been fully elucidated. Long-term ionizing radiation exposure is the only currently known risk factor, although it has been suggested that OA is the result of multiple factors, such as genetic diversity, viral infections and immune factors. The symptoms of OA are complex and depend on tumor location and size. OA commonly occurs in the supratentorial region, particularly in the frontal lobe, followed by

the temporal lobe, parietal lobe, thalamus, corpus callosum, ventricle, cerebellopontine angle region and brainstem. The tumor often crosses lobes and, therefore, may involve multiple lobes of the brain and the superficial cortex. The involvement of multiple lobes of the brain may explain the appearance of epilepsy-like symptoms in OA. Epilepsy is the most common clinical symptom in OA and ~80% of OA patients suffer from seizures (3). Other symptoms include ataxia, headaches, memory loss, personality changes and other mental changes, including intelligence decline and dementia (4). Therefore, the clinical symptoms of OA are frequently not characteristic of glioma.

The initial symptoms of the patient in the present case were atypical and contributed to the original misdiagnosis. The patient had previously suffered from optic neuritis, a condition associated with MS, and his vision had improved following corticosteroid injections. Finally, the premonitory cold symptoms, abnormal VEP and OCB reinforced the misdiagnosis of MS.

MS is a common cause of space-occupying lesions. The treatment of choice is high-dose dexamethasone to reduce the brain edema, which is empirically associated with clinical and radiological improvement in 1-3 weeks. However, if there is no clinical improvement, a stereotactic biopsy of the space-occupying lesion is recommended (3).

Although CT scans may show patchy lesions, low-density shadows and unclear edges, the image density may be lower in cases with cystic tumors and CT lacks the required specificity for OA diagnosis. Dotted, nodular and short stripe-shaped calcifications may be detected surrounding the tumor, and these characteristics may gather, in part, at one end of a quasi-circular tumor. The sensitivity and specificity of MRI are significantly better compared with those of CT for lesion detection and identification. T1-weighted images mainly show low-intensity signals, whereas T2-weighted images and FLAIR show homogeneous high-intensity signals with unclear edges. Since OAs grow slowly, vasogenic edema and mass effects do not commonly occur. Thus, T1-weighted images may be less efficient at detecting tumor boundaries. By contrast, T2-weighted images may more effectively reflect real tumor boundaries; however, it is difficult to distinguish the tumor from the surrounding edematous area. There is usually no or only a mild enhancement of the lesion area, as visualized by MRI. To visualize the infiltration range of the lesion, MRS is superior to conventional MRI. The MRS results of the patient revealed a significant decrease in NAA, a mild decrease in Cr, a significant increase in Cho and a mild increase in Lac. In contrast to this result, Cho may be decreased in highly malignant gliomas, which is likely associated with necrosis (5). The change in the ratios of Cho/Cr and NAA/Cr provides guidance for the classification of the malignant grade of the tumor and the projected survival time of the patient (6). These results indicate that a tumorigenic lesion may be underlying the observed symptoms.

Histopathological examination remains the gold standard for OA diagnosis. Indirect signs of OA, such as edema of the brain or the brain stem, basal ganglia or corpus callosum volume gain and blurring of the lateral fissure may be observed. Histological examination may show the diffuse distribution of tumor cells, which are polygonal or circular, with nuclear condensation. The immunohistochemical markers used are Olig2, a marker of oligodendrocytes; GFAP, a marker of astrocytes; EGFR, a marker associated with astrocytomas; and MGMT, a marker associated with OA (4). Immunohistochemical analysis of this patient's biopsy revealed tumor cell expression of Olig2, GFAP and MGMT, indicating that the patient had an OA.

OAs (grade II) are considered to be low-grade tumors, and they generally grow at a slower rate compared with malignant anaplastic OAs (grade III). However, OAs may evolve into anaplastic oligoastrocytomas over time. OA growth generally depends on the percentage of astrocytoma in the tumor, as astrocytomas tend to grow more rapidly compared with oligodendrogliomas.

Due to the rarity and high misdiagnosis rate of OA, it is suggested that clinical physicians update their knowledge regarding brain tumor classification and increase their awareness of rare tumors. Promisingly, the rapid advances in imaging technologies, particularly functional MRI, appears to enable accurate confirmation of the location and extent of injury in the brain. With the combination of current imaging technology, biopsy and pathological examination, it is now possible to accurately diagnose these relatively rare tumors.

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