

Primary cerebellar glioblastoma multiforme

Mustafa Kemal Demir, Tayfun Hakan, Okan Akıncı, Zafer Berkman

ABSTRACT

Primary glioblastoma multiforme of cerebellar hemispheres in adults is a rare condition. Most of them result from dedifferentiation of astrocytoma to glioblastoma. We present two cases of unusual *de novo* cerebellar glioblastomas, one of which is the giant-cell variant. We review their clinical behaviour with conventional MR imaging features and discuss the key findings that can lead to the correct diagnosis in sight of new MR imaging technologies.

Key words: • glioblastoma multiforme • posterior fossa • cerebellum • magnetic resonance imaging

Glioblastomas constitute approximately 15%-20% of the entire intracranial tumors (1). They generally occur in the fifth and sixth decades. These are infiltrating tumors located in the deep white matter or in the deep gray matter neighboring white matter, mainly in cerebral hemispheres. They develop secondary to diffuse or anaplastic astrocytomas. However, they can sometimes occur primarily (2). Occurrence of primary cerebellar glioblastoma multiforme (GBM) in adults is extremely rare; few cases have been published so far (3-5).

In this paper, clinical features and magnetic resonance (MR) imaging findings of primary cerebellar GBM in two patients are reported.

Case reports

Case 1

A twenty-eight year-old female patient presented to our hospital with sudden nausea, vomiting, and headache. In neurological examination, right cerebellar involvement and intracranial pressure increase findings were present. A 1.5 Tesla MR imaging scanner was used to perform SE T1, FSE T2, and post-gadolinium SE T1W cranial MR imaging examinations in axial, coronal, and sagittal planes. A 3-cm mass lesion with mixed solid and cystic components and surrounding edema was present in the caudal lobe of the right cerebellar hemisphere. This mass was heterogeneous and hypointense to cerebellar parenchyma on T1W sequences and heterogeneously hyperintense on T2W images. Following injection of gadolinium, the solid component enhanced heterogeneously and the cystic component enhanced in an irregularly circular fashion. Mass effect on the neighboring brain stem, and obstruction of the cerebellomedullary cistern was present. Obstructive hydrocephalus due to the obstruction of the fourth ventricle was present (Figure 1a, b). Surgery (total tumor resection) was performed. Histopathological examination following the operation revealed that the tumor was a giant-cell variant of GBM (Figure 1d). Postoperative radiotherapy was performed. However, the tumor recurred, and the patient died in the eighth month following the diagnosis.

Case 2

Neurological examination of a 17-year-old male presenting with headache, vomiting, and balance problems revealed increase in intracranial pressure, and left cerebellar findings. Cranial MR imaging was requested for suspicion of a space occupying lesion. A mass lesion with irregular contours located in the left cerebellar hemisphere and vermis, and extending from the mid-cerebellar peduncle to the pons was observed in cranial MR imaging examinations of SE T1, FSE T2, and FLAIR and post-gadolinium SE T1W sequences performed in three planes using a 1.5 Tesla MR imaging unit. On non-contrast T1W images, the mass

From the Departments of Radiology (M.K.D. ✉ demirkemal@superonline.com, O.A., Z.B.) and Neurosurgery (T.H.), Haydarpaşa Numune Training and Research Hospital, İstanbul, Turkey.

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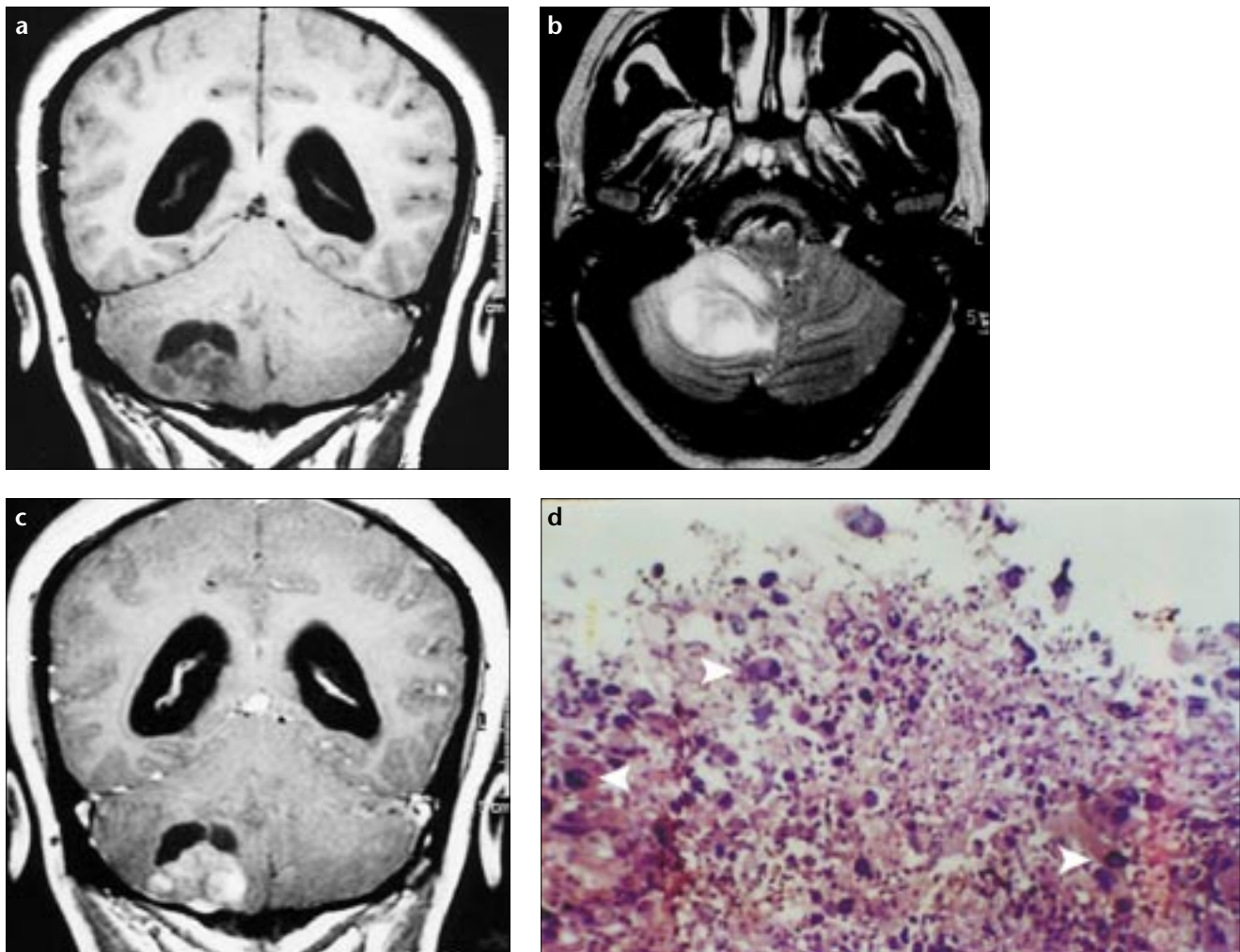


Figure 1. a-d. Giant-cell glioblastoma. On coronal precontrast T1-weighted MR image (a), a 3-cm, heterogeneously hypointense mass lesion with cystic/necrotic and solid components is observed in the caudal lobe of the right cerebellar hemisphere. On axial T2-weighted MR image (b), tumor is seen heterogeneously hyperintense to cerebellar parenchyma. Two rounded hyperintense areas within the mass are due to either intratumoral necrosis, or cystic degeneration. On coronal postcontrast T1-weighted MR image (c), irregular circular enhancement is observed around the central non-enhanced cystic/necrotic component, and non-homogeneous enhancement is observed in the solid component. Giant, irregular tumor cells with multiple nuclei are observed in the histological illustration (d) (HE, x100). Phagocytic activity is seen in tumor cells (d, arrowheads).

lesion was isointense and heterogeneously hypointense to cerebellar parenchyma. (Figure 2a). There were irregular heterogeneous areas in T2W series and FLAIR examinations (Figure 2b, c). Following intravenous gadolinium administration, irregular circular enhancement consistent with necrotic areas was observed in the mass lesion (Figure 2d). Mass effect on the fourth ventricle and hydrocephalus were present. Subtotal tumor resection and ventriculoperitoneal shunt placement were performed via sub-occipital approach. Diagnosis of GBM was made in the histopathological examination. Adjuvant chemotherapy and radiotherapy were performed. Tumor recurred after six months. The patient died following the second operation.

Discussion

Glioblastoma is the most frequent tumor among all primary intracranial tumors with a frequency about 15%-50%. It can be seen in all age groups; however, patients are generally over 50 years of age. When compared to childhood tumors, localization in the posterior fossa in adults is rare (6,7). Giant-cell variant of GBM is even much rarely encountered in adults (8).

GBM is a stage 4 tumor according to World Health Organization classification. Main differentiating characteristics from diffuse astrocytomas are prominent microvascular proliferation, tumor necrosis, increased mitotic activity, and more cellular and nuclear pleomorphism. Giant-cell variant of GBM, constitutes 5% of all GBMs. It has

multinuclear and amorphous cellular structure. Its differentiating properties are its firmness due to excessive stroma formation and well definition (9).

GBMs located in the posterior fossa may cause diverse cerebellar symptoms like headache, gait disturbances, ataxia, nausea, and vomiting. These findings can suggest the existence of a mass lesion in the posterior fossa. However, none of these are specific for GBM. Diagnostic imaging will always be required. MR imaging is favored among other diagnostic methods with its high contrast resolution and multiplanar capability. Furthermore, MR diffusion/perfusion imaging and MR spectroscopy examinations can also facilitate the characterization of the lesions and the differential diagnosis.

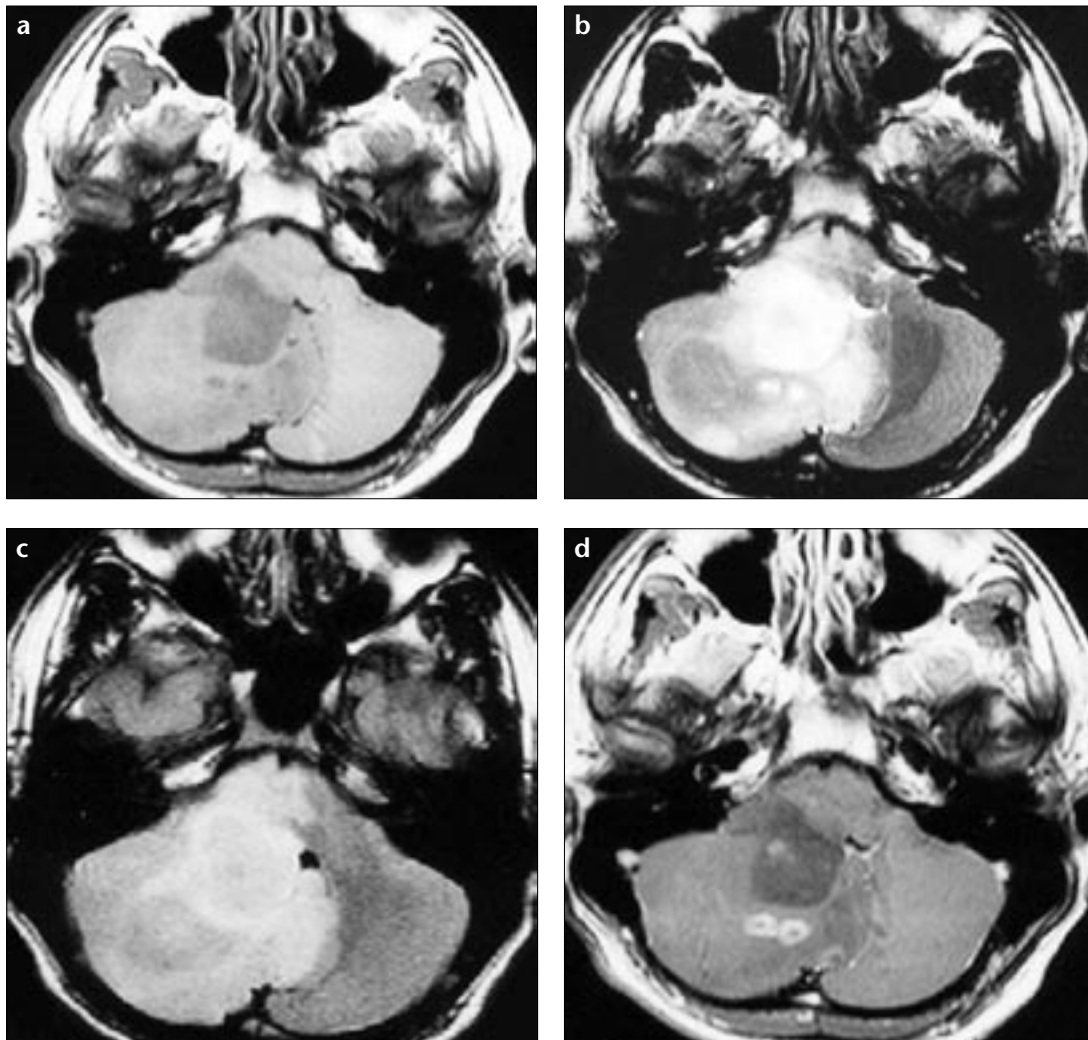


Figure 2. a-d. Primary glioblastoma multiforme in the right cerebellar hemisphere extending to vermis with mass effect on the brainstem. On axial precontrast T1-weighted MR image (a), the tumor appears to be isointense and heterogeneously hypointense to cerebellar parenchyma. On axial T2-weighted (b) and FLAIR (c) MR images, a heterogeneously hyperintense mass lesion with necrotic areas and surrounding edema is seen. Axial postcontrast T1-weighted MR image (d) shows irregular circular enhancement around the necrotic areas and nodular enhancement of the solid component in the mass.

Glioblastomas appear as heterogeneous masses on MR imaging. This heterogeneous appearance is due to the formation of necrosis and/or cysts. On T1W images, a generally centrally located hypointense area is present. The thick irregular rim surrounding this hypointense area and the solid nodules are isointense or slightly hypointense to cerebellar parenchyma. Tumors may contain foci of bleeding and calcification. Neither of these two findings was seen in our cases. Existence of these findings increases the heterogeneity of the tumor. There is a heterogeneous hyperintense appearance with variable signals on T2W images. Surrounding edema is prominent on T2W images. It should be kept in mind that neo-

plastic cells could also be present in areas other than the signal changes found on T2W sequences. Enhancement following intravenous gadolinium administration is always present. This is as rim enhancement of the thick irregular wall of the tumor. Solid nodules may be present; however, since the appearance varies it is not specific. In both cases reported here, MR imaging findings were consistent with these findings, and no characteristics that could lead to a specific diagnosis could be found.

In the differential diagnosis of GBM located in the posterior fossa in adults, diseases like metastases, abscess, hemangioblastoma, cystic astrocytoma, and entities like encephalitis, tuberculomas, or multiple sclerosis should be

considered.

MR spectroscopy is a method helpful in differentiating tumors from other diseases. In GBM, choline (Cho)/creatinine (Cr) ratio is found to increase over 3 to 1, and N-acetyl aspartate (NAA) peak is reduced. Decrease in NAA is related to neuron loss due to the tumor, decrease in creatine is related to metabolic changes, and increase in choline is due to increase in the membrane synthesis and cells. Choline concentration is reduced in infections. It has been reported that MR spectroscopy is also helpful in the classification of brain tumors. There is a clear difference in the resonance properties of choline and total creatine in low-grade astrocytomas and those of anaplastic astrocytomas. Choline signal is more

prominent in the solid components of the high-grade glial tumors. In these tumors, lactate is also increased due to tumor hypoxia. Increase in free lipid resonance in 1.3 ppm is specific for GBM and metastasis. In addition, differences in glycine/myoinositol in 3.55 ppm is also significant when differentiating between these two entities (10).

Diffusion weighted imaging (DWI) is also used in the differential diagnosis of rim enhancing cerebellar mass lesions. Cystic or solid components of brain tumors display high ADC (apparent diffusion coefficient) values and low signals in DWI with a high b value. Cystic or necrotic components of these tumors exhibit low ADC values on ADC maps, and low signal on high b-value diffusion-weighted images. To the contrary, while cavity content of abscesses is seen as high signal intensities in diffusion sequence images, ADC values are low. Therefore, DWI is very effective in the differentiation of abscesses and tumors (11,12).

In a recent study, it was found that the intensely enhancing solid components of hemangioblastomas demonstrated low signals in DWI together with high ADC values. In the same study, this finding was not observed with other tumors of the cerebellum such as metastases, ependymoma, lymphoma, and rhabdoid tumor (13).

Tumefactive demyelinating diseases can demonstrate similar clinical and radiological characteristics with brain tumors. Differentiation may not be possible even with MR spectroscopy. However, this situation is encountered more frequently with lesions located in the brain stem or a cerebral hemisphere (14).

The routine MR imaging findings of solitary metastases and GBM are sometimes not adequate for differential diagnosis. Differential diagnosis between these two entities can be possible with perfusion and spectroscopic MR examinations. The differences in vascularity and metabolite levels in the periphery of the tumor have been found to be significant for the differentiation of metastases and GBMs. Relative cerebral blood volumes in peritumoral areas calculated with perfusion-weighted MR imaging are clearly higher in gliomas when compared to metastases. In the spectroscopic examination, choline levels are high in peri-tumoral areas of gliomas and low in metastases; a difference enabling differential diagnosis (15).

In conclusion, primary cerebellar GBM and its giant-cell variant are extremely rare in adults. However, GBM must be considered in the differential diagnosis of aggressive mass lesions of the cerebellar hemisphere. Routine MR imaging findings and clinical symptoms are insufficient for an accurate diagnosis. Therefore, MR spectroscopy, DWI and brain perfusion imaging techniques must be used in prospective evaluation.

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