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Bifocal temporal ganglioglioma

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Abstract The authors present the case of a 33-year-old patient with a bifocal ganglioglioma located in the right superior temporal gyrus. He had a history of tonic–clonic seizures and developed intermittent nausea and vertigo later on. Magnetic resonance imaging showed two distinct, small lesions in the right temporal lobe. Both tumors were removed microsurgically with ultrasound guidance. Intraoperatively, two distinct tumors were found. Histological diagnosis of both tumors was of ganglioglioma WHO II. Postoperatively, the patient was free of symptoms. Bifocal occurrence or the coincidence of two distinct gangliogliomas is a very uncommon finding. So far, it has not yet been reported in benign gangliogliomas.

Key words Ganglioma · Brain tumor · Magnetic resonance imaging · Epilepsy

1. Introduction

Gangliogliomas have been described more frequently since the advent of contemporary neuroimaging studies [13, 16, 27]. Even small tumors may be a source of epilepsy. Neuroimaging studies are often unspecific, and the preoperative differential diagnosis can create considerable difficulties. Gangliogliomas usually occur as single intraparenchymal tumors. Multifocal variants have been reported only in malignant tumors. To the best of our knowledge, this is the first report on bifocal occurrence of a benign ganglioglioma.

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2. Case report

This 33-year-old man was admitted to the Department of Neurosurgery at the University of Freiburg for diagnostic evaluation of two lesions of the right temporal lobe. Five years earlier, he had suffered two tonic–clonic seizures. The computed tomography (CT) scan then was described as normal. Anticonvulsive prophylaxis with diphenylhydantoin was initiated, and no other seizures occurred. About 41/2 years later, the patient complained of intermittent nausea and vertigo.

His general physical examination was unremarkable. He was fully oriented, and there were no abnormal neurological findings. Electroencephalography was normal. During hyperventilation, a slight dysrhythmia and a few sharp waves were evoked. The CT scan showed two small hypodense lesions of the right temporal lobe without calcification. There was slight enhancement after administration of contrast medium. Magnetic resonance (MR) imaging demonstrated the topography of the two small lesions in the right superior temporal gyrus with regard to the sylvian fissure. Both tumors were isointense on the T1-weighted, nonenhanced images. There was marked enhancement after administration of gadolinium (Fig. 1). On T2-weighted images, the tumors were slightly hyperintense. Cystic components were not found. Both lesions were evident on MR angiography. The lesion located more anteriorly was in close contact to a sylvian vein (Fig. 2). Since the CT and MR findings appeared inconclusive, a transfemoral cerebral angiography was performed. The lesions were not visualized on the angiograms. The imaging findings were thought to be most likely compatible with a diagnosis of cavernomas that had not bled previously.

We decided to remove the lesions via a right frontotemporal approach. The removal was guided by intraoperative ultrasound location. Both lesions were hyperechoic. The two nodules in the superior temporal gyrus were exposed via the sylvian fissure. Both tumors were clearly separated from each other over a distance of 15 mm with normal brain tissue between. They were of solid consistency and about 10 mm and 3 mm in diameter, respectively. Some small tumor vessels were dissected and coagulated. Total resection of both tumors was achieved. The adjacent brain tissue appeared to be normal and not infiltrated by the tumor or damaged by earlier hemorrhage. The patient's postoperative course was uneventful.

For histopathological analysis, biopsy specimens of both tumors were available. The specimens showed a tumor consisting of neuronal and astroglial components (Fig. 3a). There were large

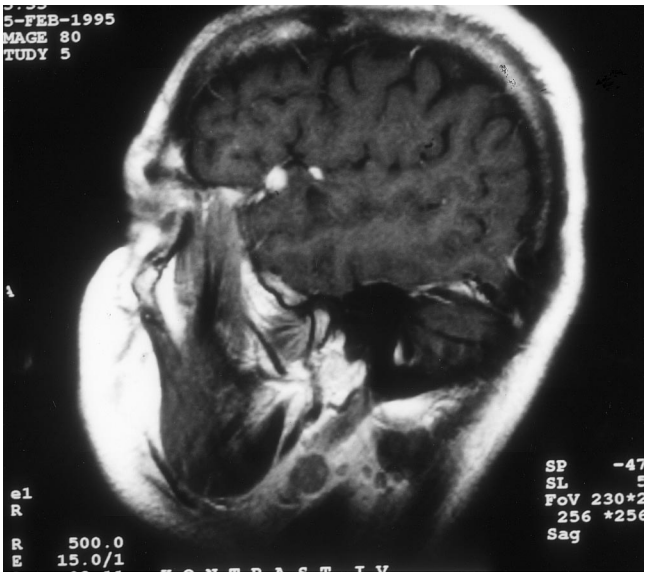

Fig. 1 Gadolinium-enhanced T1-weighted sagittal magnetic resonance image showing two small, distinct tumors in the right superior temporal gyrus close to the sylvian fissure. There are no signs of leptomeningeal involvement

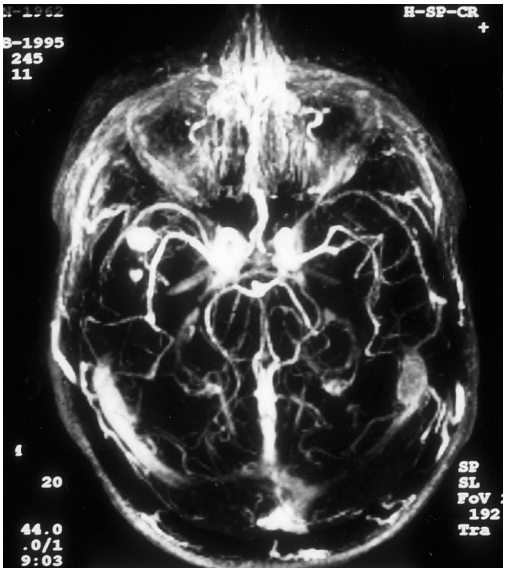

Fig. 2 Magnetic resonance angiography demonstrates enhancement of both lesions in the venous phase. The anterior lesion is in close proximity to a sylvian vein

polymorphic and rare binucleated ganglionic cells with vesicular nuclei and prominent nucleoli. Axonal processes were visible with a fascicular pattern of spindle-shaped cells. The astroglial components showed reactivity for glial fibrillary acidic protein (GFAP) (Fig. 3b), whereas synaptophysin immunoreactivity was shown in the ganglionic (neuronal) components (Fig. 3c). The neuronal component was also immunoreactive for N-CAM and neurofilament protein (not shown). Nuclear labeling for immunoreactive cells with Ki-67 (MIB-1) was observed in less than 4% of the cells. Lobules of neoplastic, partially spindle-shaped cells were focally surrounded by collagen fibrils. Both tumor specimens were classified as well-differentiated ganglioglioma WHO II.

MR scans at 3 months and 2 years postoperatively did not show any residual or recurrent tumor. The neurological status was normal. The patient did not complain anymore about headaches, vertigo, or seizures. His fitness at work and at home was good.

Discussion

Perkins introduced the term ganglioglioma in 1926 [17]. Soon thereafter, Courville reported on the first series of gangliogliomas [4]. In 1979, gangliogliomas were defined as tumors composed of neuronal and neoplastic glial elements by the World Health Organization (WHO) [28]. The latest WHO classification of brain tumors differentiates the entity of desmoplastic infantile ganglioglioma according to (1) early age of onset, (2) superficial position, and (3) frequent association with a large cyst from classic ganglioglioma [12, 21]. Gangliogliomas are rare tumors of the central nervous system and account for 0.4–1.3% of all brain tumors [27]. They may represent up to 7.6% of all brain tumors in children [3, 10]. Gangliogliomas can occur in any part of the central nervous system. The most common location, however, is the temporal lobe, where 40–84% of the gangliogliomas are found [8, 20, 27]. Usually, gangliogliomas are slow-growing, relatively benign tumors [20]. Some cases of malignant transformation have been observed [2, 5, 24]. The patients' histories often extend over years, sometimes even decades. Patients' ages at diagnosis range from 6 months to 80 years [3, 10], but those aged 50 or older are rare. About 90% of the patients present with epilepsy, which is in most cases pharmacoresistant [8, 20]. Focal neurological deficits or symptoms of increased intracranial pressure can be observed in only a few cases, mostly in patients with tumor location in the midline and affecting the optic nerve, the brain stem, or the spinal cord [10, 14]. Total tumor resection is considered the most effective treatment, while the benefits of radiation therapy are controversial [6, 8].

The clinical course of our patient with a 5-year history of epilepsy and the tumor located in the temporal lobe is typical for ganglioglioma cases[8, 13, 14, 27]. The coincidence of two distinct tumors, however, is very uncommon. Yamamoto et al. [25] reported on a multifocal neurocytoma–gangliocytoma with extensive leptomeningeal dissemination in the brain and spinal cord. The histological diagnosis in their case, however, was more problematic; and a diagnosis of dysembryoplastic neuroepithelial tumor had been discussed as well [1, 25]. Diffuse leptomeningeal involvement with multiple parenchymal foci of a ganglioglioma in a 20-month-old infant has also been described. In that case, however, focal anaplasia of the astrocytic component was found [23]. Zentner et al. [27] reported a patient with suspected but not histologically confirmed drop metastases along the CSF pathways in the fourth ventricle and the cervical and thoracic subarachnoid space 1 year after incomplete resection of an anaplastic ganglioglioma of the temporal lobe.

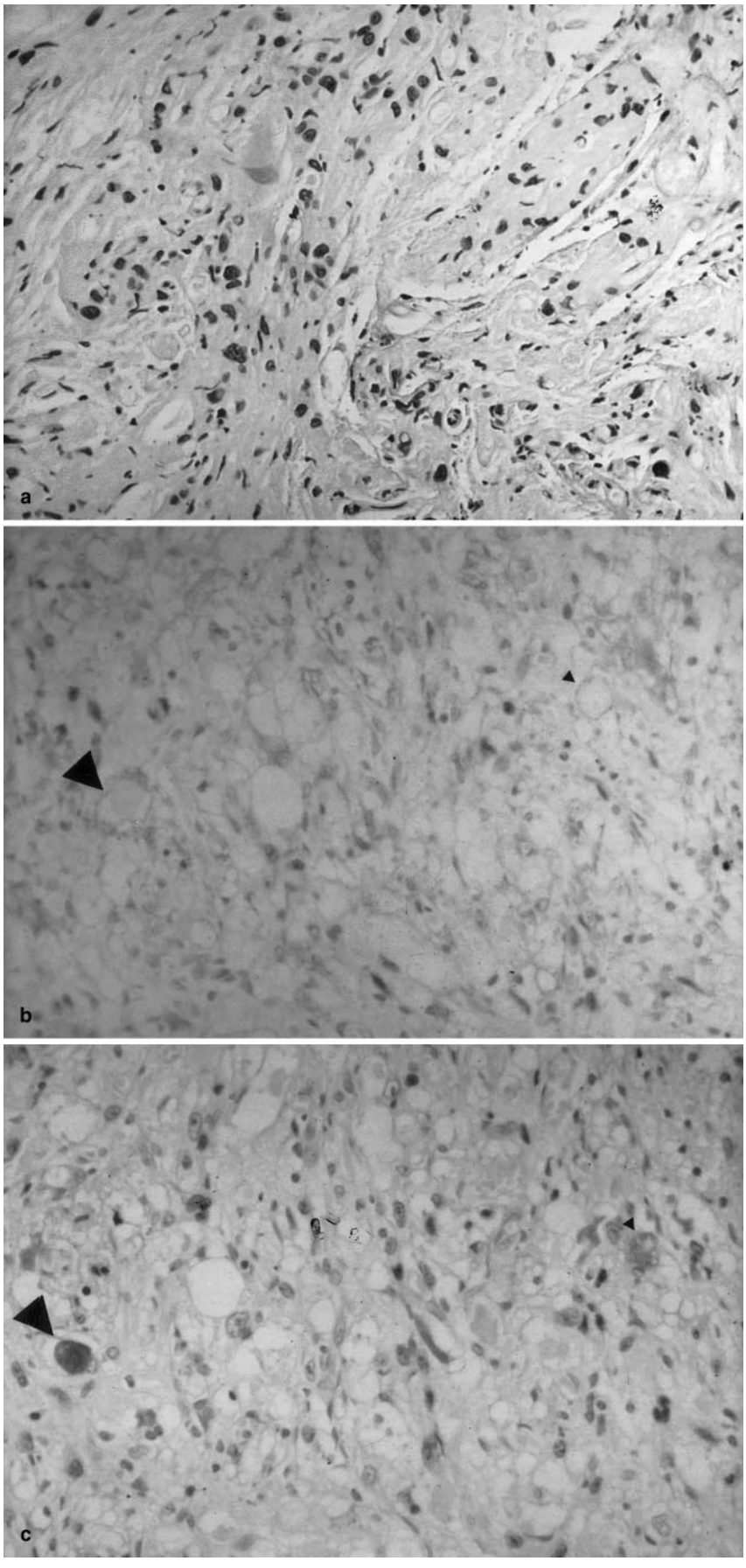

Fig. 3a–c Photomicrographs showing the results of the histopathological and immunohistochemical examinations of both specimens. **a** Differentiated ganglioglioma with polymorphic cells (second specimen). H&E, original magnification ×250.**b** Astrocytes and their processes express glial fibrillary acidic protein (DAKO, code no Z 0334) immunoreactivity in different components of the same area shown in **c**; *small and large arrow heads* point at corresponding foci. Original magnification, ×250. **c** Mature ganglionic cells show immunoreactivity to the monoclonal antibody SY38 (Boehringer Mannheim, cat. no 902322)

In our case, there were two clearly distinct tumors, both classified as ganglioglioma WHO II, without any signs of anaplasia or leptomeningeal spread. There was no recurrence 2 years postoperatively. Results of the CT and MR investigations are compatible with those of previous reports. The neuroradiological findings, however, are not pathognomonic [6, 11, 27]. In MR imaging, solid tumor components usually appear as isointense on T1-weighted images, but in some cases hypointense or even hyperintense. As in our case, T2-weighted images show hyperintense solid tumors more often than isointense or hypointense tumors. Homogeneous and inhomogeneous enhancement of solid tumors can be seen with CT as well as with MR, but are reported in less than 50% of cases. Experience with MR angiography is extremely limited.

The diagnosis of our patient's tumors as ganglioglioma WHO II was based on histopathological and immunohistochemical characteristics defined according to the WHO classification and earlier reports [7, 9, 12, 18, 24]. The classification of lesions containing neuronal and glial components such as hamartoma [22], dysembryoplastic neuroepithelial tumor [16], or ganglioglioma may be difficult in some cases. Transitional forms have been described [19]. Histopathological and immunohistochemical analysis showed two tumors with identical characteristics, both consisting of neuronal and astroglial components. In accordance with recent reports, the nuclear labeling index for the proliferation marker Ki-67, observed only in astrocytic tumor components, was less than 4%. Wolf et al. reported a significant correlation between Ki-67 and WHO grades [24]. In 74% of gangliogliomas, they found nuclear labeling for Ki-67 to be under 1%. Pathologically, ganglioglioma is not a uniform entity. Histopathological and immunohistochemical characteristics, however, allow to establish the correct diagnosis. The simultaneous occurrence of astroglial and abnormal ganglionic components with neoplastic signs such as binucleated neurons and pleomorphia is the most important criterion. Eosinophilic bodies, microcalcification, lymphocytic infiltration, microcystic degeneration, and fibrillary stroma are characteristic but not indispensable histological features [15]. Criteria of malignancy, such as anaplasia, vascular proliferation, and necrosis, have been described occasionally [2, 5]. Immunoreactivity for neuronal (e.g., synaptophysin and neurofilament proteins) and glial (GFAP) markers can be helpful in differentiating the characteristic tumor components. About 10% of gangliogliomas are classified as WHO grade II, while more than 80% are classified as WHO grade I and 5–10% as anaplastic ganglioglioma WHO grade III [24].

Our case is unique in that there has been no previous report on bifocal occurrence or the coincidence of two gangliogliomas without criteria of malignancy. We think that the classification of both tumors as ganglioglioma WHO II is reliable with regard to the histopathological and immunohistochemical features. The clinical course and neuroimaging findings, as well as the intraoperative appearance of both tumors, are compatible with the results of other studies. The bifocal development of the tumor remains unclear, and a coincidental occurrence may not be excluded. Ganglioglioma should be included in the preoperative differential diagnosis of multifocal lesions. Most importantly, our report demonstrates that multifocal occurrence of a ganglioglioma does not necessarily indicate malignancy or a poor prognosis.

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