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Glioblastoma simultaneously present with adjacent meningioma: Case report

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ABSTRACT

In this article, we report a 49-year-old woman with simultaneous meningioma and astrocytoma occurrence in the same patients without radiotherapy, phacomatosis, or any genetic disorders. We aimed to define surgical management and the etiopathogenic correlations of meningioma with glioblastoma.

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INTRODUCTION

The occurrence of multiple intracranial tumors of different cell types is not extremely rare but is usually observed in several genetic disorders, for example neurofibromatosis and tuberous sclerosis, or in the case of secondary tumors formed after cranial radiotherapy [1].

The incidence of primary brain tumors with different histological types is only 0.3% of all brain tumors [2]. The most frequent reported combination of histologically different brain tumors is meningioma and glioma [3], followed by meningioma and neurinoma [3,4], and by meningioma and pituitary adenoma [4]. The true incidence of this association may be much higher [5].

Moreover, meningiomas and gliomas may simultaneously occur by chance because these tumors are the most common primary intracranial tumors. In fact, several reports have described coexisting meningiomas and gliomas [1-9]. However, even among these reports, concurrent adjacent double tumors are rare and the adjacent occurrence implies the effect of unknown oncogenic factors unless the coexistence is because of radiotherapy or genetic disorders [1].

In this article, we report a case with simultaneous meningioma and astrocytoma occurrence in the same patients without radiotherapy, phacomatosis, or any genetic disorders. The aim of this study is to define surgical management and the etiopathogenic correlations of meningioma with glioblastoma.

CASE PRESENTATION

The 49-year-old woman was presented with weakness of the left upper limb that has developed over six months. This patient had a generalized seizure, a sudden nausea and vomiting before admission. The neurological examination revealed 4/5 left hemiparesis and grade 2 pupil edema without any other abnormality. The patient's blood type was O positive and the preoperative Karnofsky Performance Score was 90. The patient's family history was unremarkable and there were no cutaneous markers in her skin. Cranial Magnetic Resonance Imaging (MRI) revealed a right frontal lobe meningioma with intraaxial mass adjacent the meningioma compatible with high grade glioma. (Figure 2).

The patient underwent tumor excision through the right frontal approach. Macroscopically, the tumors consisted of two distinct components, grayish soft tumor

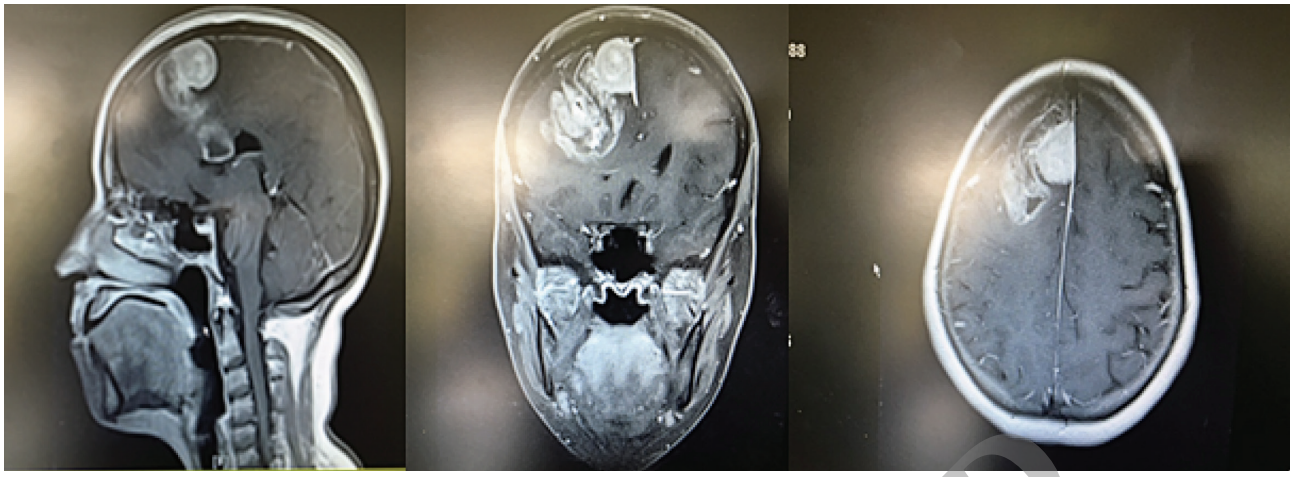

Figure 1. Preoperative cranial T1-weighted MR images with gadolinium contrast (sagittal, coronal and axial images) revealing a cystic mass lesion with irregular ring-like enhancement and a continuous well delineated mass showing strong homogeneous enhancement and dural attachment.

and reddish hard and well circumscribed tumor, separated by a relatively clear pial border. The soft glioma-like tumor had a cyst filled with yellowish fluid and had infiltrated into the surrounding normal brain. The hard hypervascular tumor was tightly attached to the dura mater of falx, suggesting a meningioma. Histological

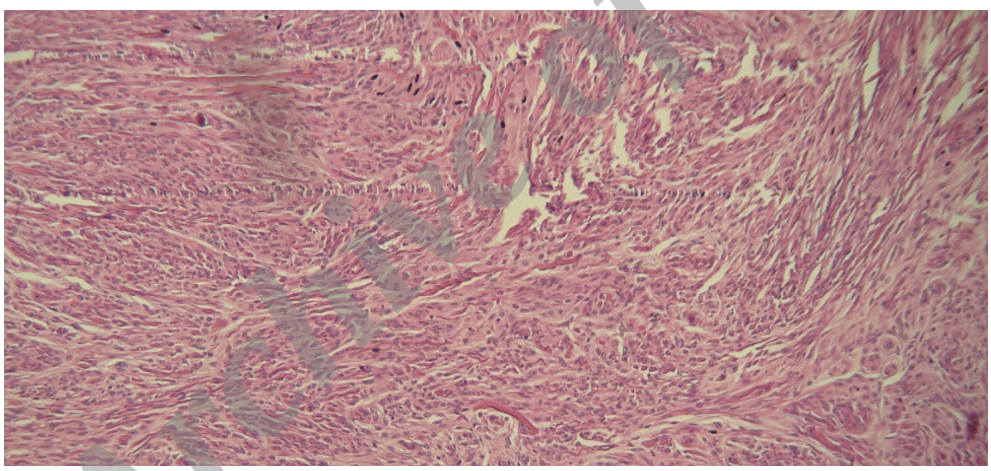

Figure 2A. Pathology of meningioma, transitional type, WHO grade I.

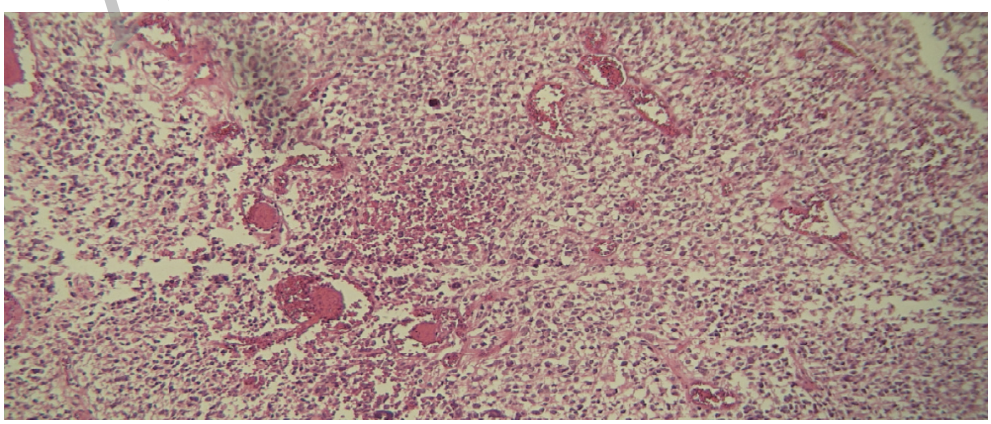

Figure 2B. Pathology of glioblastoma with oligodendroglial component WHO grade.

examination revealed two distinct tumors: the cystic lesion was a GBM and the hypervascular lesion was a meningothelial meningioma, showing typical histologic features of GBM with positive glial fibrillary acid protein (GFAP) staining and meningothelial meningioma with positive epithelial membrane antigen (EMA) staining (Figure 1).

The patient received radiotherapy (comprising of 2-Gy daily fractions of focal irradiation administered 5 days per week for 6 weeks; total dose, 60 Gy) and concomitant chemotherapy with temozolomide (75 mg/m^2/day, 7 days per week from the first to the last day of radiotherapy). After the radiochemotherapy, no residual tumor was detected on the MR images and the patient was transferred to another hospital for short-term rehabilitation without any neurological deficit.

DISCUSSION

Primary central nervous system neoplasms may be multifocal including a small percentage of gliomas in the setting of von Hippel-Lindau disease, and meningioma in the setting of neurofibromatosis [6,7]. The simultaneous or even collision occurrence of primary intracranial tumors without neurofibromatosis II and cranial radiotherapy is reported infrequently. Meningioma has an increased probability of developing another primary or secondary brain tumor. Meningioma is the most common central nervous system tumor to host a metastatic cancer [8,9]. Among them, the simultaneous or coexistence of an intracranial meningioma and an astrocytoma seems to be one of the most commonly encountered type of tumor [10]. In fact, several reports have described coexisting meningiomas and gliomas [11,12].

Several hypotheses have been proposed to explain the simultaneous occurrence of two (or more) primary intracranial tumors of different germinal origins in the same individual unrelated to radiotherapy or phacomatosis, but none have gained conclusive support [11].

We have reviewed the literature and found cases of concurrent astrocytoma and meningioma similar to our cases, excluding brain injury, phacomatosis or genetic disorders and cranial radiotherapy.

Multiple theories have been postulated in the literatures for the simultaneous or collision occurrence of these tumors. However, the exact mechanism underlying this observation is yet to be defined. Exposure to biochemical substances, genetic factors, prior trauma or surgery and immunological mechanisms may be the causative or contributory factors in the development of these tumors [6,13].

Some studies believe that such cases are largely incidental in their nature [14]. Meningioma is relatively a common tumor of the CNS constituting about 18 % of brain tumors. Similarly, glioma accounts for 40-50 % of primary brain tumors [15]. The incidence of multiple intracranial tumors of different histology is 10–15 cases per 100,000 who develop primary brain tumors [16], and from a statistical perspective chances of recurrence in the same patient is possible. Meningioma and glioma, whether they exist together or separate are relatively common forms of neoplasms involving the brain, and their concurrence in many cases maybe coincidental [10].

Many genetic factors may also be involved and a genetic study in such cases with this condition is advisable [17].

Several common abnormalities are known to be present in the signal transduction pathways of GBM and meningioma, including the p53, RTKs, Notch and Wnt pathways [18-22]. Among RTK signaling molecules, it has been suggested that expression of epidermal growth factor receptor (EGFR), platelet-derived growth factor receptor (PDGFR), insulin growth factor (IGF), and vascular endothelial growth factor (VEGF) are involved in the tumorigenesis and malignant progression of meningioma [21,22]. As the p53, EGFR and PDGF signaling are closely related to gliomagenesis [18], we performed immunohistochemical analysis to identify the common pathways activated in GBM and meningioma. The p53-positivity rates were high in both GBM and meningioma.

Amatya et al. 2[3] reported that the p53-positivity rate was less than 5% in all cases of benign meningioma, whereas it was more than 10 in 19% of cases of atypical meningiomas and in 70% of cases of anaplastic meningiomas. Other studies have also suggested the involvement of the p53 pathway in the development of meningioma [19,20]. In our case, the histological grade of the meningioma indicated that the tumor was benign (World Health Organization (WHO) grade I) and the MIB-1 labeling index was2%, which indicated a tumor with benign nature and low proliferation activity. However, high p53 positivity rate in this meningioma indicates dysfunction of the p53 pathway. On the other hand, p53 dysfunction is generally regarded as a key cause of secondary GBMs. In the case of GBM, the high positivity of p53The result of immunohistochemical analysis of the proteins involved in signaling pathways can explain other aspects of tumorigenesis. First, EGFR was strong and low EGFR expression indicate a secondary GBM showing stepwise progression. As p53 dysfunction was observed in both GBM and meningioma, genetic disorder

such as Li–Fraumeni syndrome could be regarded as the potential cause.

Another theory suggests that, astrocytoma may develop due to neoplastic transformation of the reactive glial cells surrounding a meningioma [30-32]. Juxtaposition of these diverse germinal origin tumors in the same patient suggests that one tumor may act as an irritating agent for the local proliferation and growth of the other. This hypothesis let us speculate that the collision tumor might have been caused by malignant transformation of the reactive gliosis surrounding the meningioma. However, this theory fails to explain why this transformation happened in this particular case and not in the vast majority of intracranial meningioma. This hypothesis also fails to explain the simultaneous occurrence in some cases with the two tumors far apart from each other [10]. Concurrent glioma and meningioma have been reported by several authors, some of whom have concluded that this phenomenon was most likely a random statistical coincidence rather than the result of common pathway abnormalities [33-35].

However, adjacent double tumors indicate that they may have a common causal background or may occur under the same conditions. Because the paracrine and juxtacrine systems exert their functions among different cell types, we hypothesized that if this coexistence is caused by a common causal background, the signal transduction pathways may play an important role in the tumorigenesis of adjacent double tumors. The proliferation rates of the two tumors suggest that meningioma occurs first and induces GBM by causing p53 dysfunction and RTK activation. The pathway abnormalities may then promote neuronal and oligodendroglial differentiation in GBM tissues [1].

CONCLUSION

We report a rare case of GBM and meningioma occurring simultaneously in adjacent sites. PDGF-mediated paracrine signaling may be a potential factor in inducing the generation of one tumor from another.

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