



Double Extremes of Brain Tumors – Dilemma of Decision-making and Pitfalls of Image: A Case Report and Literature Review

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Coexistence of multiple primary intracranial tumors has been reported previously. However, most of simultaneous tumors occurred after intracranial radiotherapy or in high association with heredity. Both primary intracranial tumors arising simultaneously at synchronous discrete sites were introduced without prior radiation or genetic disorders. These tumors showed the same characteristic according to preoperative images. Two distinct tumors, meningioma and anaplastic oligoastrocytoma were revealed by postoperative histopathological findings. We present this unusual case to exhibit the rare possibility that two distinct primary brain tumors can occur in the same patient. Although magnetic resonance image were used to define the tumor patterns in almost cases, some diagnostic pitfalls may occur with coexistent primary brain tumors. Hence, a discrepancy between clinical impressions and radiological findings should raise a further survey for potential different natures. Reviewing the literature, we should remove the symptomatic tumors based on mass effect and presenting symptoms first, whether it is a benign-looking meningioma or a malignant astrocytoma. Surgical priority for two distinct synchronous tumors from each other needs individual evaluation carefully.

Key words: Meningioma, anaplastic oligoastrocytoma, radiotherapy, chromosome 1p and 19q, p53, receptor tyrosine kinases

INTRODUCTION

The simultaneous occurrence of multiple primary intracranial tumors has been reported previously. However, most of these tumors occurred after cranial radiotherapy¹⁻³ or in high association with family heredity.⁴ The incidence of different histological types of primary brain tumors is about 0.3% of all brain tumors.⁵ Courville reported that incidence of multiple gliomas account for 4.3% of intracranial tumors.⁶ Cushing reported a case of malignant gliomas adjacent to benign meningiomas.⁷ Subsequently, Fisher reported meningioma and malignant glioma appearing in the same patient and summarized cases since 1910.⁸ Double extremes tumors of different pathology without genetic disorders or intracranial radiotherapy are very uncommon. Moreover, several authors already published that meningiomas and gliomas are the most common simultaneously primary intracranial tumors by statistical analysis.⁹⁻¹⁵ However, concurrent occurrence of meningioma and anaplastic oligoastrocytoma (AO), WHO

Grade III at synchronous discrete sites without radiation or genetic disorders are rare case as we know. Spallone *et al.* reported that recognition of one intracranial lesion may miss other coexistent brain lesions easily.¹³ Several possible hypotheses had been proposed to explain this situation.¹⁶ Nestler *et al.* revealed the result of comparative genomic hybridization and chromosome analysis in two patients who presented with concurrent meningioma and glioblastoma multiforme (GBM).¹⁷ Chromosome and genetic testing of tumor cells should be performed routinely when different histological types of brain tumors are present.¹⁷ Reviewing the literature, surgical priority for two distinct synchronous tumors needs individual consideration carefully. We should remove the symptomatic tumors based on progressive larger size and mass effect first, whether it is a benign-looking or less malignant tumors.^{14,16}

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CASE HISTORY

The 39-year-old female experienced disorganized behavior without weakness of limb for 1 week before admission. After checking hemogram and electrolyte, computed tomography (CT) of brain without contrast [Figure 1a and b] was arranged which showed two hyperdense lesions over the left frontal and parietal lobes. Gadolinium-enhanced magnetic resonance imaging (MRI) of the brain revealed two distinct extra-axial tumors of the left frontal and parietal lobes [Figure 1d and e]. These tumors showed the same characteristic according to preoperative gadolinium-enhanced MRI and CT of the brain. According to symptomatic frontal tumors with mass effect, the left frontal tumor was totally removed and surgical histopathological findings confirmed the diagnosis of meningioma [Figure 2] while the smaller one waited for observation. Six months later, she presented with severe headache and right-sided hemiparesis (MP: 3/5). Follow-up brain CT [Figure 1c] and brain MRI [Figure 1f] demonstrated progression of the smaller lesion was with central necrosis and surrounding edema. A second craniotomy with total removal of tumor was performed and postoperative histopathological findings confirmed the AO, WHO Grade III [Figure 3]. After secondary surgery, she was gradually recovery without new neurological deficits. Although magnetic resonance image were used to define the tumor patterns in almost cases, some diagnostic pitfalls may

occur with coexistent tumors. Discrepancy between clinical impression and radiological findings should raise a further survey for potential lesions of different natures.

DISCUSSION

Possible pathophysiology of concurrent intracranial tumor of distinct origins

Several authors have published simultaneous intracranial tumors of both mesenchymal and neuroepithelial origin.^{6-8,18-20} Concurrent meningioma and gliomas were also reported,^{13-17,21-24} and meningioma and glial tumor were the most common coexistent primary brain tumor.⁹⁻¹⁵ Most of these coexistent tumors occurred after cranial radiotherapy¹⁻³ or in high association with heredity.⁴ Mechanism of radiation-related neoplasms is multifactor and we still do not understand well. However, radiation takes an important part in not only treatment of tumor but also a potential risk factor of cancer.³ Ionizing radiation has also been hypothesized and was a risk factor of glioma formation.^{9-15,25}

Cellular genetic background of concurrent intracranial tumors

Neoplastic transformation to astrocytoma from the reactive surrounding meningioma were reported by several authors.²⁶⁻²⁸ Therefore, several common abnormalities: signal transduction pathways of GBM and meningioma had been present, including

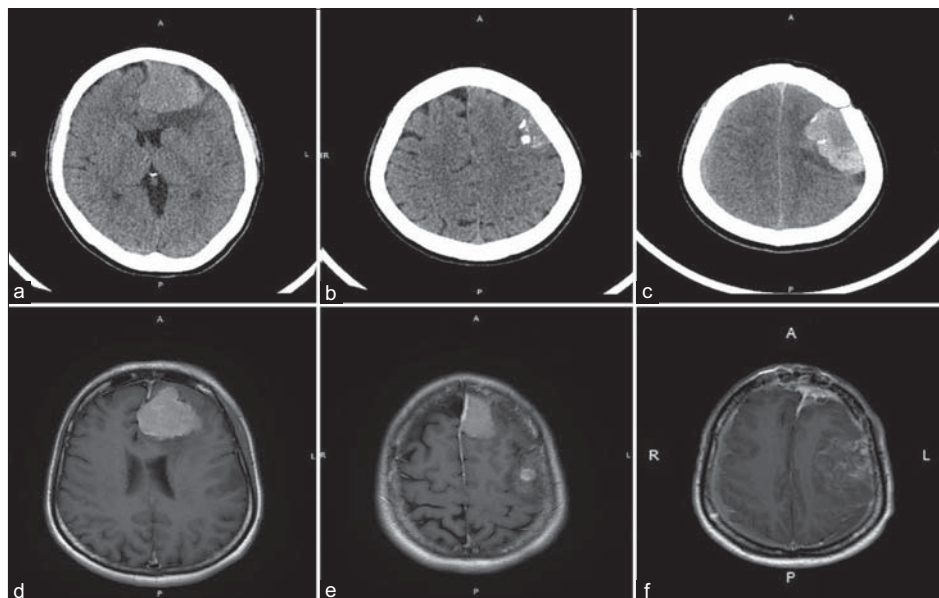


Figure 1: (a and b) Noncontrast computed tomography of brain showed two high-density lesion over left frontal and left parietal lobe; (d and e) Gadolinium-enhanced magnetic resonance imaging revealed two homogenous enhanced lesion of the left frontal and parietal lobe; (c and f) Six months later, non contrast computed tomography and gadolinium enhanced magnetic resonance imaging demonstrated progression of the previous left parietal lesion with central necrosis and surrounding edema

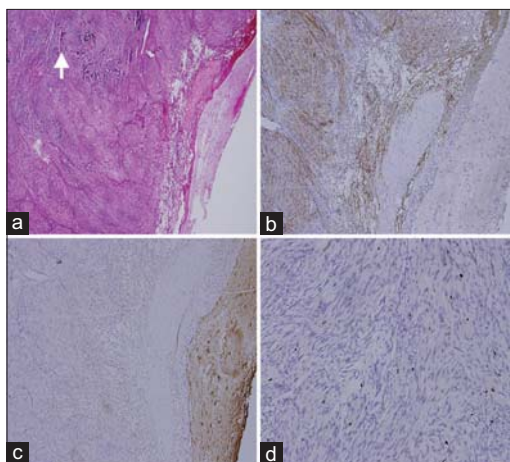


Figure 2: (a) Histopathology confirmed the diagnosis of the left frontal tumor is a meningioma, WHO Grade I, which shows typically syncytial and whorl-like growth pattern with occasional psammoma bodies (white arrow). In immunohistochemical studies, it reveals positive reactivity to anti-endothelial antibody (b), but negative to anti-gliofibrillary acidic protein (c). Furthermore, the Ki-67 of this tumor is around 2-3% (d) indicates its low proliferation index and should be classified as WHO Grade I

the p53, receptor tyrosine kinases (RTKs), Notch, and Wnt pathways.²⁹⁻³² Neuronal and oligodendroglial differentiation of GBM tissues may be promoted by the abnormal signal transduction pathways, meningioma occurs first, and GBM may be formed by causing p53 dysfunction and RTK activation.¹²⁻¹⁶ Codeletion of chromosome arms 1p and 19q mainly occurs in oligodendrogliomas and anaplastic oligodendrogliomas, as well as in oligoastrocytomas and AOs.³³ Chromosome t (1p; 19q) is meaning that consequence of an unbalanced translocation between chromosomes 19 and 1.³⁴ However, chromosome 19q and 1p is a predictive factor of response to chemotherapy as well as radiotherapy.³⁵ Analysis of chromosomes was used to estimate prognosis and further management of concurrent brain tumors.

Surgical priority

When clinical impressions and radiological findings are discrepant, we need further survey for potential different natures. When unpredicted clinical deterioration develops either before or after the removal of intracranial tumor, we never forget possibility of different natures.¹⁶ However, the surgical priority of two distant synchronous tumors needs individual evaluation carefully. We should remove the symptomatic tumors based on progressive larger size and mass effect first, whether it is a benign-looking or a less malignant tumors.^{14,16}

CONCLUSION

We present an analysis of concurrent meningioma and glioma and discussion of mechanism, gene, and treatment

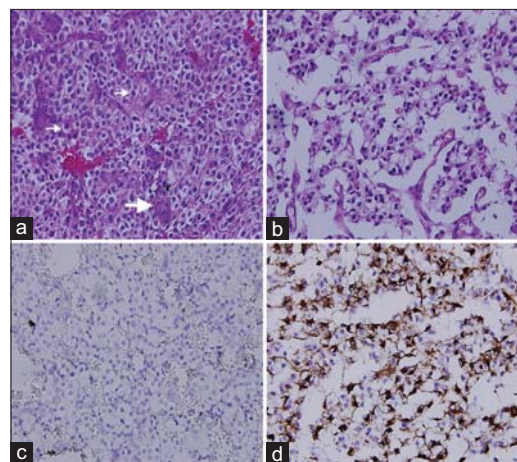


Figure 3: Pathology of the left parietal lesion reveals an anaplastic oligoastrocytoma, WHO Grade III, characterized by mixed oligodendrocytic components (a), relative round and vesicular nuclei with perinuclear halo and astrocytic components (b), irregular and hyperchromatic nuclei with eccentrically located nuclei and eosinophilic cytoplasm. Figure (a) showed increased mitotic figures (white arrow) and endothelial proliferation (big white arrow). In immunoreactivity to anti-gliofibrillary acidic protein, astrocytic component (d) compares to the oligodendroglial region (c), that confirms this tumor's separate components

modalities. Our case demonstrated the benign and malignant lesions could mask the surgeon's decision based on radiological interpretation. Hence, a discrepancy between clinical impressions and radiological findings was noticed; we must take further survey for potential different natures. Most importantly, we should remove the symptomatic tumors based on mass effect and presenting symptoms first, whether it is a benign-looking meningioma or a less malignant astrocytoma. Chromosome and genetic analysis should be performed routinely when different histological types of brain were diagnosed. Consequently, some diagnostic pitfalls may occur with coexistent primary brain tumors.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient has given her consent for her images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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