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Glioblastoma multiforme: An incidental finding?

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Abstract

Incidents of patients diagnosed with concomitant primary glioblastoma multiforme (GBM) and meningioma lesions are extremely rare but have been reported dating back to the 1970s. The majority of documented cases of concurrent GBM and meningioma portray the tumors to be in close proximity and in comparable stages of development. Herein, we report a case of primary GBM and a giant meningioma tumors that not only developed at opposite poles of the brain parenchyma, but were also of vastly different sizes and stages of development upon initial presentation. These differences ultimately prevented simultaneous diagnosis and resection of the tumors. Upon resection, pathological analysis of the giant tumor showed that it was indeed a meningioma and demonstrated evidence of brain invasion and microvascular involvement. The other lesion demonstrated classic signs of GBM on pathologic work-up. The case presented highlights the complexity of patients presenting with concomitant neuro-oncologic disease and the need to systematically address individual issues at their individual appropriate time.

Keywords

glioblastoma multiforme; meningioma; concomitant development; gliomagenesis; oncogenic signaling cascade

Abbreviations

GBM: Glioblastoma Multiforme; CT: Computed Tomography; MRI: Magnetic Resonance Imaging; PDGF: Platelet Derived Growth Factor; RTK: Receptor Tyrosine Kinase; EGFR: Epidermal Growth Factor Receptor; VEGF: Vascular Endothelial Growth Factor

Introduction

Concomitant primary glioblastoma multiforme (GBM) and meningioma lesions are extremely rare. Initial reports site the use of radiosurgery for one lesion as the cause of the development of the other. There have been several reports of concomitant lesion dating back to the 1970s [1]. The majority of these documented cases demonstrate the tumors to be in close proximity, in comparable stages of development, and involving the same anatomical structures. In a report by *Maiuriet al.* on several concomitant meningiomas and other intracranial tumors, the close proximity and presumably similar staging of the tumors allowed for simultaneous identification and resection of both tumors, often via the

same surgical approach [2].

Herein, we report a case of primary GBM and meningioma tumors that not only developed at opposite poles of the brain parenchyma, but were also of vastly different sizes and stages of development upon initial presentation. These differences ultimately prevented simultaneous diagnosis and resection of the tumors. Clinical manifestations, imaging findings, possible mechanisms, and impact on management are discussed.

Clinical Summary

A 60-year-old patient presented to the emergency department with altered mental status and features of confusion and acute paranoia with delirium. Initial computed tomography (CT) findings showed a giant left frontal meningioma and a small right parieto-occipital hypodense lesion; findings that were confirmed on magnetic resonance imaging (MRI). The patient subsequently underwent a bi-frontal craniotomy and complete resection of the meningioma was performed. The patient's presenting symptoms appeared to be related only to the meningioma and its associated edema. Because of the urgency in needing to remove the giant meningioma for decompression of mass effect and a subsequent complicated post-operative course, no immediate further investigation of the parieto-occipital lesion was performed.

Post-operative recovery was complicated by prolonged encephalopathy and respiratory failure. The patient's status required trach and PEG tube placement prior to discharge to a nursing home facility at approximately one month post-op. During recovery in a nursing home, the patient's condition continued to deteriorate. This deterioration was partly attributed to dysfunction of his feeding tube and progressive weight loss associated with malnutrition. During re-admission to the hospital for his malnutrition the patient had follow-up imaging to evaluate for possible hydrocephalus, cranial infection or other cause of his progressive neurological decline.

On this follow-up imaging the previously small right parieto-occipital lesion had grown significantly with expansion of the associated gyri, demonstration of associated cerebral edema and progression across the posterior corpus callosum – all of which features were considered radiographically to be consistent with GBM. Multiple conversations ensued with the patient's family regarding the likely diagnosis and potential outcome for his progressive brain tumor. Ultimately the patient was transitioned to hospice care.

Pathological Findings

Pathological analysis of the tumors showed that the giant tumor was indeed a meningioma and demonstrated evidence of brain invasion and microvascular involvement. Additionally, the parieto-occipital lesion was confirmed to be a glioblastoma multiforme tumor by virtue of the classical signs seen on the pathological work-up. GBM analysis demonstrated a focus of necrosis, cellular atypia, evidence of pseudopalisading, and microvascular proliferation. These features are typical of GBM tumors.

Discussion

Among the various case reports on the phenomenon of simultaneous development of two primary intracranial tumors, several hypotheses have been posited. Recent publications support the

common belief that chance represents the predominant driving force while alternatively proposing the idea that treatment methodologies for one tumor may potentiate the development of the other, either because of the carcinogenic potential of the antineoplastic treatment itself or possibly due to shared oncogenic pathways [3]. Historically, there have been a few case reports of GBM arising in close proximity to a previously resected or radiotherapy-treated meningioma [4,5].

Close proximity of these tumors also raises suspicion of a shared common molecular pathway in their pathogenesis[6]. One signaling molecule that may play a role in the development of these simultaneous tumors is platelet derived growth factor (PDGF). PDGF receptor α and β were found to be overexpressed in cases of dual tumor development, suggesting their involvement in the oncogenic signaling cascade. Furthermore, vascular endothelial growth factor (VEGF) expression has been observed in such cases, illustrating a pro-oncogenic angiogenic effect. Receptor tyrosine kinase (RTK), Notch, and Wnt abnormalities have also been found in cases of simultaneous GBM and meningiomas. Epidermal growth factor receptor (EGFR), a component of the RTK pathway, has been implicated in gliomagenesis and has been found in 20% of benign meningiomas [3,7]. Li-Fraumeni syndrome has also been tied to a case of simultaneous GBM and meningioma, indicating that the p53 pathway may be just as important for the development of these dual primary tumors as it is with other malignancies [8].

Our patient presented with tumors that were geographically distant – being located in the frontal and parieto-occipital areas of the opposite hemispheres of the brain. The fact that the meningioma was at a later development stage compared to the GBM raises the possibility that over time the meningioma might have changed the neural and immunological landscape of the brain which in turn may have facilitated the subsequent rapid development of the GBM. Furthermore, previous reports involved tumors that presented with similar size and stage. Our patient's tumors were not only at different locations, but also of vastly different sizes and stages of development. Ultimately, the clear presentation of symptoms from the giant meningioma and its distant location from the ultimately identified GBM prevented simultaneous pathological diagnosis and treatment of both lesions.

Figures

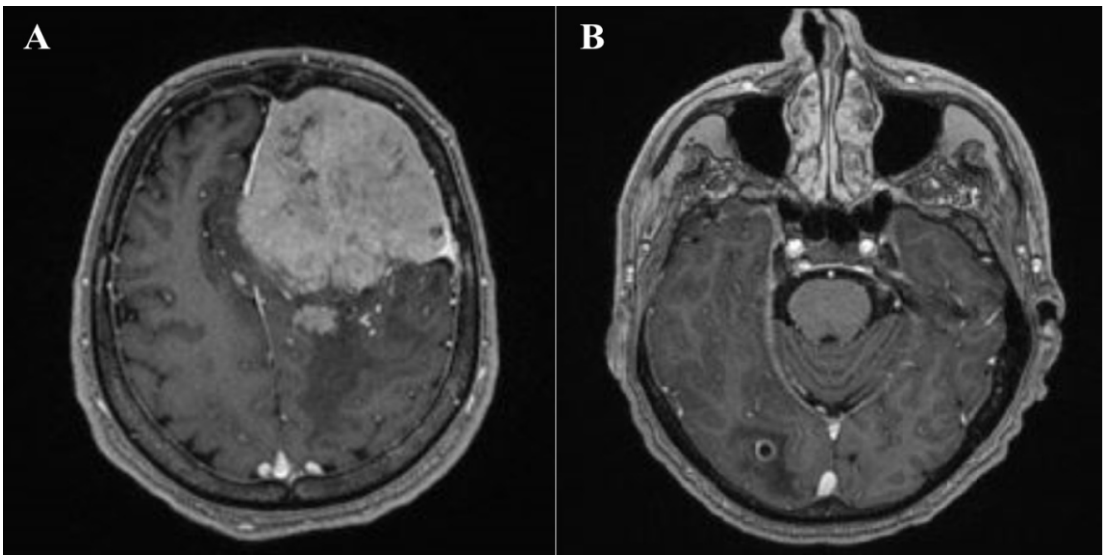

Figure 1: Pre-operative MRI of the giant Meningioma: A) Axial T2 weighted MRI with contrast of the giant meningioma in the right frontal lobe showing mass effect and midline shift; B) Axial T2 weighted MRI with contrast showing a small ring enhancing lesion in the right parieto-occipital lobe.

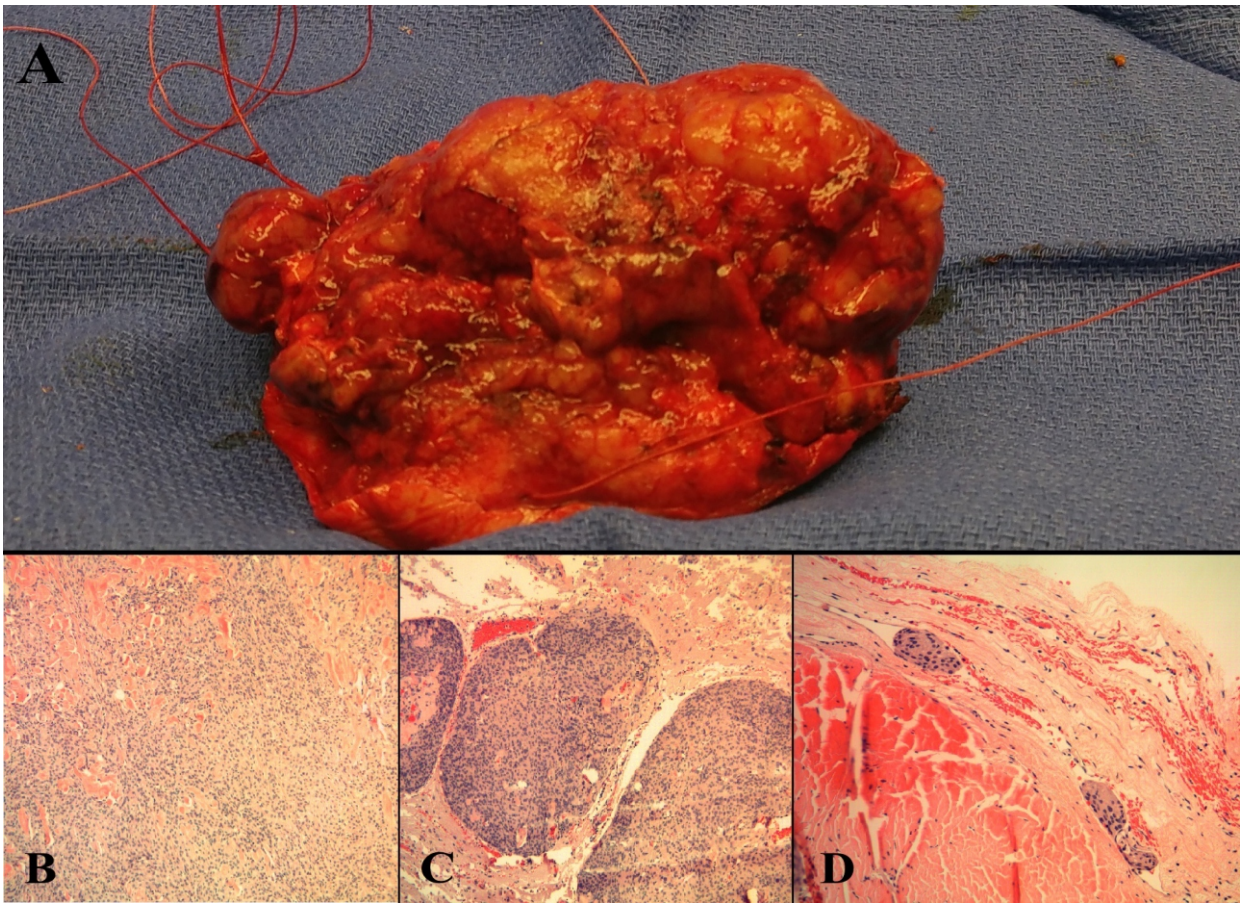

Figure 2: Post resection pathology of the giant meningioma: A) Gross resection mass; B) H&E stain of tumor parenchyma; C) H&E stain of architecture of the tumor demonstrating invasion of the brain parenchyma;D) H&E stain of tumor periphery demonstrating vascular involvement.

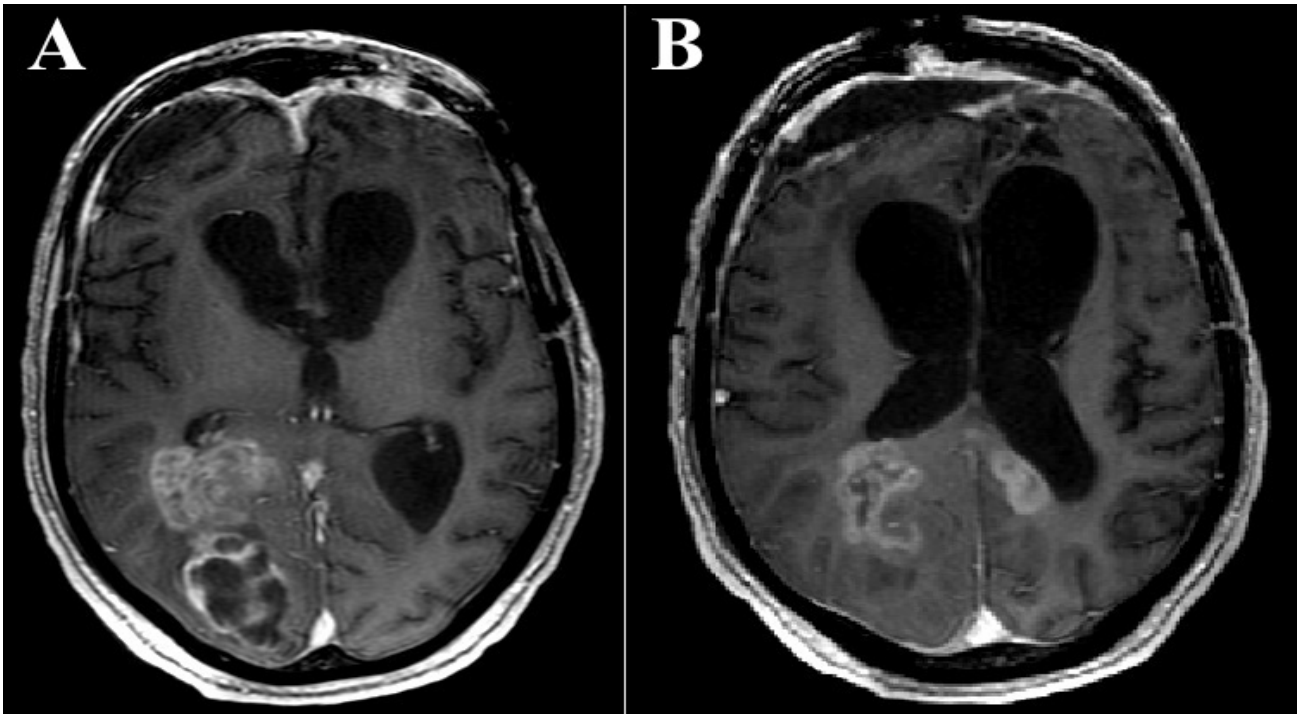

Figure 3: Subsequent MRI revealing a significantly developed Glioblastoma Multiforme in the right parieto-occipital lobe: A) Axial T2 weighted MRI with contrast show mass effect and lateral ventricular compression within the right parieto-occipital lobe; B) Axial T2 weighted MRI with contrast showing contralateral hemisphere involvement- a classic "butterfly" sign- and mass effect

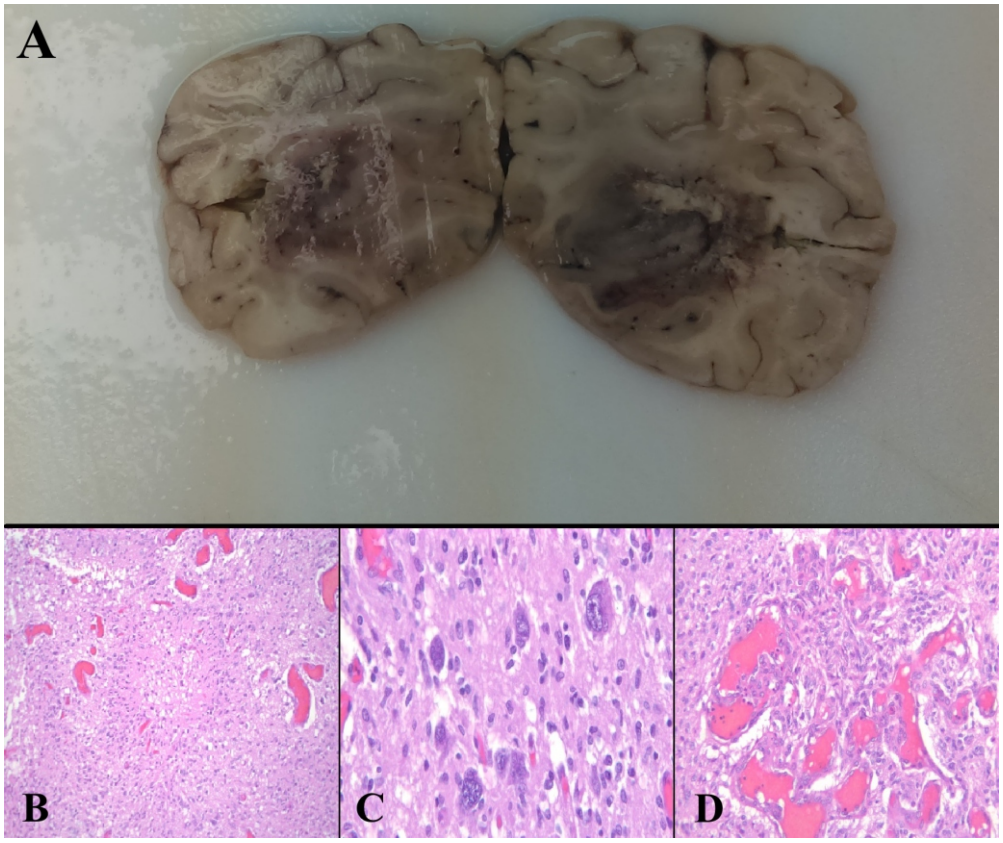

Figure 4: Post mortem images and pathological analysis: A) Gross picture of GBM demonstrating extensive bilateral hemispheric involvement on gross pathology; B) H&E stain of tumor parenchyma demonstrating a focus of necrosis and evidence of pseudopalisading; C) High power view of H&E stain tumor parenchyma demonstrating cellular atypia and neoplastic proliferation; D) H&E stain of gross tumor demonstrating angiogenic proliferation.

Conclusion

The case presented highlights the complexity of patients presenting with neuro-oncologic disease and the need to systematically address individual issues at their individual appropriate time. The patient presented with symptoms that were completely related only to the very large benign tumor, but on imaging at presentation also had concern for CNS malignancy. Close clinical and radiological follow up are imperative to try to maximize outcomes for patients with potential synchronous tumor presentations. Unfortunately in this case the patient's clinical condition never sufficiently improved to allow further treatment of what was ultimately determined to be incidental glioblastoma.

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