Case Report

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Three distinct co-existent primary brain tumors in a patient

ABSTRACT

A rare case of simultaneous occurrence of three entirely distinct intracranial tumors is described. A 55-year-old male with no evidence of phacomatoses or history of radiation therapy presented with complaints of increased drowsiness, headaches, and dysarthria. Investigations revealed an olfactory groove meningioma, a glioblastoma multiforme in the left medial temporal lobe, and a diffuse glioma in the brain stem. Occurrence of multiple varieties of tumors at the same time is extremely rare. Theories that explain their occurrences including the role of common carcinogens, autocrine growth factors, and tumor suppressor genes are discussed.

KEY WORDS: Multiple primary neoplasms, meningioma, glioblastoma multiforme, glioma

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INTRODUCTION

The occurrence of three primary intracranial tumors, in the absence of phacomatoses or prior radiation therapy is rare. In such cases, the most common coincidental occurrence is of meningiomas with gliomas.[1] We present a case with the simultaneous occurrence of gliomas with multiple localizations, and a meningioma. Accurate preoperative diagnosis of these tumors is difficult, although, with the recent advances in neuroimaging, more such synchronous tumors are detected.

CASE REPORT

A 55-year-old male presented with complaints of progressively increasing headache, drowsiness, and decreased speech output for about 2 months. During this period, he had two episodes of generalized seizures. On examination, the patient was drowsy, with decreased attention span and impaired memory for both recent and past events. There was no focal motor and sensory deficit.

A plain and contrast MRI study of the brain was performed along with MR (magnetic resonance) spectroscopy. The study showed a large, intensely enhancing, solid olfactory groove meningioma [Figure 1] and its related mass effect. A second tumor, an intra-axial space-occupying lesion, was identified in the left medial temporal lobe in the region of the amygdaloid nucleus and the entire hippocampus [Figure 2A]. The peripheral wall of this tumor was solid, irregular with an intense postcontrast enhancement. The predominant central component was necrotic and nonenhancing [Figure 2B]. Extensive intra-lesional hemorrhage was seen as susceptibility on gradient-recalled echo (GRE) imaging. There was mass effect on the left cerebral peduncle. The radiological features were suggestive of a high-grade glioma. A third tumor was observed in the right side of the brain stem involving the midbrain, pons, and medulla and also extending into the posterior limb of the internal capsule. It was seen as an area of abnormal signal intensity [Figure 3A], with minimal patchy postcontrast enhancement [Figure 3B] and not associated with intralesional hemorrhage, perilesional edema, or mass effect. Radiologically, this lesion was thought to represent a grade III glioma of the brain stem due to the patchy postcontrast enhancement. MR spectroscopy of this lesion showed a spectral pattern that was consistent with the diagnosis of a tumor [Figure 3C].

Under general anesthesia, a bicoronal incision with bifrontal craniotomy and left temporal craniotomy was performed. The olfactory groove meningioma was completely resected and a partial excision of the left medial temporal lesion was done. The brain stem lesion was not biopsied.

The histopathological report confirmed the presence of an olfactory groove transitional meningioma with nests, lobules, and whorls of meningothelial cells, fibroblastic tissue, and a few psammoma bodies [Figure 4]. The medial temporal lesion was a moderately cellular tumor composed of cells with hyperchromatic nuclei lying amidst edematous, focally myxoid, fibrillary

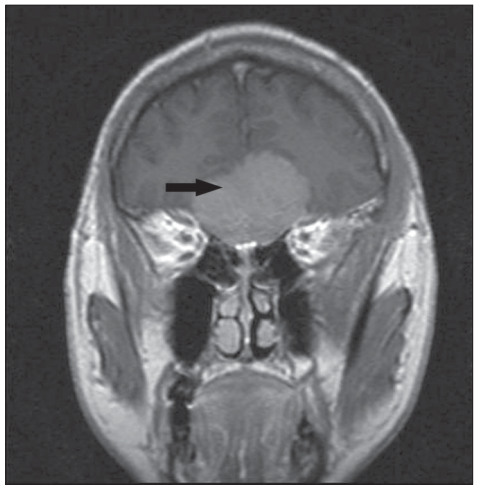

Figure 1: Postcontrast coronal T1 weighted image shows a solid, intensely enhancing olfactory groove meningioma (arrow)

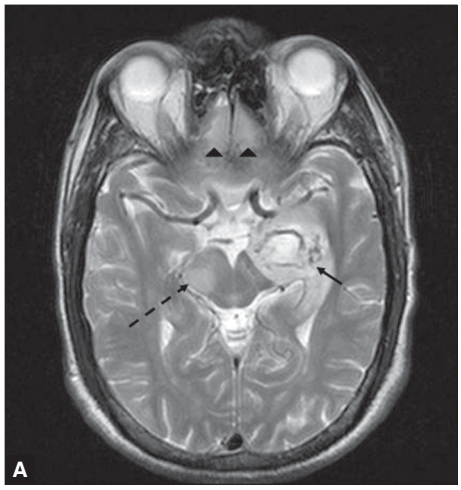

Figure 2(A): Axial, T2 weighted image of the brain shows a high-grade intra-axial, left temporal lobe tumor (solid arrow) with intralesional hemorrhage. Also noted in this image is the inferior part of the olfactory groove meningioma (arrowhead). The third tumor, a low-grade glioma, is seen in the right cerebral peduncle (dashed arrow).

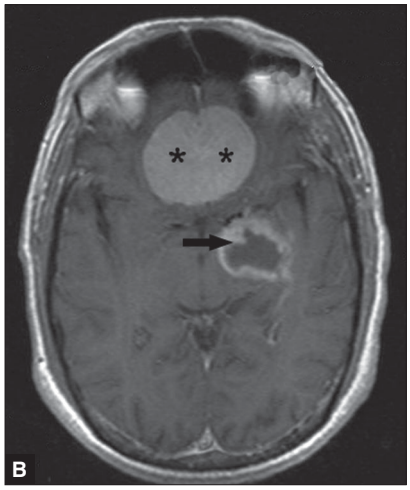

Figure 2(B): Postcontrast T1 weighted axial image of the brain shows the left temporal lobe tumor predominantly necrotic with an irregular, solid, enhancing wall (arrow). The olfactory groove meningioma is also seen in this image (asterisks)

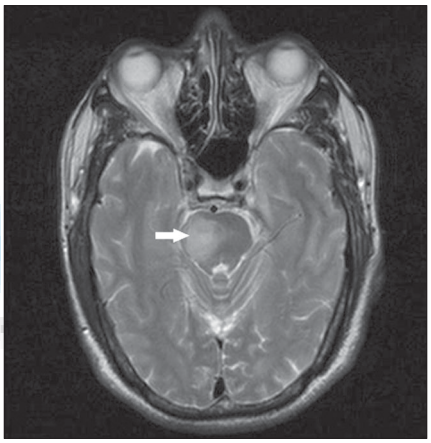

Figure 3(A): Transverse T2 weighted image of the brain reveals a lesion in the right side of the pons showing abnormal hyperintense signal (arrow)

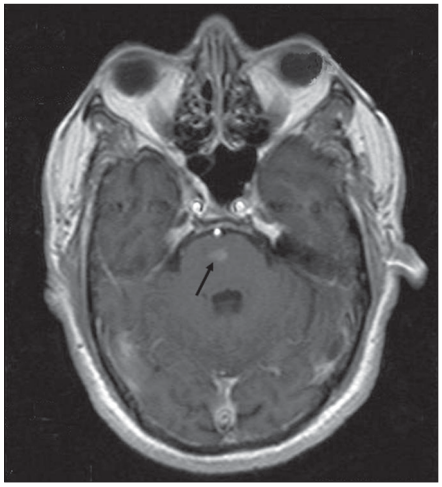

Figure 3(B): Postcontrast T1 weighted axial image of the brain shows a patchy enhancement of the brain stem lesion (arrow)

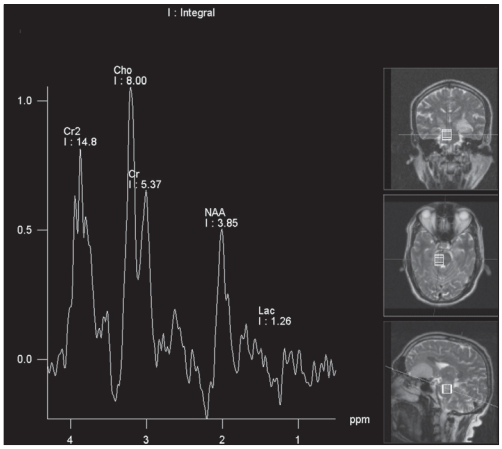

Figure 3(C): MR spectroscopy of the brain stem lesion using a single voxel and intermediate TE (time-to-echo) value shows diminished NAA (N-acetylaspartate), elevated choline, and a lactate peak, consistent with the tumor

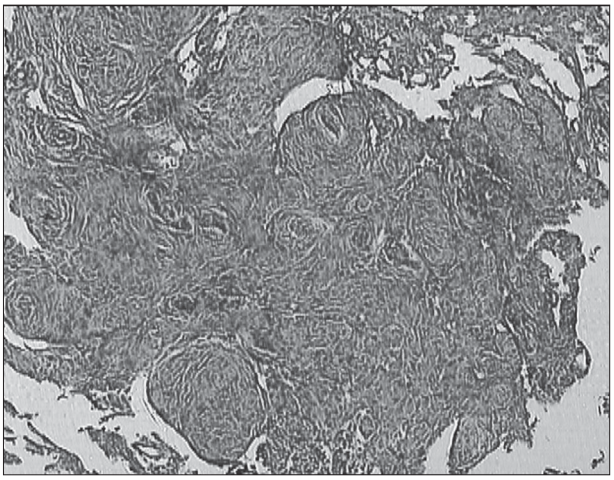

Figure 4: Photomicrograph shows a tumor composed of meningothelial cells in syncitium and whorls (H & E, ×250)

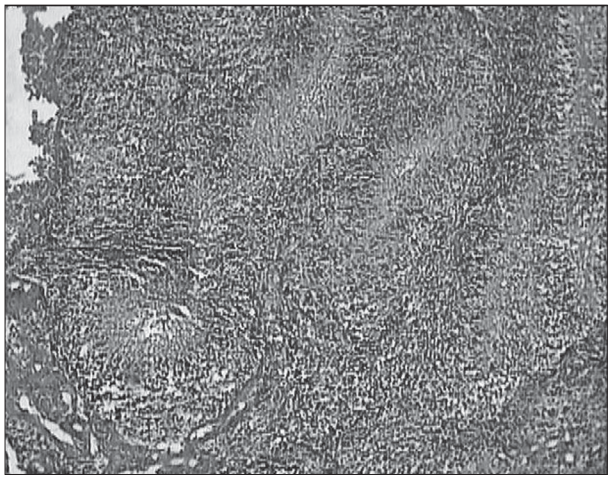

Figure 5: Photomicrograph showing necrotic foci palisaded by tumor cells (H & E, ×250)

matrix. There was moderate nuclear atypia, mitosis, focal vascular endothelial cell proliferation, and large areas of necrosis including foci of palisading necrosis. These features represented a glioblastoma multiforme (GBM) [Figure 5]. The patient subsequently underwent focal conformal radiation treatment to the region of glioblastoma and brainstem glioma. The patient reportedly died after an acute illness in his village within 2 months of surgery. Details of events prior to death were not available. No postmortem study was possible.

DISCUSSION

Synchronous primary intracranial tumors are rare and their occurrence is not well understood. The GBM and the brainstem glioma in this case may represent multicentric gliomas at different stages of biological progression. Multicentric gliomas are widely separated lesions, occurring in different cerebral lobes or hemispheres, whose spread cannot be explained by either commissural or other pathways, local metastasis, or by spread via cerebrospinal fluid channels.[2] However, the true occurrence of multicentric gliomas can only be established at autopsy, when no gross or microscopic connection is shown between tumors.

On imaging studies, the presence of edema which is remote from the site of primary tumor should prompt one to look for additional lesions. In this patient, both the GBM and meningioma were associated with significant edema and mass effect. The brain stem lesion, however, did not appear to be associated with perilesional edema. The findings on MR spectroscopy were useful in the characterization of this lesion, in the absence of histological confirmation.

Multiple theories have been postulated in the literature for the simultaneous occurrence of these tumors. One school of thought suggests that the initial tumor might have stimulated oncogenesis in either the cerebral parenchyma or the meninges.[3] Growth of human tumor cells is autonomous and autocrinous, due to production of both growth factors and receptors for these factors. Platelet-derived growth factor (PDGF) is a likely mediator. Three subunits of PDGF, the PDGF-AA, PDGF-BB and PDGF-AB, are secreted by astrocytomas.[4] There are two receptor subtypes; PDGF-α-R and PDGF-β-R. Astrocytomas have the PDGF-α-R receptor and their growth is stimulated by PDGF in an autocrine fashion.[5] Meningiomas have the PDGF-β-R receptor and PDGF-BB acting on these receptors is shown to stimulate cell division.[6] Thus, the GBM may stimulate growth in adjacent arachnoid cells by production of a common growth factor.

Common genes may be involved in the development and progression of meningiomas and glioblastomas. In a recent study, a meningioma-associated tumor suppressor gene (TSG) was found on the long arm of chromosome 14. Identified as the NDRG2 (N-myc downstream-regulated gene 2), it was commonly inactivated in clinically aggressive meningiomas.[7] An earlier study showed that this same gene was expressed in normal brain tissue but down-regulated in GBM.[8] Thus, inactivation of NDRG2 may play a role in the pathogenesis of both meningioma and GBM. Studies of 10q deletions in grade II meningiomas[9] and glioblastomas[10] have shown overlaps with the region of the TSG called deleted in malignant brain tumours 1 (DMBT1). Further studies are needed to determine the exact gene whose deletion may act in the progression of meningioma to higher grades, but evidence suggests that it may overlap with those regions found deleted in GBM.

Another theory suggests the presence of an unidentified common carcinogenic stimulus, which leads to tumors in different tissues.[11] Although it has been suggested in the past that the presence of residual embryonic structures could subsequently become the basis for multiple tumors, this hypothesis may not be relevant any more.[12]

The reasons for the simultaneous occurrence of different

primary intracranial tumors in the absence of phacomatoses or prior radiation exposure are at present speculative, and these tumors could be merely coincidental. Our understanding of multiple, distinct intracranial tumors will gradually improve as more cases are reported and studied.

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