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Case Report

Glioblastoma imitating a cavernoma radiologically: A unique image report

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ABSTRACT

Background: Glioblastoma is the most common primary malignant brain tumor with characteristic radiological features in most cases.

Case Description: We highlight an unusual case of a 54-year-old woman, neurologically intact, with a diagnostically challenging lesion. The patient's magnetic resonance imaging revealed a left frontal lesion with surrounding edema and a hemosiderin ring, misleading it to be a cavernoma. Intraoperatively, the lesion was found to be a solid tumor with hematoma and was confirmed to be glioblastoma on histopathology.

Conclusion: The dilemma associated with our patient's radiological findings and longstanding history of epilepsy is rare and a diagnostic challenge.

Keywords: Cavernoma, Epilepsy, Glioblastoma, Hemorrhage, IDH-1

INTRODUCTION

Glioblastoma is the most common and malignant solid tumor of the brain, accounting for 57% of all gliomas and 48% of all primary central nervous system malignant tumors, with a median survival time of fewer than 2 years.[17] While the typical presentation of glioblastoma on magnetic resonance imaging (MRI) is easily identified, occasionally, non-characteristic presentations are misinterpreted as vascular disease,[7] as was the case with our patient, whose glioblastoma was initially mistaken to be a cavernoma, an aberrant vascular lesion characterized by a "popcorn ball" appearance on MRI [Figure 1].[1] Cavernomas are seen rarely, occurring in 0.5% of the general population and accounting for 5–15% of all vascular diseases of the brain.[15]

Therefore, to holistically appreciate glioblastoma progression, morphological and genetic alterations have been combined with traditional pathological descriptions of the disease to produce a dichotomous classification.[3] At the core of this classification lies the Isocitrate dehydrogenase IDH-1 mutation status; thus, glioblastoma can now be categorized as either wild-type or mutant, which are near-perfect analogs to the previous WHO classification of primary and secondary glioblastoma, respectively.[9] IDH-1 wild-type glioblastomas

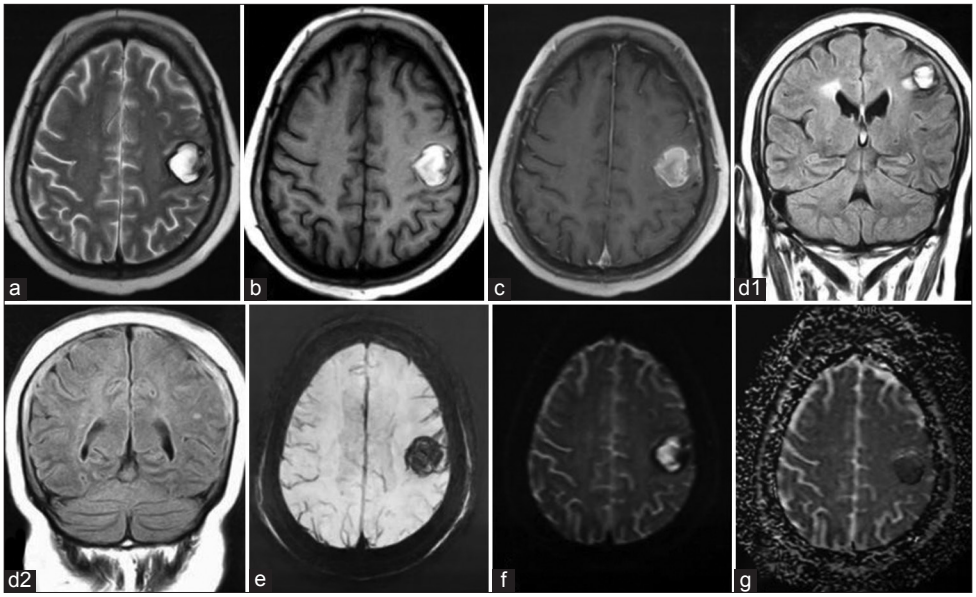

Figure 1: Multiplanar and multisequential magnetic resonance imaging of the brain (a) T2WI hyperintense lesion with peripheral hemosiderin ring. (b)T1 without and with (c) contrast showed patchy enhancement on the lateral aspect. (d1) Fluid-attenuated inversion recovery (FLAIR) image surrounding edema noted at the medial aspect of the lesion. (d2) FLAIR image with punctate hyper-intensities in the left cortical region. (e) Susceptibility-weighted imaging lesion had diffuse signals drop-out (f and g). Diffusion-weighted imaging and apparent diffusion coefficient sequences showing diffusion restriction.

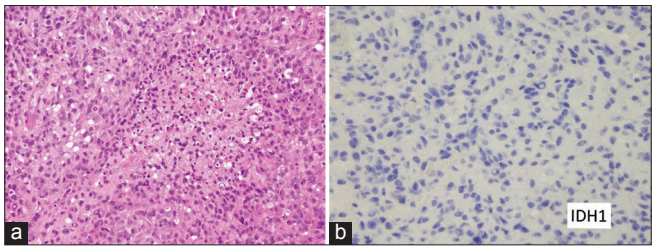

Figure 2: Histopathology of glioblastoma multiforme. (a) H&E staining showed neoplastic cells with hyperchromatic nuclei and inconspicuous nucleoli with moderate amounts of eosinophilic cytoplasm. Multiple gemistocytes and areas of palisading tumor necrosis are also seen in the background. (b) Isocitrate dehydrogenase immunohistochemical staining negative for IDH mutation.

are the most frequent (90%) and are predominant in patients over 60 years of age, whereas IDH-1 mutant is less frequent (10%) and arise in younger patients with a history of lower-grade glioma.[9,13]

A wide range of secondary neurological manifestations are associated with glioblastoma, including headaches, alteration in personality and cognition, gait imbalance, visual and olfactory disturbances, and epilepsy.[12] Epilepsy presents as a frequent comorbidity and an initial manifestation of the disease.[6] Seizures are relatively less common in glioblastomas (25–33%) as opposed to in lower-grade gliomas.[8,13,14]

CASE PRESENTATION

A 54-year-old woman presented with complaints of transient right hand and arm numbness, along with facial twitching for 3 months. The patient had a 20-year history of epilepsy. Her neurological examinations were largely unremarkable.

On MRI [Figure 1], abnormal signal intensity was noted on the left medial frontal region, predominantly hyperintense on T2/fluid-attenuated inversion recovery (FLAIR), and showed diffusion restriction on diffusion-weighted imaging sequence. Peripherally, the hemosiderin ring was appreciated on T2 sequences with signal dropout on susceptibility-weighted imaging. It showed patchy post-contrast enhancement on the contrast sequence. However, due to high signals on pre-contrast T1, it was difficult to comment on the extent of post-contrast enhancement. Surrounding edema and punctate foci of hyperintensities on the subcortical white matter with chronic ischemic changes were noted on T2/FLAIR sequences. Findings were therefore, suggestive of a cavernoma. It clearly lacks the typical features of glioblastoma, including irregular enhancement and significant surrounding edema.

Elective neuronavigation-guided craniotomy for maximus safe resection of the lesion was performed. Intraoperatively, it was noted to be an intra-axial soft to firm lesion with xanthrochromic discoloration throughout the lesion. Some

abnormal vessels were difficult to coagulate; it was a clue that it could be a high-grade lesion rather than just a cavernoma.

The histopathological examination revealed neoplastic glial cells with hyperchromatic nuclei, inconspicuous nucleoli, and a moderate amount of eosinophilic cytoplasm. Multiple gemistocytes and areas of palisading tumor necrosis alongside areas of mitoses were seen. However, no microvascular proliferation was appreciated. Genetic analysis revealed that glial fibrillary acidic protein (GFAP) was positive, p53 and IDH-1 were both wild types, SOX10 and Cytokeratin AE1/AE3 (CKAE1/AE3) were negative, and Ki67 index was 20%. The patient was thus diagnosed with glioblastoma, IDH-1 wild type [Figure 2].

DISCUSSION

To effectively grasp the oddity that the radiographic image of this patient presents, the differences between cerebral cavernous malformations (CCMs) and glioblastoma on MRI must be accurately delineated.

CCMs or cavernomas are vascular abnormalities of the brain primarily composed of a collection of irregular, hyalinized capillaries circumscribed within a gliotic margin showing hemosiderin deposits.[10] Coexistence and even mimicry of such lesions have been previously reported in the literature, albeit rarely.[15,2] In general, CCMs can be differentiated from gliomas by the absence of mass effect and peripheral edema. However, these features are observed in the presence of hemorrhage,[16] as were the case for our patient.

On a genetic basis, it is well documented in the literature that IDH-1 mutations are frequently observed in what was previously defined as "secondary" Glioblastoma (73–85%),[9,4] which develops from a preexisting lower-grade glioma; a disease state that is in line with the diagnosis of the case, we present. However, these mutations are rarely, if ever present in "primary" Glioblastoma,[4] with the converse, the relationship of wild-type with glioblastoma origin status, holding true as well. Further, IDH-1 mutations have been linked to younger patients who concomitantly suffer from either astrocytoma, anaplastic astrocytoma, anaplastic oligoastrocytoma, or glioblastoma.[11] Finally, it has also been observed that patients with lower-grade gliomas tend to suffer from epilepsy as opposed to those with higher-grade gliomas.[8]

Thus, it is clear that the case we present is unique in relation to currently published literature on the subject, as not only did our patient's Glioblastoma present as a mimetic CCM, her 20-year long history of epilepsy (which, according to the epidemiological data above, puts her below the mean age) points to her affliction being a lower-grade glioma primarily, which then progressed into a glioblastoma; however, the molecular profile of the patient signifies the development of a de novo glioblastoma, due to the absence of an IDH-1 mutation. Similarly, a consistent association of increased serum GFAP concentration has been seen in relation to the development of IDH-1 wild-type Glioblastoma,[5] a factor additionally present in the molecular profile of the patient we present.

CONCLUSION

Due to the hemorrhage superimposing our patient's glioblastoma, the lesion bore close resemblance, radiologically, to a cavernoma. In addition, IDH-1 wild-type glioblastoma predominantly manifests in older patients (>55). Existing literature and nomenclature-defining guidelines have shown that they are diagnosed only if specific genetic, molecular, and histopathological factors are present. The distinct nature of our case is predicated on the fact that, not only did our patient present with a rare case of mimicry, superimposed on this was an opposing epidemiological profile to IDH-1 wild-type glioblastoma, related closer to IDH-1 mutant glioblastoma while her other parameters were diametrically opposed; a situation distinctly unique within published literature on the subject.

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Declaration of patient consent

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Conflicts of interest

There are no conflicts of interest.

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