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Well-Circumscribed, Minimally Enhancing Glioblastoma Multiforme of the Trigone: A Case Report and Review of the Literature

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Summary: Glioblastoma multiforme (GBM) is known to present within the lateral ventricle but is relatively infrequent and predominantly found in the frontal horn or body of the ventricle. A GBM located within the trigone is rare, and one that appears well-circumscribed, homogeneous, and minimally contrast enhancing, as demonstrated in this patient, is highly unusual.

Intraventricular neoplasms are uncommon, representing just 1–10% of all CNS tumors (1–4). Glioblastoma multiforme (GBM) is known to present within the lateral ventricle but is relatively infrequent and, when present, is found predominantly in the frontal horn or body, presumably from a paraventricular origin (1, 2, 5). Not unexpectedly, contrast enhancement is typical of an intraventricular GBM, and an infiltrative, irregular appearance on imaging can also be present (6–8). In this report, we present a highly unusual case of GBM located primarily within the trigone that not only appeared well circumscribed, homogeneous, and noninfiltrative, but also enhanced minimally with contrast.

Case Report

The patient was a 32-year-old, right-handed woman without significant past medical history who presented for evaluation of headaches and intermittent short-term memory loss. She also reported mild nausea, but was otherwise asymptomatic. Her headaches had begun approximately 3 months before her presentation. On neurologic examination, no deficit was appreciated. She underwent a head CT (Fig 1) with the finding of a large, poorly enhancing right occipital-parietal mass that appeared to be located within the lateral ventricle. Subsequent MR imaging scanning (Fig 2) confirmed the location of the tumor in the trigone with local expansion of the ventricle. Similar to the CT, minimal enhancement was noted. On the basis of the imaging characteristics, a low-grade astrocytoma was felt to be the most likely diagnosis. In light of the size of the tumor and its location, a parietooccipital surgical approach was performed. The tumor appeared grayish and was predominantly firm, necessitating piecemeal removal. The tumor was

not particularly vascular, and a distinct plane between tumor and ependyma was identified, but there were several areas where the tumor appeared to infiltrate into adjacent brain parenchyma. Frozen-section pathologic analysis was described as abnormal and cellular but was not specifically diagnostic. Tumor resection was continued until a near-total removal was accomplished. Postoperatively, the patient remained without neurologic deficit. Follow-up MR imaging showed near-total removal of the tumor.

Histologic sections were examined by light microscopy. The neoplasm was hypercellular with necrosis and endothelial cell proliferation, hallmarks of GBM, World Health Organization (WHO) classification grade IV (Fig 3E, F) (9, 10). Gemistocytes were distributed throughout the neoplasm with rare mitoses. These cells had hyaline, eosinophilic cytoplasm, and eccentric, hyperchromatic nuclei, some of which were large and pleomorphic (Fig 3A). Immunostains for glial fibrillary acidic protein (GFAP), S-100 protein, vimentin, and neurofilament were positive (Fig 3B, -C, -D), whereas immunostains for muscle-specific actin, alpha smooth muscle, and synaptophysin were negative. MIB-1 was positive, with a low proliferation index. The morphology and GFAP positivity suggested a diagnosis of diffuse gemistocytic astrocytoma; however, the tumor necrosis and microvascular proliferation raised the tumor grade to grade IV GBM.

Because of the unusual radiographic appearance and location, the histologic slides were also reviewed by physicians at the Armed Forces Institute of Pathology (Bethesda, MD), who confirmed the initial diagnosis. Whole-brain radiation and chemotherapy were subsequently instituted. At 2-year follow-up, the patient complained of headaches but remained neurologically intact with no evidence of tumor progression on MR imaging.

Discussion

Intraventricular tumors can be categorized into those that originate from structures within the ventricular system or those that arise from the ventricular wall and subsequently grow into the ventricle (2, 11). Choroid plexus tumors and meningiomas are typical examples of tumors arising from an intraventricular structure, the choroid plexus (12, 13). By contrast, intraventricular gliomas likely originate from a paraventricular location before growth into the ventricle. Regardless of origin, a tumor is considered intraventricular if it is located primarily within the ventricular system and causes a local expansion of the ventricle with growth. Most lateral ventricular tumors enlarge slowly and typically do not cause symptoms until reaching a size large enough to cause obstructive hydrocephalus or compression of surrounding eloquent structures (4, 5). The most common symptom is headache, followed by visual deficits and signs of elevated intracranial pressure, including papilledema

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FIG 1. Precontrast (A) and postcontrast (B) CT images showing a large, poorly enhancing mass that appears to be within the right lateral ventricle.

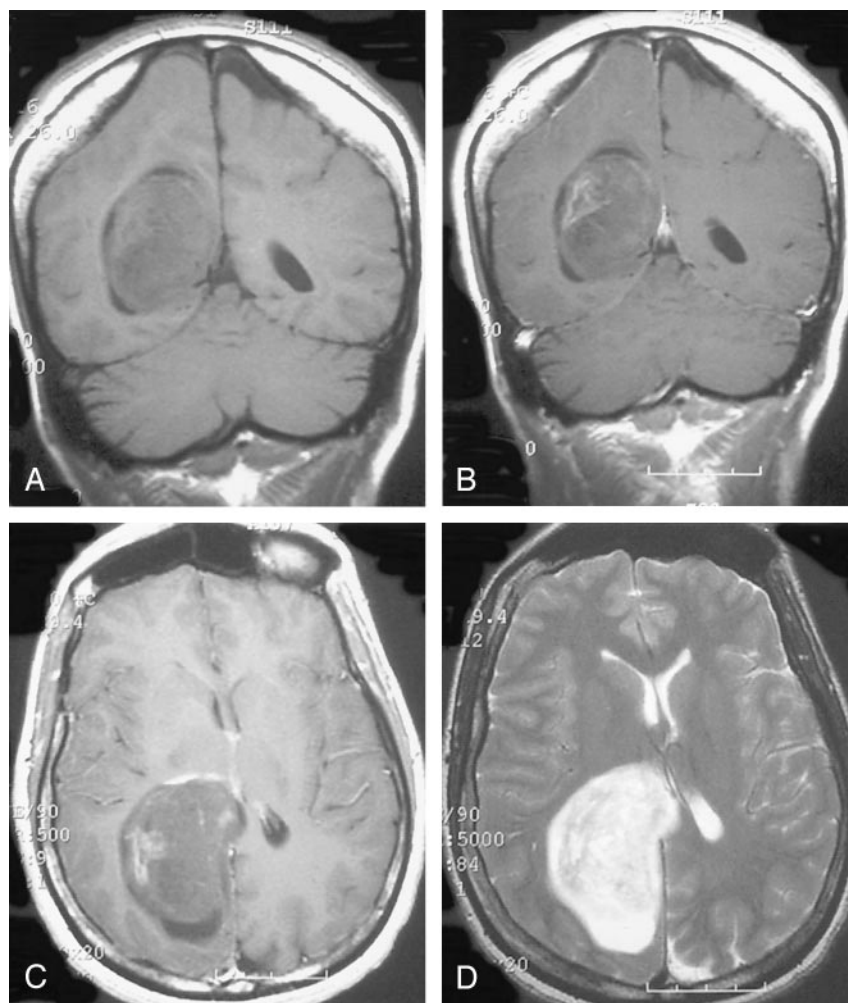
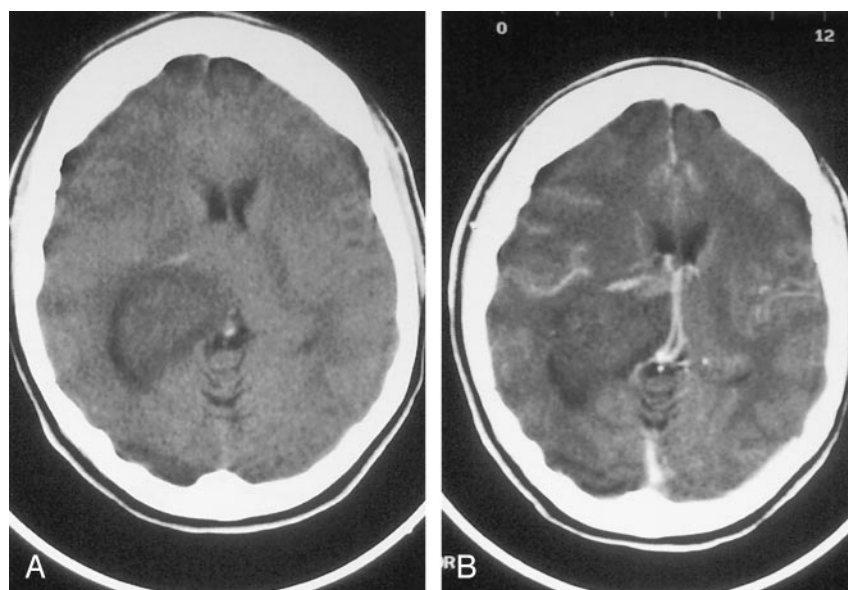


FIG 2. Precontrast coronal (A), postcontrast coronal (B), postcontrast axial (C), and T2-weighted axial (D) MR images redemonstrating a minimally enhancing mass within the trigone. The mass is homogenous and well-defined and appears to cause local expansion of the ventricle.

(2, 4, 11, 12, 14). Less common symptoms are memory loss, seizures, mental status changes, ataxia, and focal motor deficits. Usually, the interval from symptom onset to presentation is short, measured in weeks to months (2). The primary problem of headaches be-

ginning approximately 3 months before presentation for the patient in this case study is consistent with a large ventricular tumor.

Although intraventricular neoplasms are relatively rare overall, a large number of tumors have been

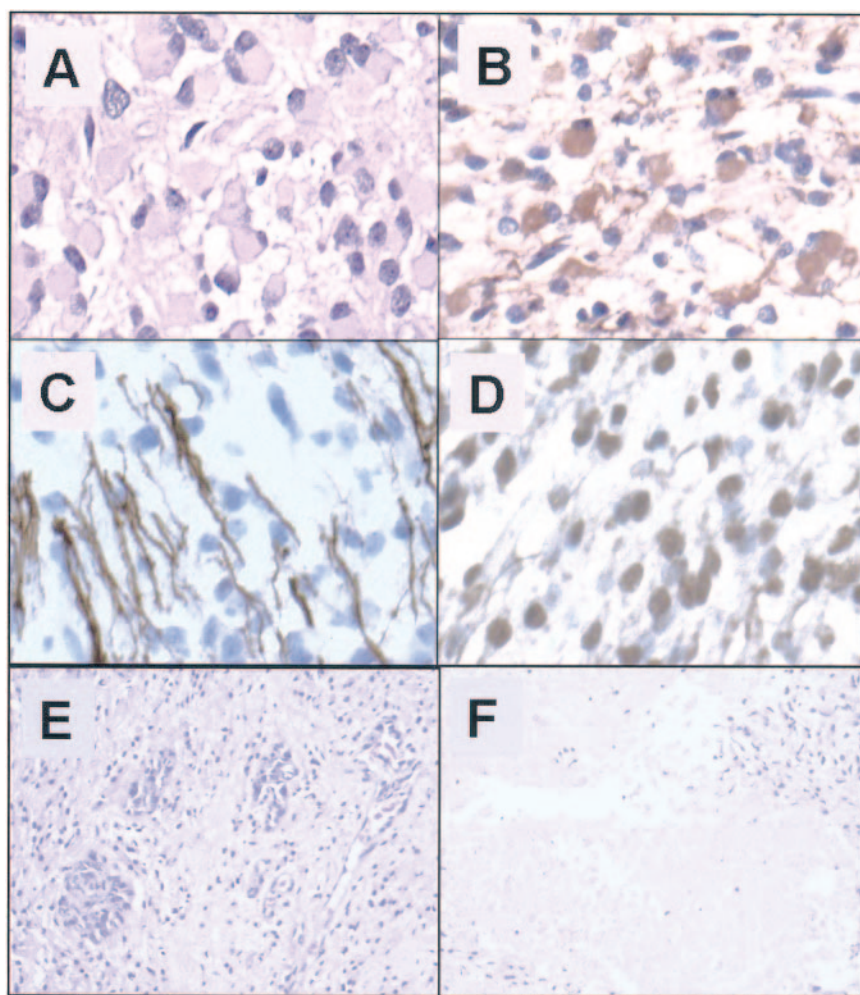


FIG 3. Glioblastoma multiforme. Gemistocytes were the most common cell type within the neoplasm (A; hematoxylin and eosin, original magnification $\times 400$). Immunostains for GFAP (B), neurofilament (C), and S-100 protein (D), are all at original magnification $\times 400$. Areas of vascular endothelial cell proliferation and necrosis (E and F, respectively; original magnification $\times 100$) characterize this lesion as a grade IV GBM.

Most common tumors based on age and location (1, 2, 4, 5, 12, 21)

	Frontal Horn	Foramen of Monro	Body	Trigone
Children (<10 yrs)	PNET SEGA	SEGA	PNET	CPP CPC
Adults (10 to 30–40 yrs)	Astrocytoma Central Neurocytoma	Colloid Cyst SEGA	Astrocytoma GBM Ependymoma Oligodendroglioma Central Neurocytoma	Astrocytoma Ependymoma Meningioma
Adults (>30–40 yrs)	Central Neurocytoma Subependymoma	Colloid Cyst Subependymoma	GBM Subependymoma Metastasis	Meningioma

Note.—PNET indicates primitive neuroectodermal tumor; SEGA, subependymal giant cell astrocytoma; CPP, choroid plexus papilloma; CPC, choroid plexus carcinoma; and GBM, glioblastoma multiforme.

reported to present within the lateral ventricle, including central neurocytoma, colloid cyst, subependymal giant cell astrocytoma, subependymoma, ependymoma, primitive neuroectodermal tumor, choroid plexus papilloma, choroid plexus carcinoma, meningioma, astrocytoma, GBM, oligodendroglioma, metastasis, lymphoma, teratoma, epidermoid, fibroma, and hemangiopericytoma (1, 5, 6, 11–20). Although CT or MR imaging can assist in the localization of the tumor, radiographic studies alone are often inade-

quate to make a precise diagnosis (5). The imaging characteristics for most intraventricular neoplasms are nonspecific with conventional T1-weighted/T2-weighted MR imaging protocols. Many studies, therefore, advocate use of the location of the tumor and the age of the patient to narrow the differential diagnosis (1, 2, 5, 12, 21). In most of these articles, patient age was arbitrarily divided into <10 years, between 10 and 30–40 years, and >30–40 years of age. Table 1 is a composite of the articles and lists only the most

common tumors based on location and patient age. Tumors involving just the temporal horn are rare and most often are meningiomas (2). In addition to age and tumor location, other factors such as a hereditary syndrome or systemic illness can influence the differential diagnosis. Specifically, patients with tuberous sclerosis have a predisposition to develop subependymal giant cell astrocytomas, and patients with AIDS are much more likely to have an intraventricular lymphoma (2, 21, 22).

For adults, meningiomas, astrocytomas, and ependymomas are most common at the trigone. Contrast enhancement is a characteristic of all three tumor types, although the degree of enhancement in astrocytomas varies (1, 5). A GBM presenting within the trigone is uncommon, with most presenting within the frontal horn and body of the lateral ventricle. To the best of our knowledge, there have been only five definite cases of a GBM at the trigone (2, 5, 6). When present, intraventricular GBMs have the typical imaging characteristics of intraparenchymal, high-grade gliomas, including contrast enhancement and, at times, inhomogeneity and infiltrative, irregular borders (1, 2, 5–7). The well-circumscribed, minimally enhancing appearance of the trigonal GBM in this case is highly unusual and has not been reported in the literature previously. Because contrast enhancement in astrocytomas is variable and astrocytomas are relatively common at the trigone, we suspect that this tumor was originally a low-grade astrocytoma that was in the process of transforming into a GBM at the time of presentation. This neoplasm was unusual in that portions demonstrated the distinctive morphology of a gemistocytic astrocytoma, WHO classification grades II–III (10). The presence of extensive necrosis and endothelial cell proliferation, however, raises this to a WHO grade IV glioblastoma.

Conclusion

The prognosis for most patients with a diagnosis of GBM is dismal, with an average survival of approximately 12 months (23). There are, however, a small number of patients (up to 5%) who survive 5 years or longer (24). An analysis of these long-term survivors suggests that a prolonged disease-free interval after initial, aggressive surgical resection followed by multitechnique treatment is a significant positive prognostic indicator (24). Other favorable prognostic factors include a young age (<50 years), high Karnofsky score, and a low mitotic rate as reflected by a low Ki-67 or MIB-1 labeling index (23, 25). The patient in this case study has had a near total resection and has undergone multitechnique treatment involving radiation and chemotherapy. In addition, she has a number of the aforementioned positive indicators, including

young age, high functional status, and a low MIB-1 index, all of which has likely led to a longer survival.

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