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Case Report

Imaging findings in the progression of a giant cell glioblastoma

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ABSTRACT

First described in 1909, giant cell glioblastoma (GC) is a histologic variant of glioblastoma multiforme (GBM) that accounts for 1% of cases of primary GBM. It is characterized by a predominance of bizarre giant cells with abundant eosinophilic cytoplasm, and may portend an improved prognosis over classic GBM. Due to the rarity of GC, there is a paucity of reports that describe its associated radiologic findings. This case report chronicles the progression of a GC that was incidentally discovered in a 74-year-old male with coincident subdural hematoma and empyema. Serial brain imaging was obtained as part of this patient's continued work-up that documents the radiologic characteristics of the GC over a period of months. To our knowledge, this manuscript is the most extensive radiologic documentation of the progression of GC to date.

Introduction

Giant cell glioblastoma (GC) is a rare histologic variant of glioblastoma multiforme (GBM) characterized by a predominance of bizarre multinucleated giant cells with abundant eosinophilic cytoplasm [1]. It was first described as a "monstrocellular" tumor by Schmincke in 1909, and has since been reported to account for 1% of cases of primary GBM [2]. GC may portend an improved prognosis over GBM [2]. Yet, despite having been first described in the literature over 100 years ago, GC has been incompletely characterized to date due to its rarity. We present a case of GC coincident with a subdural hematoma and empyema that radiologically details the development of this rare neoplasm.

Case report

A 74-year-old male presented to the ED with sudden onset altered mental status and aphasia. His medical history was notable for hypertension, atrial fibrillation for which he was on warfarin, and recurrent oral cavity squamous cell carcinoma (OSCC) for which he had undergone right mandibulectomy with neck dissection and a partial glossectomy. The patient had a seizure in the ED and was admitted to the ICU for further workup. On hospital day (HD) 2, a noncontrast MRI

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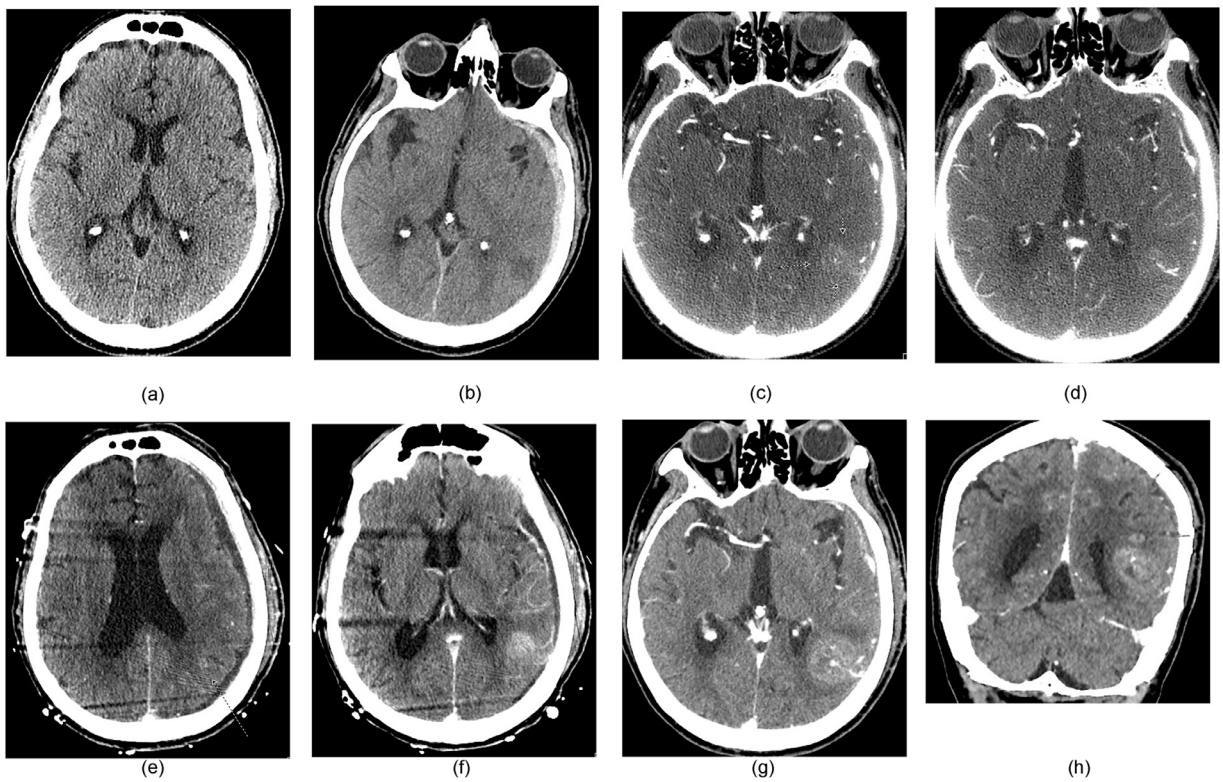


Fig. 1 – (a) Initial presentation. CT head in ED shows no abnormality. (b) Initial presentation, hospital day 2. CT head shows acute subdural and temporal hypodensity corresponding to FLAIR hyperintensity. (c and d) 47 days after initial presentation. CTA head obtained for new stroke-like symptoms demonstrates subtle enhancement in this region. There is a central vascular structure running through this area. (e and f) 48 days after initial presentation. CECT obtained for worsening AMS. Purulent drainage from burr hole. MRI was difficult to arrange due to pacemaker. CT head shows enhancing lesion in left posterior superior temporal lobe and additional small satellite focus. (g and h) 78 days after initial presentation. CECT shows likely recurrent subdural empyema and enlarging temporal cortical lesion with prominent central vessel.

brain showed a left convexity subdural hematoma as well as a 1.7 cm rounded focus of transcortical T2/FLAIR hyperintensity in the left temporal lobe demonstrating central susceptibility signal loss, initially thought to represent a venous infarct. Post contrast MRI sequences for further characterization of this lesion showed linear gyriform enhancement and internal microhemorrhage, which supported a diagnosis of subacute venous infarct. The subdural was managed conservatively and the patient was discharged home after 1 week. CTs 1 and 2 weeks out from discharge showed a relatively stable subdural.

Three weeks after discharge (28 days after initial presentation), the patient re-presented to the ED from neurology clinic for acute change in mental status. A noncontrast CT (NECT) showed expansion of the subdural hematoma to 1.9 cm with increased midline shift. Neurosurgery evacuated the hematoma via 2 burr holes and placed a subdural drain, and the patient was discharged to a skilled nursing facility (SNF) 1 week later. The temporal lesion was not visualized or poorly visualized on all the CT scans performed over this time period.

The patient represented a little over a week later (47 days after initial presentation) after a fall at his SNF and was noted to have facial droop and pronator drift. A NECT showed a new hyperdense collection tracking from the patient's parietal burr hole. The incision over this burr hole was also draining a small amount of purulent fluid raising concern for empyema. A second NECT the same day was unchanged from the first with regard to the parietal collection, but demonstrated interval development of a hyperdense collection in the left posterior temporal region corresponding to the area of hypodensity identified on the CT from his first admission. The region measured up to 3 cm and was concerning for a hemorrhagic transformation of what was still presumed to be a venous infarction. On hospital day 1, additional NECT scans showed slight posterior expansion of the parietal collection and a third contrast-enhanced CT (CECT) showed slight enhancement of the temporal lesion, suggesting blood–brain barrier breakdown, as well as a 2-mm area of satellite enhancement immediately superior to the lesion. On HD 3, contrast-enhanced MRI (CEMRI) confirmed a subdural empyema and demonstrated the temporal lesion as a hyperintense T2/FLAIR signal with enhancement and anterior peripheral restricted diffusion. Concern was raised in the MRI interpretation that, while this area could represent a venous infarct, a hemorrhagic metastasis could also have this appearance. A craniotomy was performed for

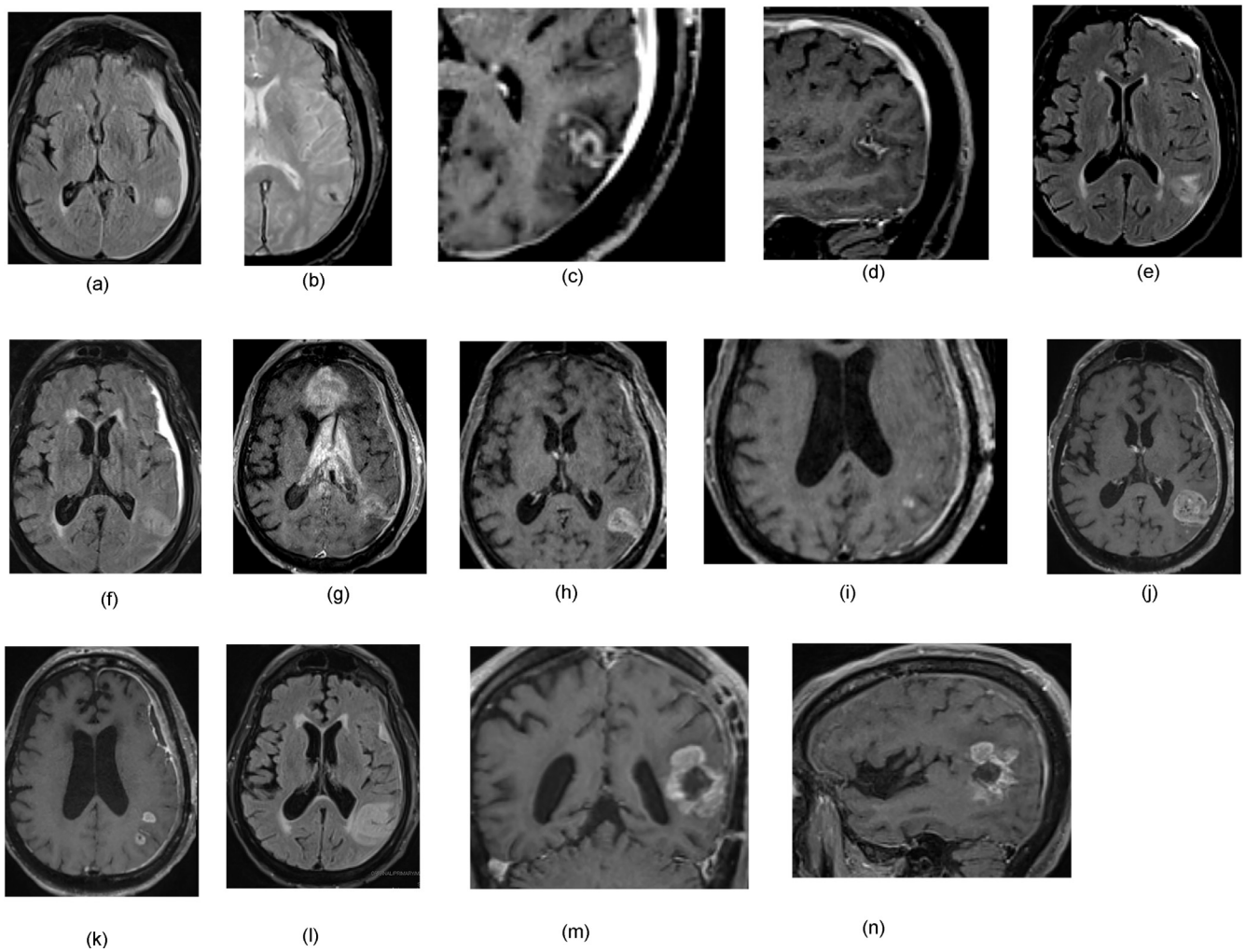
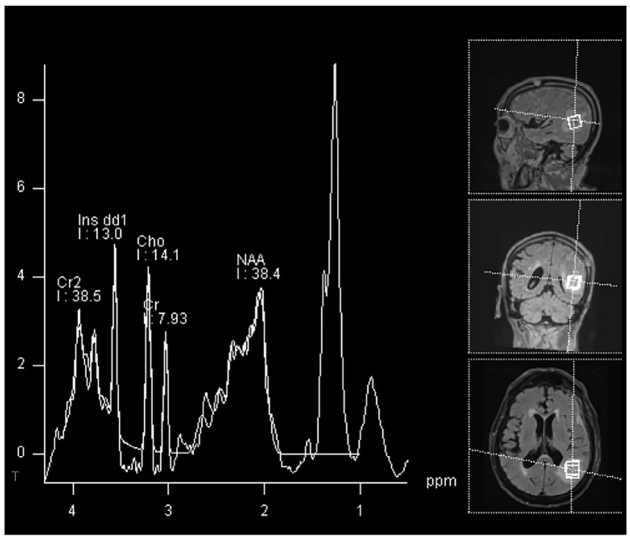


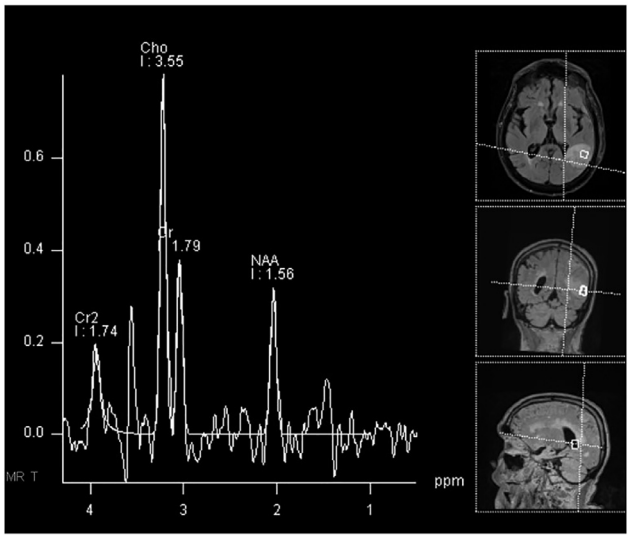
Fig. 2 – (a) Initial presentation, hospital day 2, FLAIR demonstrates small focus of transcortical hyperintense signal in the left posterior superior temporal lobe and acute subdural hematoma. (b) Initial presentation, hospital day 2, GRE demonstrates mild central gradient blooming. (c and d) Initial presentation, hospital day 6, CEMRI demonstrates unusual serpentine enhancement. (e) Initial presentation, hospital day 6. FLAIR demonstrates gyral swelling and surrounding edema. (f and g) 48 days after initial presentation. MRI obtained to evaluate empyema. FLAIR and CET1WI demonstrate focal gyral swelling and mild hyperintense FLAIR and enhancement. (h and i) 54 days after initial presentation. MRI obtained post empyema wash out for follow up. Continued gyriform enhancement with punctate satellite foci of enhancement. (j–l) 79 days after initial presentation. MRI head shows enlarging left temporal mass and satellite lesions with increased hyperintense FLAIR signal. (m and n) 131 days after initial presentation, 42 days post resection. CETIWI at first follow up prior to adjuvant chemoradiation. Peripheral nodular enhancement worrisome for disease progression.

subdural empyema evacuation. The patient's neurologic status waxed and waned over the next few days but returned to baseline by discharge on HD 10.

Three weeks after discharge (78 days after initial presentation), he represented with altered mental status. A CECT was obtained that redemonstrated an enhancing cortical lesion in the left temporal lobe with a prominent central vessel, measuring $3.3 \times 2.9 \times 1.8$ cm (AP by TV by CC), progressively enlarging when compared to previous studies. A CEMRI also showed an increase in the size of adjacent enhancing nodular lesions and increased surrounding T2/FLAIR hyperintensity possibly representing vasogenic edema or tumor infiltration. Spectroscopy was obtained for further characterization in preparation for possible resection. Both single- and multivoxel spectra in the contralateral parenchyma demonstrated a normal Hunter's angle. On the multi-voxel spectroscopy, there was a significant drop in the absolute choline peak between the lesion and contralateral parenchyma demonstrated in multiple voxels but most pronounced along the posterior margin of the lesion. There was also reversal of Hunter's angle with a significant choline:NAA ratio of over 2:1. A peak at 1.3 ppm likely represented lactate. On the single-voxel spectroscopy, there was flattening of Hunter's angle without significant reversal. A large lactate peak was also demonstrated. The mass, thought at the time to most likely be a squamous cell metastasis, was excised and by permanent section discov-



(a)



(b)

Fig. 3 – (a) SVS at TE 34 shows flattening of Hunter's angle but a Cho:NAA ratio of ~1:1. (b) CSI at TE 144 shows reversal of Hunter's angle with Cho:NAA ratio of ~ 2:1.

ered to be a giant cell glioblastoma, IDH1-mutant type, MDMH promoter methylation positive. A follow-up MRI 1 month after resection and prior to adjuvant chemoradiation demonstrated nodular enhancement surrounding the resection cavity.

Discussion

We present a case of GC that was incidentally noted during neuroimaging obtained for an acute, symptomatic subdural hematoma. The lesion rapidly progressed but co-occurrence with additional acute findings as well as an atypical imaging appearance for GBM resulted in a mildly delayed diagnosis. GC is a histologic variant of GBM and has been reported to account for 1% of primary GBM [2]. The significance of the histologic difference is not known, owing in large part to the paucity of cases. However, studies have reported GC may have a more favorable prognosis compared to GBM [2]. The radiologic appearance of GC has not been well documented. Our patient's serial imaging demonstrating the development of a GC is, to our knowledge, the most extensive radiologic documentation of the progression of this rare neoplasm.

Previous case reports that radiologically describe GC are few and have reported somewhat conflicting characterizations, as well as difficulty distinguishing GC from other pathologic processes using imaging alone. From the few reports that do radiologically describe GC, it appears to infrequently present with the classic radiologic features of GBM. One reported case describes a hemorrhagic lesion in a young girl that was mistaken for embolic stroke before pathology revealed GC [3]. Another report by Nagao, et al. described a well-circumscribed T1 hypointense, heterogeneously T2 hyperintense peripherally enhancing mass with T2 prolongation in the surrounding white matter. Based upon the conventional MRI sequences and relative cerebral blood volume values on perfusion-weighted MRI, this lesion in a 64-year-old woman was initially suspected to be a metastasis [4]. It was only after resection and pathologic examination that its glial origin was discovered. The CT and MRI findings of a case of giant cell glioblastoma were also described by Zipp, et al. [5], and Parekh et al., in a 1993 paper, also published the CT findings of a case of multifocal GC [6]. Older cases including a radiologic description have also been published by Asklen, et al., who noted the radiologic appearance of the tumor to be well demarcated but otherwise without distinguishing features [7, 8]. All of these descriptions are of relatively advanced cases, whereas our manuscript catalogs the appearance of the tumor as it progresses.

As in several of the above cases, imaging studies alone did not allow for confident radiologic diagnosis of our patient's lesion. Nagao, et al., report that the well-circumscribed appearance of their patient's lesion on conventional MRI was further cause to suspect metastasis. Indeed, MRI GBM is typically irregular with T2/FLAIR hyperintensity surrounded by vasogenic edema [9]. Our patient's lesion was hyperintense with surrounding edema on T2/FLAIR, but initially lacked the irregular, poorly defined, enhancing borders classically seen in GBM. It has also been reported that GC can exhibit both solid and cystic components on CECT [10].

Concern was raised for cerebral metastasis due to our patient's history of OSCC. This was the presumptive diagnosis at the time of resection. However, reports of cerebral metastases from OSCC are exceedingly rare. It is unknown whether cerebral involvement truly is an anomaly or if its occurrence is simply underrecognized and underreported [11]. OSCC classically first spreads to the cervical lymph nodes and features advanced local or regional disease before spreading more distantly [11,12]. Given our patient's history of local and regional OSCC, a metastatic etiology was a reasonable concern.

This unique case illustrates that while we often search for a single diagnosis to explain a patient's constellation of symptoms, we must be cognizant that the most obvious imaging

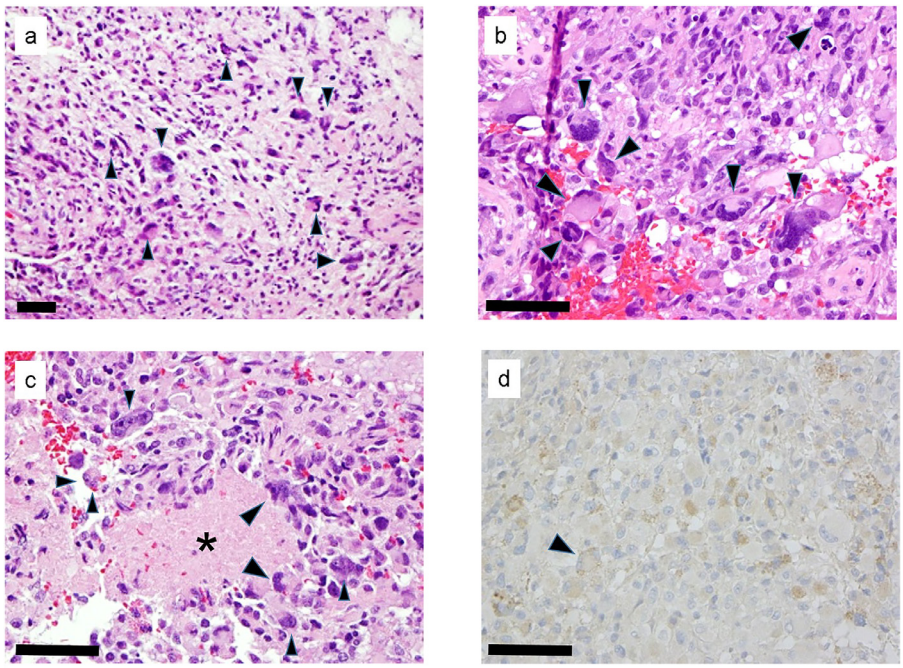


Fig. 4 – Histopathology of giant cell glioblastoma. The mass contains infiltrating neoplastic glial cells with nuclear and cytoplasmic atypia (all panels). Areas of the neoplasm have high cell density and contain several multinucleated giant cells (arrowheads, panels a–d). There is extensive confluent necrosis of neoplastic cells (asterisk, panel c). Some tumor cells including giant cells were positively stained (brown) with antibody against a mutant form of IDH-1 (panel d). Panels a through c show hematoxylin and eosin staining. Scale bars: 100 microns.

findings, as well as the most likely interpretation of those findings, may not adequately explain a patient's condition. Our patient's lesion was found incidentally on imaging obtained for a symptomatic subdural hematoma. The lesion in question displayed characteristics that initially raised suspicion for a venous infarct rather than a neoplasm. However, once radiologic findings were determined to also support the diagnosis of a hemorrhagic neoplasm, a metastatic origin was the logical first concern due to the patient's history of OSCC. Yet, after resection and subsequent permanent section, the unexpected diagnosis of GC was discovered.

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