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Case Report

Paroxysmal dysphasia in a 68 year-old man: Enhancing the MRI spectrum!

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ABSTRACT

Brain tumor-related epilepsy is a common complication of primary and metastatic brain tumors with seizures often representing the first manifestation of the tumor. The size and location of the tumor can make detection of epileptiform discharges on scalp electroencephalogram and safe surgical resection challenging. We describe a case of a patient with glioblastoma multiforme presenting as dominant temporal lobe epilepsy. Seizures were manifest as episodes of speech arrest on a background of long-standing history of episodic speech difficulty and headache. In this case, recognizing a change in semiology allowed diagnosis of a high-grade glioma. Use of electrocorticography during surgical excision of the tumor guided safe maximal excision without damage to eloquent cortex and helped confirm the diagnosis of brain tumor-related epilepsy.

1. Introduction

Glioblastoma multiforme (GBM) is a malignant primary brain neoplasm with variable presentation depending on the location of the tumor. GBM is often rapidly progressive with an estimated median survival of 14 to 16 months [1]. Symptomatic seizures are common in patients with primary brain tumors [2]. Tumor-related epilepsy can be the first manifestation of GBM and present in the absence of other neurologic symptoms or focal deficits on examination. Depending on tumor size and location, scalp electroencephalogram (EEG) may not identify epileptiform discharges or electrographic seizures, representing a diagnostic challenge.

Treatment of GBM involves maximal safe surgical resection followed by radiation therapy and adjuvant temozolomide chemotherapy [3]. In patients with GBM, gross total resection has been associated with two to three month improved survival [4]. The infiltrative nature of GBM and proximity of tumor to eloquent cortex can make surgical excision challenging. Use of electrocorticography for intraoperative monitoring during an awake craniotomy can guide safe surgical excision. Intracranial EEG can also identify epileptiform discharges undetected on scalp EEG, helping confirm a diagnosis of tumor-related epilepsy.

2. Case description

A 68-year-old right-handed man presented with a four-week history of paroxysmal neurological episodes characterized by incomprehensible speech lasting several minutes. He also reported episodes dating back to when he was 16 years old, described as word-finding difficulty lasting several minutes. These were followed by a headache and occurred once or twice a year. At age 23, the events of altered speech became associated with migratory paresthesias in the upper extremities. During his sixth decade of life, the events became accompanied by visual symptoms including jagged lines, floaters, and spiral-shaped light. His recent episodes of dysphasia represented a change in semiology as they did not include paresthesias or visual symptoms and they were not followed by a headache. The episodes involved no abnormal body movements, loss of awareness, or loss of bowel or bladder function. The neurological examination was normal.

Given new episodes on the background of a long-standing history of spells, a broad differential was considered, including vascular, infectious, inflammatory, and neoplastic etiologies. Outpatient electroencephalogram (EEG) revealed mild left temporal slowing without evidence of epileptiform discharges (Fig. 1A). Brain MRI demonstrated a T2 hyperintense lesion in the left temporal lobe that enhanced with gadolinium (Fig. 1B, C). Scattered areas of periventricular T2 hyperintensity were also noted (Fig. 1D). There were no diffusion weighted imaging (DWI) or apparent diffusion coefficient (ADC) changes.

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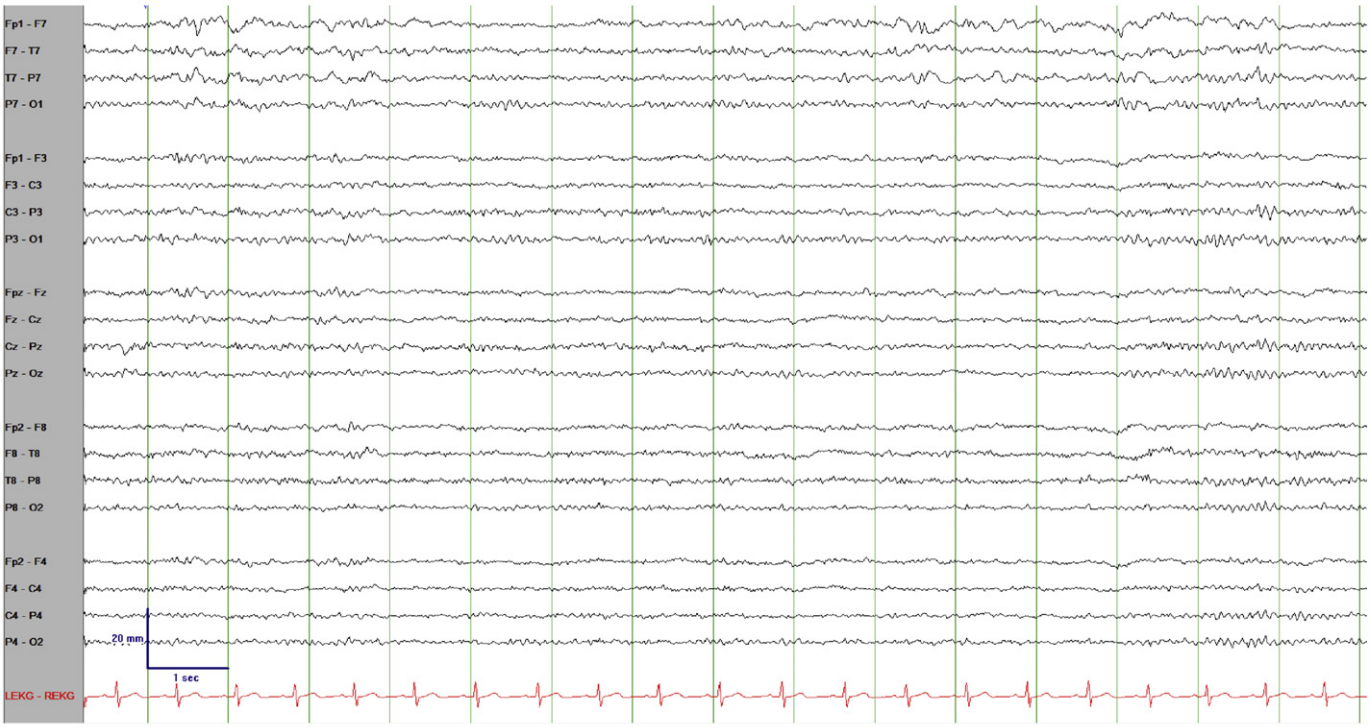
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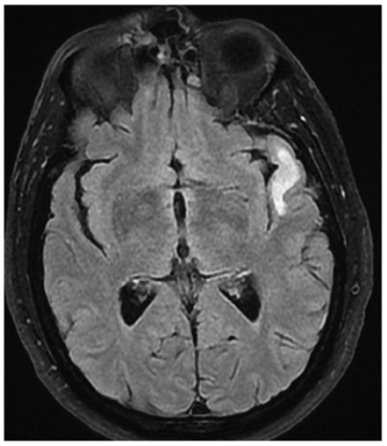

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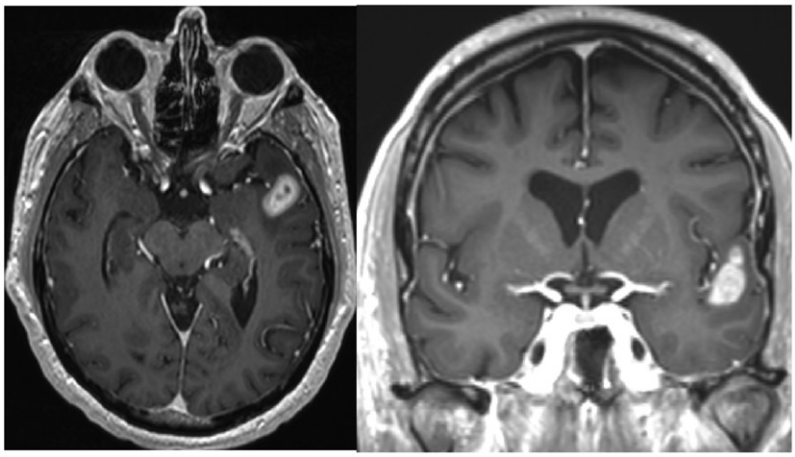

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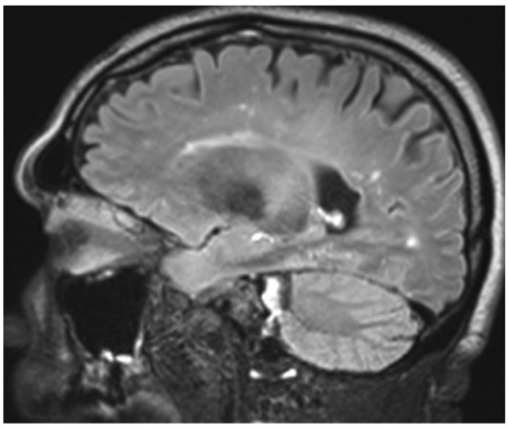

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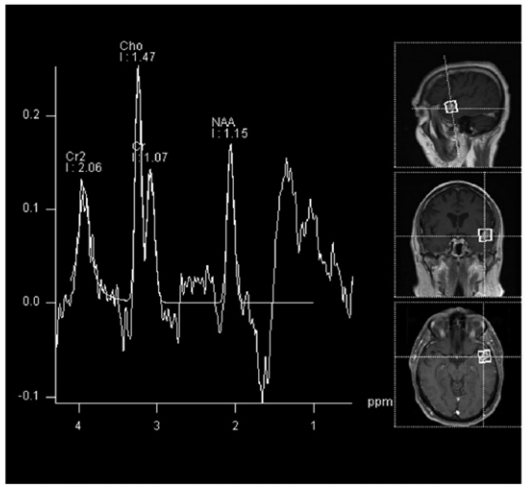
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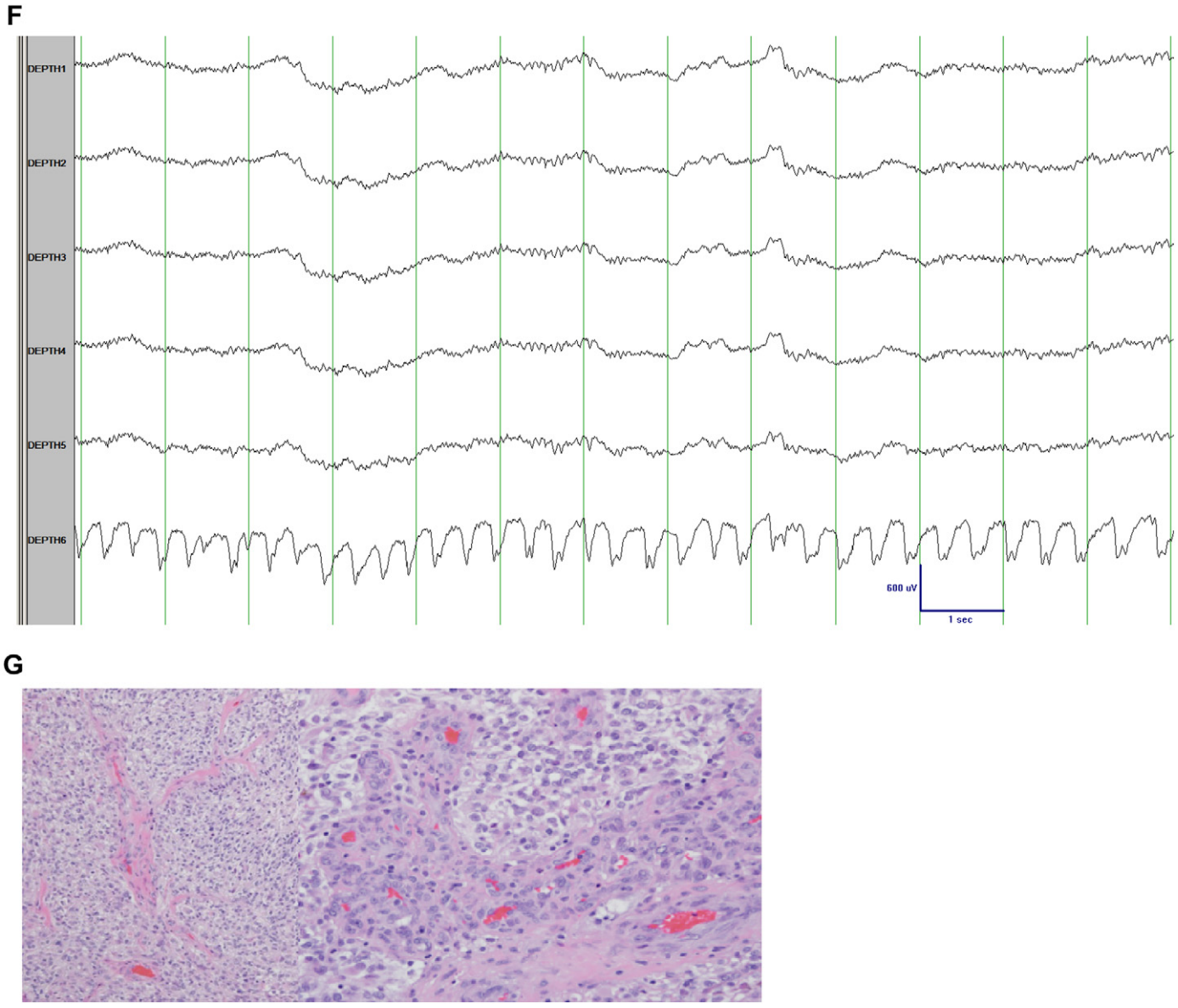

Fig. 1. A: Scalp EEG showing mild left temporal slowing without evidence of epileptiform discharges. B: Axial MRI brain T2 FLAIR image indicating a left temporal mass lesion with no significant mass effect or edema. C: Axial and coronal T1 post-gadolinium MRI brain images demonstrating a left temporal mass lesion with contrast enhancement. D: Sagittal MRI brain T2 FLAIR image indicating scattered periventricular hyperintensities. E: MR spectroscopy showing elevated choline to creatine peaks as well as decreased N-acetyl aspartate, consistent with neoplasm. F: Intracranial EEG demonstrating a focal electrographic seizure arising from a single contact of the depth electrodes. G: Pathology indicating cellular atypica, endothelial proliferation, and necrosis consistent with a diagnosis of glioblastoma multiforme.

The patient was admitted to the epilepsy monitoring unit (EMU) for seizure classification. Despite four days of monitoring, no episodes of speech arrest were captured. Interictal EEG demonstrated left temporal slowing without epileptiform discharges. Cerebrospinal fluid (CSF) analysis revealed 5 white blood cells, normal glucose at 78 mg/dL, and elevated protein at 56 mg/dL. Oligoclonal band assay was negative. CSF cytology was negative for malignancy.

Magnetic resonance spectroscopy (MRS) was requested to further characterize the lesion. MRS performed over the left superior temporal gyrus showed elevated choline to creatine peaks with decreased N-acetyl aspartate (Fig. 1E), a pattern suggestive of neoplastic etiology.

Patient underwent left-sided supratentorial awake craniotomy for resection of the left temporal lobe lesion and histopathological analysis. Intraoperative electrocorticography with electrocortical stimulation for language mapping was performed during the procedure with an 8×8 high-density grid placed over the left lateral temporal lobe. Functional mapping localized eloquent cortex for language and subsequently excluded from surgical resection. The anterior temporal lobe with the bulk of the tumor was resected. Electrocorticography demonstrated lateralized periodic discharges over the temporal lobe lesion with a focal electrographic seizure arising from a single contact of the depth electrode (Fig. 1F).

On histopathological analysis, the surgical specimen was consistent with an isocitrate dehydrogenase (IDH) wild-type GBM (Fig. 1G). Methylguanine-DNA methyltransferase (MGMT) methylation status was indeterminate. No complications from surgery arose and the patient was referred for stereotactic radiation and temozolomide chemotherapy. He was also discharged on a maintenance dose of levetiracetam.

3. Discussion

Our patient's spells that started at age 16, described as transient word-finding difficulty, sensory changes, and visual changes followed by headache most consistent with migraine. Reversible visual, sensory, and speech symptoms lasting several minutes followed by a headache are suggestive of migraine with aura. Migraine peaks between ages 15 and 19 in males, which coincides with the onset of our patient's spells at age 16 [5]. Additionally, patients with migraine may have subclinical white matter lesions on MRI imaging, though similar MRI findings can also represent chronic microvascular ischemia [6].

However, the more recent episodes of speech arrest represented a new type of spell and suggested focal seizures arising from the dominant temporal lobe. Brain MRI identified an enhancing temporal lobe lesion with no significant peri-tumoral edema and little mass effect. The MRI features of the lesion were concerning for a high grade glioma, which are T2 hyperintense contrast-enhancing mass lesions. The temporal lobes are the second most common anatomical location for GBM [7].

Non-invasive diagnostic measures including MRS also suggested a neoplasm. Conventional in vivo MRS uses protons to detect the concentration of brain metabolites including N-acetyl aspartate, choline, creatine, lactate, myoinositol, and glutamate in order to determine whether a lesion is neoplastic, inflammatory, or ischemic [8]. In general, astrocytomas have an increase in choline, indicating high glial cellularity and decreased N-acetyl aspartate reflecting neuronal replacement by tumor tissue, which was observed in the left superior temporal gyrus MRS performed for our patient [8].

A definitive diagnosis was attained upon excisional biopsy. The location of the mass lesion in the dominant temporal lobe represented a surgical challenge, since the presenting symptom of speech arrest indicated that language function could be compromised by resection of the mass. Incorporation of awake craniotomy with electrocortical stimulation and functional language mapping was crucial to ensure maximal resection without adversely affecting eloquent cortex [9]. The diagnosis of brain tumor-related epilepsy secondary to GBM was made and treatment planning was completed without undue risk for the patient. Electrocorticography also revealed frequent epileptiform discharges and a brief focal seizure, which was not identified despite four days of EMU stay. This underscores the limitations of scalp EEG in identifying seizures arising from deep epileptic foci remote from recording electrodes.

Although brain tumors account for 4% of all epilepsies, symptomatic seizures can occur in up to 85% of patients depending on tumor type and location [2]. TRE occurs in up to 30–50% of patients with GBM [2]. Molecular markers such IDH mutation and MGMT methylation status are important predictors of tumor behavior and provide prognostic information for GBM cases [10]. IDH mutations are associated with a better prognosis in gliomas, likely representing an early event in glioma genesis [10]. In our patient, IDH wild-type status confers a poorer prognosis. MGMT is a DNA repair enzyme whose activity can be silenced by methylation, making tumors more susceptible to alkylator chemotherapy with agents such as temozolomide [10]. In our patient, the MGMT methylation status was indeterminate, conferring a poorer prognosis. Radiotherapy with concomitant temozolomide and adjuvant temozolomide improves two-year survival in patients with GBM [3], which was prescribed to our patient.

4. Conclusions

This case highlights that even in the apparent setting of a long-standing neurological process, it is important to recognize new symptoms that signify a difference condition and potential pathophysiology. In this case, a repeat evaluation uncovered a new diagnosis of GBM.

The case also underscores the potential benefits of electrocorticography, which allowed for safe maximal surgical excision of the mass lesion without causing speech deficit or damage to other eloquent cortex. Electrocorticography was also instrumental in identifying epileptiform discharges that could not be detected on scalp EEG, helping confirm the diagnosis of brain tumor-related epilepsy and guiding medical management.

Authors' contributions

Study concept and design: Drs. Sener and Feyissa.
Acquisition of data: All authors.
Manuscript preparation and literature review: Drs. Sener and Feyissa.
Critical review of the manuscript: Drs. Tatum, Quinones-Hinojosa, Mahato, and Feyissa.

Disclosures

Drs. Sener, Mahato, and Tatum report no disclosures relevant to the manuscript.

Drs. Feyissa and Quiñones-Hinojosa were attending physicians receiving compensation for care provided to the patient described in this case report.

Dr. Tatum is Editor-in-Chief of Epilepsy Behavior Case Reports.

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