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Limbic System Glioblastoma Extending to the Papez Circuit: A Case Report

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ABSTRACT

Background: Glioblastoma is the most common malignancy of the central nervous system. Symptoms vary significantly depending on tumor location and size.

Case Report: A 55-year-old man presented with mild memory deficits, occasional eye twitching, and throat irritation for two months. Magnetic resonance imaging revealed a glioma centered in the piriform cortex, infiltrating the amygdala, hippocampus, bilateral fornices, mammillary bodies, anterior cingulate gyrus, and anterior commissure.

Conclusion: Despite extensive involvement of the limbic system and the Papez circuit, the patient exhibited a remarkable paucity of symptoms and maintained his daily functioning. This discrepancy was elucidated by diffusion tensor imaging tractography, which demonstrated that the tumor primarily displaced, rather than destroyed, the adjacent white matter tracts.

Keywords: Diffusion tensor imaging, glioblastoma, limbic system, tractography.

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INTRODUCTION

Glioblastoma (GBM) is the most aggressive malignant brain tumor of astrocytic origin, and its etiology is currently poorly understood.[1] Although GBM can occur at any age, including childhood, its incidence increases sharply after the age of 54 and peaks between 75 and 84 years of age.[2] The preliminary diagnosis is typically based on characteristic tumor-related radiological findings, initially identified by computed tomography and confirmed by magnetic resonance imaging (MRI). A definitive histopathological diagnosis is obtained through tumor resection or biopsy. Functional MRI and diffusion tensor imaging (DTI) enable the integration of patient-specific anatomical and functional data into preoperative planning. Moreover, data obtained from DTI can be used for tractography, a three-dimensional (3D) reconstruction technique that allows assessment of neural tracts. Tractography provides valuable information not only for surgical planning but also for postoperative evaluation.[3] Therefore, imaging modalities play a crucial role in guiding tissue sampling for surgical resection, establishing histological diagnosis, and performing postoperative assessment.

CASE REPORT

A 55-year-old male patient with an unremarkable medical history was diagnosed with GBM following a biopsy. Neurological examination revealed no cognitive or behavioral deficits, and the patient reported no functional impairment in daily life other than mild memory problems. Despite the absence of focal neurological findings, the patient was admitted to the hospital with complaints of progressive forgetfulness regarding recent events over the preceding two months, occasional twitching of the right eye, and a tickling sensation in the throat.

The MRI scan was performed using a 48-channel head coil on a 3 Tesla scanner. A T2-weighted fat-saturated turbo spin-echo (TSE) sequence (TR=3000 ms, TE=75 ms, slice thickness=3 mm, and gap=0.5 mm) and DTI using a single-shot spin-echo echo-planar imaging sequence (TR=3443 ms, TE=93.3 ms, slice thickness=2.5 × 2.5 × 2.5 mm, and gap=0 mm) were acquired in the axial plane. DTI data were obtained using 32 different diffusion directions with b-values of 0 s/mm^2 and 800 s/mm^2.

MRI revealed a glioma centered in the piriform cortex, infiltrating the perirhinal cortex, amygdala, and hippocampus. The lesion demonstrated significant midline extension, involving the bilateral fornices, mammillary bodies, anterior cingulate gyrus, and anterior commissure. Furthermore, it invaded the subcallosal area and multiple regions of the corpus callosum, including the genu, rostrum, isthmus, and splenium, ultimately crossing into the contralateral hemisphere (Fig. 1).

Alterations in white matter tracts affect diffusion tensor anisotropy and orientation, resulting in distinct patterns on directional DTI color maps.[4] By differentiating intact, edematous, and disrupted fibers on these maps, we observed evidence of both fiber destruction and fiber displacement, with some tracts displaced by the glioma without complete structural disruption. In this case, intact, edematous, and disrupted fibers were individually identified on the DTI color map shown in Figure 2.

Orientation and integrity of the white matter tracts were also demonstrated by DTI. Several fiber bundles, including the fronto-

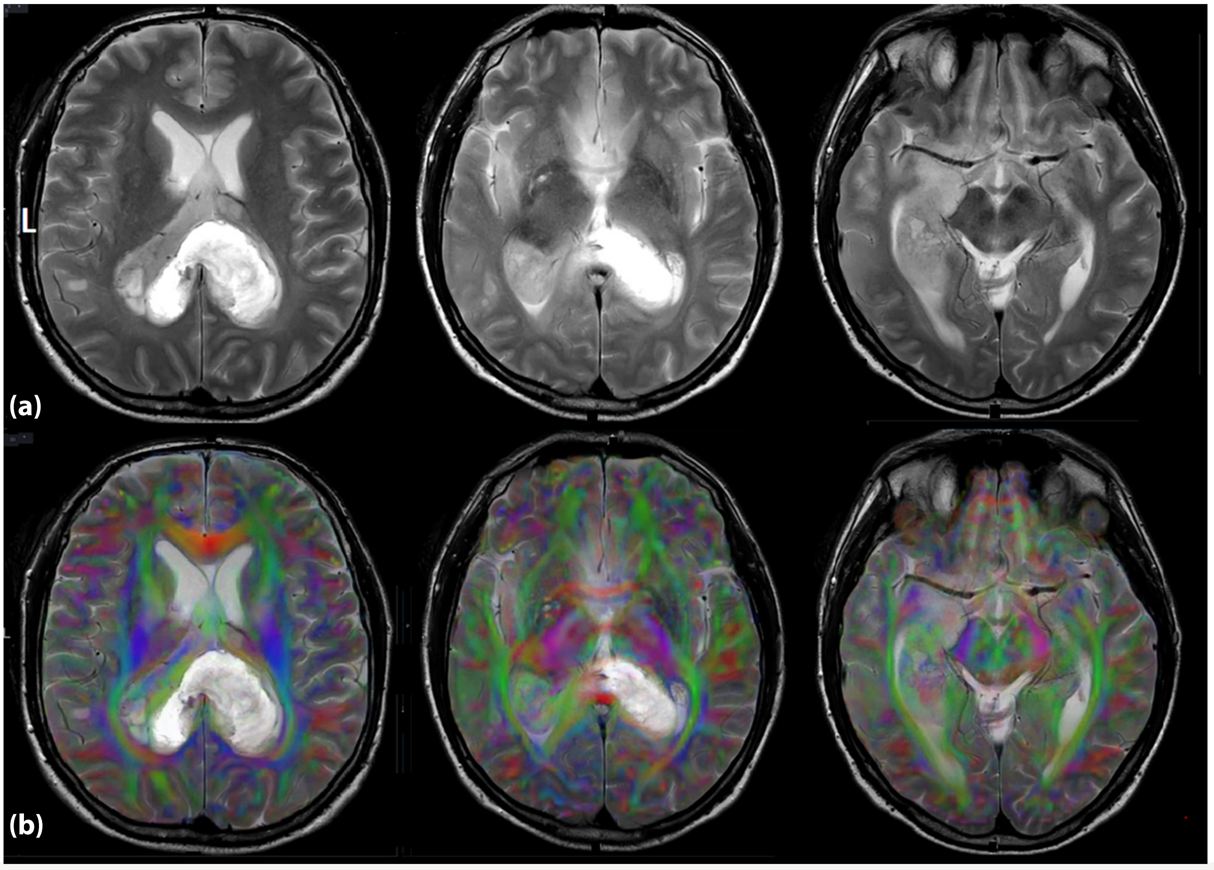

Figure 1. Consecutive axial T2-weighted images reveal an extensive lesion centered in the left anteromedial temporal lobe, involving the mesial temporal structures, limbic pathways, and the splenium of the corpus callosum, with extension into the contralateral hemisphere. Additional cortico-subcortical involvement is observed in the left insular, parietal, and posterior temporal regions **(a)**. Corresponding color-coded fractional anisotropy (FA) maps demonstrate displacement, deviation, and disruption of adjacent white matter tracts caused by the lesion **(b)**.

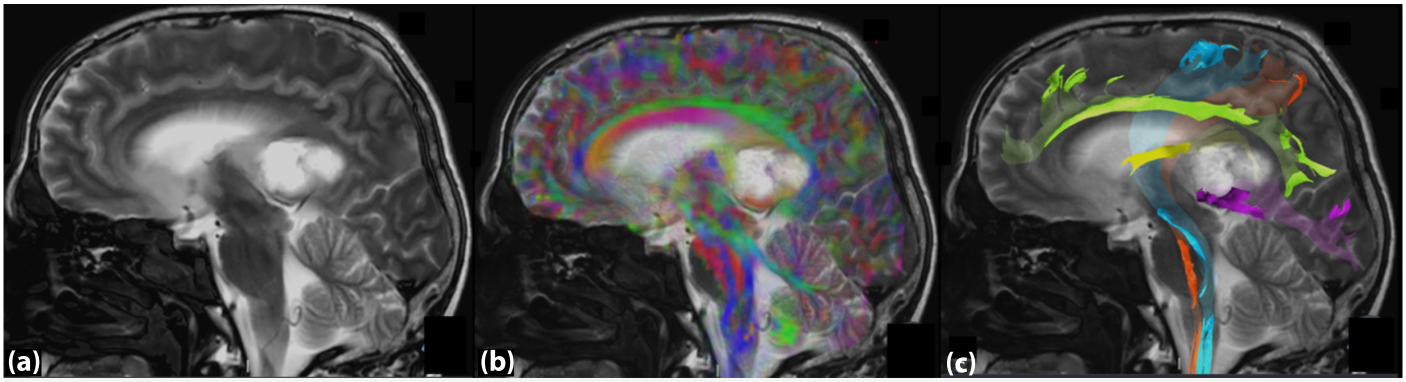

Figure 2. A sagittal T2-weighted image **(a)**, color-coded fractional anisotropy (FA) map **(b)**, and tractography reconstruction **(c)** demonstrate lesion-induced displacement of the corticospinal tract (CST, red), medial lemniscus (ML, blue), fornix (FX, yellow), and cingulum (CI, green). The forceps major (FM, pink) exhibits both displacement and disruption secondary to the lesion.

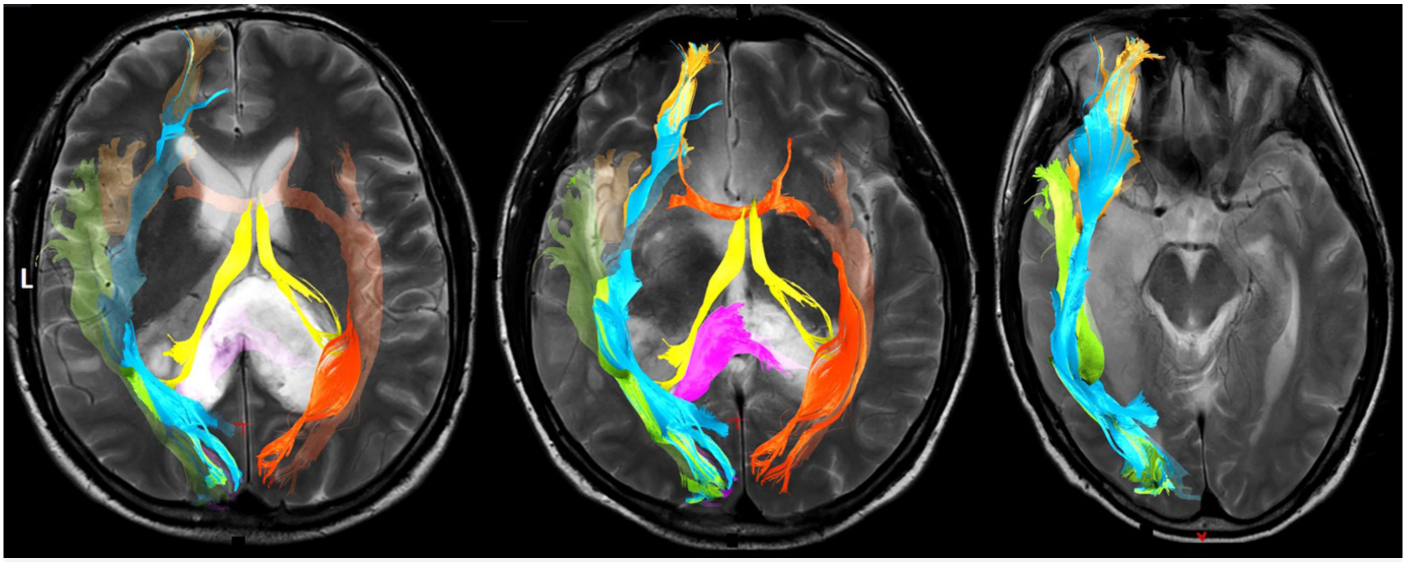

Figure 3. Tractography images demonstrate lesion-related disruption of the left temporal extension of the anterior commissure (AC, red) and the right occipital extension of the forceps major (FM, pink). The fornix (FX, yellow), inferior longitudinal fasciculus (ILF, green), and fronto-occipital fasciculus (FOF, blue) show displacement and deviation due to the lesion. The uncinate fasciculus (UNC, orange) remains intact and follows its normal anatomical course.

occipital fasciculus, inferior longitudinal fasciculus, and fornix, were displaced by the tumor, whereas the left temporal extension of the anterior commissure and the right occipital extension of the forceps major were disrupted (Fig. 3). In addition, the patient's optic radiation was affected by tumor infiltration, which may explain ocular complaints such as twitching.

DISCUSSION

While GBM typically involves the cerebral lobes,[5] this rare case demonstrates extensive involvement of the limbic system and its associated white matter. As noted by Capizzano et al.,[6] central nervous system (CNS) tumor classification prioritizes histology over anatomical origin, often overlooking so-called "limbic" tumors. Given the biological significance of anatomical origin, greater consideration should be given to tumors arising within the limbic system.

Classically, Papez[7] proposed a model linking specific brain structures to emotional processing and memory consolidation. This network, termed the Papez circuit, connects the hypothalamus, anterior thalamic nuclei, cingulate gyrus, and hippocampus. Subsequently, these cortical and subcortical structures, along with their associated fiber tracts, were collectively described as the limbic system. This system has been implicated in various neurological and psychiatric disorders.[8]

In this rare case, there was widespread involvement of the Papez circuit, including the hippocampus, amygdala, bilateral fornices, mammillary bodies, and anterior cingulate. The tumor's expansion also involved the anterior commissure and multiple subregions of the corpus callosum, extending from the rostrum and genu to the isthmus and splenium, ultimately crossing the midline into the contralateral hemisphere. Most of the brain structures and fibers affected by the tumor correspond to components of the extended version of the Papez circuit. In this respect, the present case supports the concept of an expanded Papez circuit. Owing to the resolution limitations of current neuroimaging modalities, comprehensive *in vivo* visualization of the entire Papez circuit is challenging. Consequently, very few studies have successfully delineated the full pathway in living subjects.[9]

A striking feature of this case is the relative preservation of emotional and cognitive functions despite the extensive involvement of the Papez circuit, with the patient exhibiting only mild memory deficits. As demonstrated on the DTI color maps, the tumor did not completely destroy all white matter tracts, rather, some fibers displaced without structural disruption. Therefore, the displaced white matter fibers may have remained functional.

Given this potential for functional preservation, surgical management of GBM cases involving the limbic system should emphasize not only anatomical resection but also preservation of functional networks. While standard imaging techniques may delineate tumor margins, they may be inadequate for visualizing white matter displaced or infiltrated by the tumor. In this context, tractography plays a critical role in surgical planning and assists in the preoperative mapping of vital subcortical connections, such as the Papez circuit. Thus, while aiming for maximal safe tumor resection, the patient's cognitive and emotional integrity may also be preserved.

CONCLUSION

The temporal lobe is unique in that it contains both predominant isocortex and allocortex.[6] Tumors originating from the limbic lobe may exhibit distinctive characteristics compared to those arising from extralimbic temporal regions. Since Yaşargil et al.[10] described the characteristics of limbic tumors more than three decades ago, primarily focusing on surgical aspects, the concept has received relatively little attention in the pathological and radiological literature. Further discussion and clearer characterization of limbic tumors are needed.

Moreover, this case is rare because of its extensive spread along the Papez circuit. It also supports prior imaging studies that have successfully visualized the entire circuit, as the tumor spread followed the anatomical course of the Papez circuit. In this case, the fact that a tumor affecting the limbic system to this extent did not result in behavioral or emotional disturbances, other than mild memory impairment, can be explained by the DTI color maps, thereby underlining their importance in understanding the symptoms.

Ethics Committee Approval: This is a single case report, and therefore ethics committee approval was not required in accordance with institutional policies.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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