Multicentric Low-Grade Gliomas

Vishwajith Sridharan[1], Laura M. Urbanski[3], Wenya Linda Bi[1,3], Katrina Thistle[3], Michael B. Miller[2], Shakti Ramkissoon[2], David A. Reardon[4], Ian F. Dunn[1]

BACKGROUND: **Multicentric low-grade gliomas are rare entities that occur in disparate regions of the brain. They can present with distinct pathologic and imaging findings and may harbor a worse prognosis. We present a case of multicentric low-grade gliomas and highlight their pathogenesis, imaging characteristics, and molecular signatures, with implications for clinical management.**

CASE: **A 49-year-old man presented with left-sided headaches for 3 months. Magnetic resonance imaging revealed concurrent non-enhancing lesions in the left medial temporal lobe and superior cerebellum. Increased size and the development of contrast enhancement in the temporal lesion promoted a left temporal craniotomy. Pathology revealing a grade II ganglioglioma. Three months later, the cerebellar lesion also acquired new contrast enhancement and was found to be a grade II astrocytoma following a supracerebellar infratentorial approach for resection. At 2 years follow-up, the patient remains clinically stable, receiving adjuvant chemotherapy for new non-enhancing, unresectable pontine lesion.**

CONCLUSION: **Tumor growth rate, detailed pathologic findings, imaging characteristics, and molecular signatures influence the clinical course of multicentric low-grade gliomas. *PDGFRA* amplifications and *IDH1* wild-type status may act in a concerted fashion to produce an accelerated course of radiologic changes and tumor recurrence, as noted in our case. Additional research is needed to stratify the risk of transformation in patients with multicentric low-grade glioma and to guide management strategies.**

INTRODUCTION

Low-grade gliomas (LGG), defined as World Health Organization (WHO) grade I–II, account for 15% of all primary brain tumors diagnosed in adults annually and 35% of pediatric brain tumors (3, 25). Among adults, the most frequent LGGs are astrocytomas, oligodendrogliomas, oligoastrocytomas, and ependymomas (11). Co-occurrence of 2 distinct low- or high-grade gliomas in the same patient has been reported in 2%–9% of cases (28), or less than 1% of all brain tumors.

Concurrent brain tumors in different locations can be classified as multifocal or multicentric. Multifocal tumors are presumed to share a common origin, with subsequent spread through commissural pathways, cerebrospinal fluid, blood, or local metastasis. Multicentric tumors are widely separated, often in different lobes or hemispheres, with distinct causes not directly attributable to the above pathways (15). Reports of pure multicentric LGGs are sparse in the literature (28). We report an unusual case of an adult with concurrent ganglioglioma and diffuse astrocytoma in discrete locations, associated with rapid evolution on imaging.

CASE

A 49-year-old man presented with escalating left-sided headaches over 3 months. Examination revealed no focal neurologic deficits, with fluent speech and preserved motor function. Magnetic resonance imaging (MRI) revealed concurrent T1-hypointense,

Key words
- Astrocytoma
- Ganglioglioma
- Low-grade glioma
- Multicentric glioma
- Platelet-derived growth factor receptor amplification
- Tumor progression

Abbreviations and Acronyms
IDH1: Isocitrate dehydrogenase 1
LGG: Low-grade glioma
MRI: Magnetic resonance imaging
PDGFRA/B: Platelet-derived growth factor receptor, alpha-type/beta-type
RT: Radiation therapy
WHO: World Health Organization

From the Departments of [1]Neurosurgery and [2]Pathology, Brigham and Women's Hospital, Harvard Medical School; [3]Department of Cancer Biology and [4]Center for Neuro-Oncology, Dana-Farber Cancer Institute, Harvard Medical School, Boston, Massachusetts, USA

To whom correspondence should be addressed: Ian F. Dunn, M.D. [E-mail: idunn@partners.org]

Citation: World Neurosurg. (2015) 84, 4:1045-1050.
http://dx.doi.org/10.1016/j.wneu.2015.05.021

Journal homepage: www.WORLDNEUROSURGERY.org

Available online: www.sciencedirect.com

T2-hyperintense, non-enhancing lesions in the left medial temporal region and superior cerebellum (Figure 1). The left temporal lesion was noted to increase in size over 3 months with the development of scant contrast enhancement, coincident with increased headaches in the patient, prompting a left frontotemporal craniotomy. A gross total resection was achieved through a trans-sylvian approach. Pathology was consistent with a WHO grade II ganglioglioma, with an increased MIB-1 proliferative index of 19.1% (Figure 2A–E). Immunohistochemistry stains were positive for glial fibrillary acidic protein, oligodendrocyte transcription factor, NeuN (scattered) and synaptophysin, but negative for isocitrate dehydrogenase 1 (IDH1) mutation. Exome sequencing (OncoMap) revealed no additional mutations.

Follow-up MRI 3 months later demonstrated stable post-operative changes in the left temporal resection cavity but new homogeneous enhancement of the superior cerebellar lesion. Because of concern for malignant transformation, a supra-cerebellar infratentorial approach was pursued and a gross total resection of this lesion was achieved. Final pathology revealed a WHO grade II astrocytoma (Figure 2F–J). The lesion had an MIB-1 proliferative index of 1.8%, prominent gemistocytic

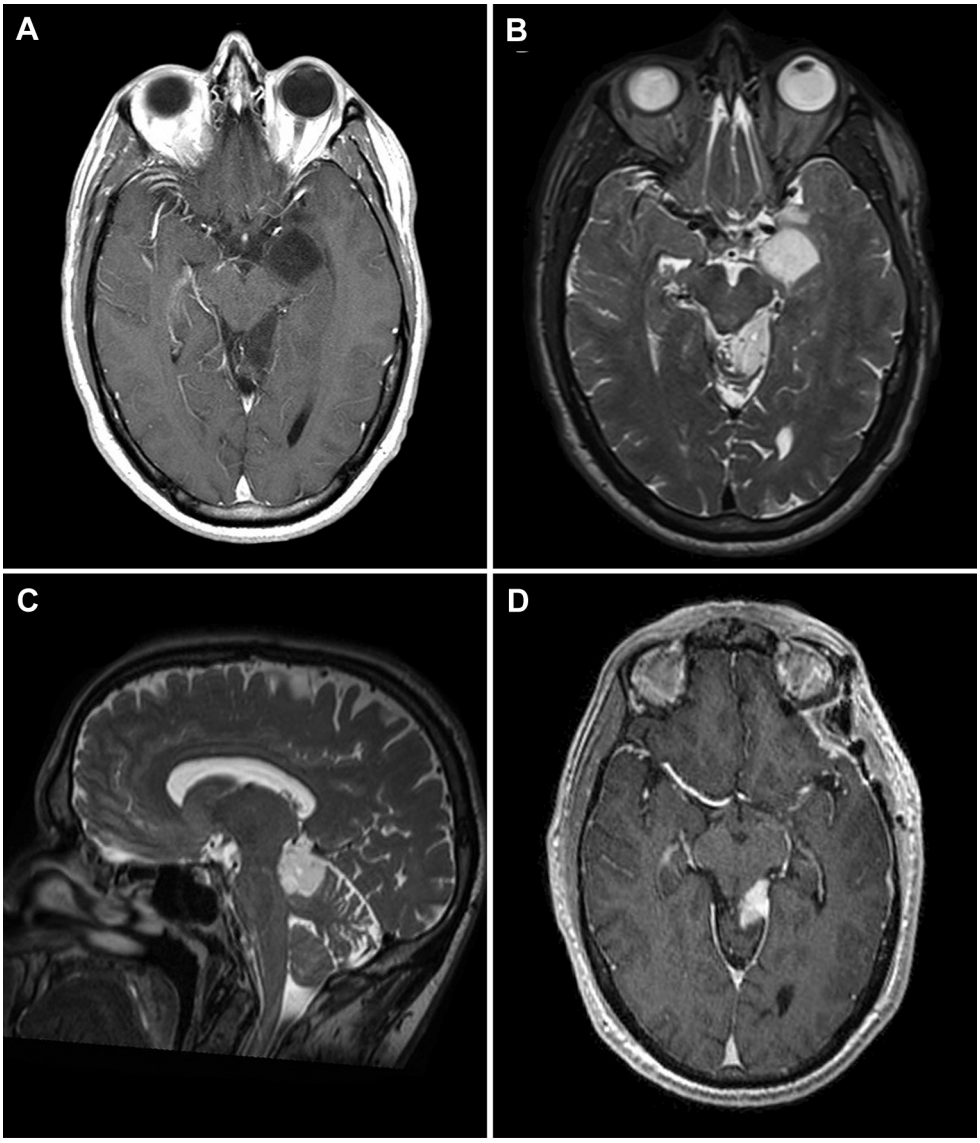

Figure 1. Magnetic resonance imaging on presentation revealed concurrent (**A**) non-enhancing T1-hypointense and (**B**) T2-hyperintense left medial temporal and superior cerebellar lesions in axial view. After gross total resection of the left medial temporal lesion, the superior cerebellar lesion (**C**) grew in size on a sagittal T2-weighted sequence and (**D**) developed avid gadolinium enhancement after 2 months of observation, prompting a second surgery. (continues)