



Multicentric Leptomeningeal Glioblastoma Mimicking Meningioma: A Case Report and Systematic Review

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Abstract

Background Extra-axial glioblastoma is rare. We report the first case of multicentric extra-axial sellar glioblastoma mimicking a meningioma and systematic review on its pathogenesis following the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) guidelines. The case report follows the CAsE REport guidelines. With this review a series of cases, including our case, is presented.

Methods Case presentation: A 73-year-old gentleman had an extra-axial lesion in the sellar region and a left clinoid mimicking a meningioma. Dense dural and vessel adhesions restricted resection to subtotal decompression. Histopathology was isocitrate dehydrogenase (IDH) wild-type glioblastoma.

Systematics Review We searched databases as per the PRISMA guidelines for articles on extra-axial glioblastoma, leptomeningeal glioblastoma, and cases where glioblastoma mimic meningioma. We analyzed demographics, clinical presentation, surgical challenges, histopathology, and immunohistochemistry.

Results We identified 793 articles, of which 9 articles, 12 patients (including our case), matched our inclusion criteria. Most of the patients were elderly with a mean age of 56.9 years (range; 33–74 years); male:female of 8:4. The majority had headaches without raised intracranial pressure. The most common mimicking pathology was meningioma. Adhesions to brain, major vessels, and pial invasion made complete excision impossible in most patients. IDH wild-type tumors had middle meningeal artery blush in angiogram.

Conclusion Extra-axial/primary-intracranial-leptomeningeal-glioblastoma is a tumor subtype with specific clinical/radiological features, extent of resection, and outcomes. As glioblastoma prognosis differs significantly from meningioma, extra-axial glioblastoma's identification is essential for decision-making and prognostication. There is an early trend suggesting that primary leptomeningeal glioma prognosis may not be worse than classic glioblastoma. This case adds to knowledge on pathogenic mechanisms and variable representation of glioblastoma.

Keywords

- ▶ glioblastoma
- ▶ primary intracranial leptomeningeal glioblastoma
- ▶ sellar glioblastoma
- ▶ meningioma
- ▶ multicentric glioblastoma
- ▶ case report

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Key Message

Extra-axial/primary-intracranial-leptomeningeal-glioblastoma is a tumor subtype with specific clinical/radiological features, extent of resection, and outcomes. As glioblastoma prognosis differs significantly from meningioma, extra-axial glioblastoma's identification is essential for decision-making and prognostication. Complete resection is not often possible due to dense adhesions.

Introduction

Glioblastoma is reported in all possible locations, with reports at leptomeninges, cranial nerves (CNs), and internal auditory canal.¹⁻⁴ Glioblastoma is rare in the sellar, parasellar region, dorsum sellae, clinoid, and sphenoid wing. Sellar glioma is usually astrocytoma, optic pathway hypothalamic glioma, chordoid glioma, and low-grade astrocytoma. Deng et al⁵ reported only one patient with glioblastoma in a study of 27 sellar gliomas. Description of extra-axial lesions such as meningioma mimicking astrocytoma in the sphenoid wing exists.^{6,7} However, we could not find any description in the literature that reports glioma mimicking extra-axial lesion in these regions.

This article presents first report of such an occurrence and a systematic review of leptomeningeal glioblastoma that mimic an extra-axial lesion. We created a case series of extra-axial primary leptomeningeal glioblastoma with this review to present the results and novel findings. We aimed to find an answer to the question: Are extra-axial/primary-leptomeningeal-glioblastoma a different entity for clinical/radiographical features, extent of resection, pathogenesis, and outcomes?

Materials and Methods

Case Report

The case report followed the consensus-based clinical care reporting (CAsE REport) guidelines.⁸

Search Strategy and Selection Criteria

We searched PubMed, Web of Science Core Collection, ScieLo science index, Google Scholar, and Scopus databases till July 2021 to identify citations for intracranial glioblastoma mimicking as meningioma. The Preferred Reporting Items for Systematic Review and Meta-Analyses Protocols⁹ guidelines were used in this systematic review. Our search strategy used Boolean operators for keywords and Medical Subject Headings (MeSH) terms. Keywords used were: Leptomeningeal glioblastoma, extra-axial glioblastoma, glioblastoma, and meningioma. Example of search strategy used for PubMed was: (“glioblastoma”[MeSH Terms] OR “glioblastoma”[All Fields]) AND mimicking[All Fields] AND (“meningioma”[MeSH Terms] OR “meningioma”[All Fields]) OR (Extraaxial AND (glioblastoma OR glioma OR “malignant neoplasm”[tw])) OR “Leptomeningeal glioblastoma”. Two reviewers (R.M. and A.A. G.) independently searched the database and performed screening process independently. Mutual consensus resolved

any difference in opinion. Screening was based on the title and abstract and full text of the potentially eligible articles was retrieved. Additional citations were identified through the references of included articles and institutional repository.

Inclusion Criteria

Human studies reporting leptomeningeal glioblastoma, extra-axial glioblastoma, or glioblastoma mimicking meningioma were included. There was no restriction on the time of publication. Only English language articles were included. Eligible studies were case reports, case series, prospective or retrospective studies, and experimental or observational study design. Case reports were included because we believed that literature would be limited due to rarity of the entity.

Exclusion Criteria

Studies reporting meningioma mimicking glioblastoma and collision tumors were excluded. Nonhuman studies, reviews, and systematic reviews or meta-analysis were excluded. Also, publications in language other than English were excluded.

Data Extraction

Study identity, country, publication year, study design, and demography were collected to represent the studies' general characteristics. Clinical details of presentation, headache, sensorimotor neurological deficits, papilledema, pupils, ocular movements, tumor location, and whether the lesion was solitary or multicentric were collected. In addition, radiological details, surgical details, tumor characteristics, extent of resection, histopathology, immunohistochemistry (IHC), adjuvant therapy, and follow-up were extracted from the included studies.

Quality Scoring and Statistical Analysis

Only case reports matched our inclusion criteria. Methodological quality of the included studies was assessed using the tool proposed by Murad et al.¹⁰ As there were limited studies with many studies not reporting all the parameters, mean statistics was used to represent categorical variables.

Results of Systematic Review

Using the search strategy, we identified 793 citations, and 766 were left after removing duplicates. Only nine articles (11 patients)^{4,11-18} matched our inclusion criteria. All were case reports. The study search and selection process is as shown in ► **Fig. 1**. Four articles were from Japan, two from the United States, and one each from Greece, China, and India. General characteristics of included studies for 12 patients (including ours) are as shown in ► **Table 1**. Mean age of the patients (including ours) was 56.9 years (range: 33-74 years) with male:female of 8:4. Six patients had headache, two had motor deficits, and two had CN deficits. The lesion was in the temporal lobe ($n=5$), frontal ($n=3$), parietal ($n=2$), cerebellopontine angle ($n=1$), with our case in the clinoid and parasellar region. All were solitary except ours, which was multicentric. Laterality was right in six, left in three,

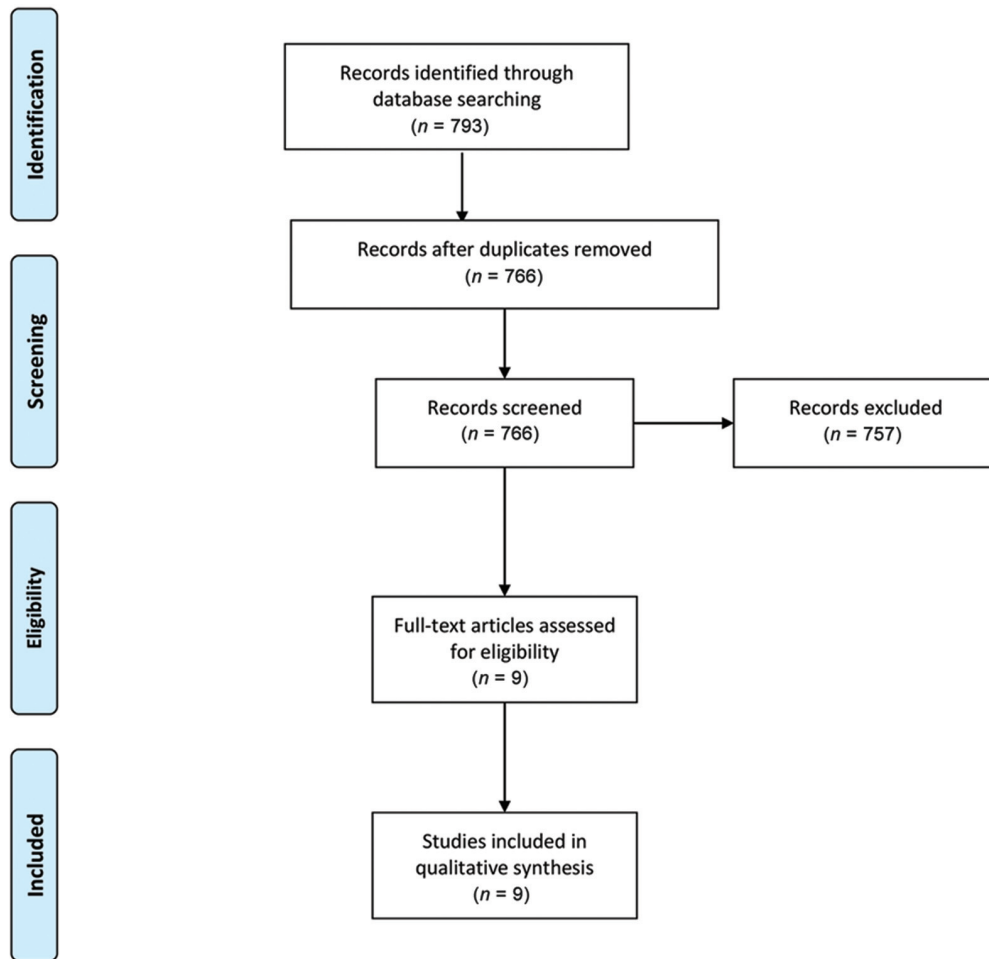


Fig. 1 Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) flowchart showing study search, screening, and selection process.

bilateral in two, and not reported in one patient. Two patients had extension to the neighboring brain regions. In all cases, the tumor was T1 hypo/iso and hyper on T2-weighted magnetic resonance imaging (MRI) sequences with heterogeneous contrast enhancement (►Table 2). In cases where angiogram was performed, blush from middle meningeal artery (MMA) was noticed. In most of the cases, the tumor mimicked meningioma (►Table 3). Due to adhesions to the brain surface, major intracranial vessels, and pial invasion, complete excision was not possible in most of the patients. Three patients had good outcomes reported at last follow-up, seven died at last follow-up, and no follow-up was available in two patients. Isocitrate dehydrogenase (IDH) was reported for four and all were IDH wild-type. Follow-up duration was 2 to 52 months (►Table 4). All the studies were of moderate quality as per the tool devised by Murad et al¹⁰ except three studies,^{13,14,18} which were of high quality.

Our Case Presentation

History and Examination

A 73-year-old gentleman with dull frontotemporal headache for 4 months and drooping of the right eyelid for 2 months

was evaluated. There was no history of fever, loss of consciousness, memory disturbances, deviation of angle of mouth, or limb weakness. On examination, the patient was moderately built and nourished. There were no neurocutaneous markers, and he was conscious, alert, and oriented. His visual acuity was 6/12 in the right eye and 6/9 in the left eye. The right pupil size was 5 mm, and it was nonreactive to light; the left pupil was 3 mm and reactive to light. Right side third nerve motor weakness was present in the form of incomplete ptosis. There were no sensory or motor limb deficits.

Laboratory Examination at Admission was within Normal Limits

Neuroimaging

Computed tomography (CT) brain plain showed a mass lesion in the dorsum sella with extension to the medial temporal region and homogenous contrast enhancement without any cystic change or calcification. There was no focal or perilesional edema. MRI brain plain and contrast showed a right sellar/suprasellar lesion, T1 hypointense and T2 hyperintense near the dorsum sella extending to the medial temporal region, and cerebral peduncle of size

Table 1 Characteristics of studies, demographics, and clinical presentation of patients

Serial no.	Study ID	Year	Country	Title	Study design	Age (y)	Gender	Presentation	Headache	Loss of vision	Visual fields loss	Duration of symptoms	Comorbidities	History
1.	Kakita et al ¹²	1992	Japan	Primary leptomeningeal glioma: ultrastructural and laminin immunohistochemical studies	Case report	74	Female	Hemiplegia	No	No	No	Two months	Nil	Nil
2.	Wakabayashi et al ¹⁷	2002	Japan	Primary intracranial solitary leptomeningeal glioma: a report of 3 cases	Case report	72	Female	N/A	N/A	N/A	N/A	N/A	N/A	N/A
3.	Wakabayashi et al ¹⁷	2002	Japan	Primary intracranial solitary leptomeningeal glioma: a report of 3 cases	Case report	33	Male	N/A	N/A	N/A	N/A	N/A	N/A	N/A
4.	Stavrinou et al ¹⁶	2010	Greece	Primary extracerebral meningeal glioblastoma: clinical and pathological analysis	Case report	53	Male	Headache	Yes	N/A	N/A	One month	Nil	Nil
5.	Wu et al ⁴	2011	China	Primary glioblastoma of the cerebellum: report of 2 cases	Case report	60	Male	Hearing loss and facial palsy	No	No	Normal	Two months	Nil	Nil
6.	Patel et al ¹⁵	2016	USA	Glioblastoma mimicking meningioma: report of 2 cases	Case report	57	Female	Headache, ataxia, and memory loss	Yes	N/A	N/A	One month	Nil	N/A
7.	Yamamoto et al ¹⁸	2017	Japan	Glioblastoma fed by middle meningeal artery and displaying cyst formation soon after repeated implantation of carmustine wafers: a case report	Case report	66	Male	Headache and seizures	Yes	Nil	Nil	One week	Nil	Nil
8.	Katsuhara et al ¹³	2018	Japan	Solitary primary intracranial leptomeningeal glioblastoma invading the normal cortex: case report	Case report	55	Female	Headache and nausea	Yes	Nil	Nil	Few weeks	Nil	Thymoma removal at 40
9.	Doddamani et al ¹¹	2018	India	Ambiguity in the dural tail sign on MRI	Case report	17	Male	Headache, vomiting, vision loss, and altered sensorium	Yes	Yes	Nil	N/A	Nil	Nil
10.	Michaelson and Connerney ¹⁴	2020	USA	Glioblastoma multiforme that unusually present with radiographic dural tails: questioning the diagnostic paradigm with a rare case report	Case report	63	Male	Falls and seizures	N/A	N/A	N/A	Two weeks	Diabetes, hyperlipidemia, and peripheral vascular disease	Developmental delay
11.	Michaelson and Connerney ¹⁴	2020	USA	Glioblastoma multiforme that unusually present with radiographic dural tails: questioning the diagnostic paradigm with a rare case report	Case report	60	Male	Right hemiparesis	No	N/A	N/A	N/A	Nil	N/A
12. Present	Present case	—	India	Multicentric leptomeningeal glioblastoma mimicking meningioma: a case report and literature review	Case report	73	Male	Headache and drooping of right eyelid	Yes	No	No	Two months	Nil	Nil

Abbreviations: MRI, magnetic resonance imaging; N/A, not available.

Table 2 Neurological findings in the patients

Serial no.	Study ID	Papilledema	Pupils	Ocular movements	Sensory-motor neurological deficits	Visual fields on examination	Location of tumor	Multiple or solitary	Laterality	Extension
1.	Kakita et al ¹² 1992	N/A	Normal	Normal	Right hemiplegia	N/A	Parietal	Solitary	Left	Nil
2.	Wakabayashi et al ¹⁷ 2002	N/A	N/A	N/A	N/A	N/A	Frontal	Solitary	Bilateral	Nil
3.	Wakabayashi et al ¹⁷ 2002	N/A	N/A	N/A	N/A	N/A	Temporal	Solitary	N/A	Nil
4.	Stavrinou et al ¹⁶ 2010	Yes	Normal	Normal	Left weakness	Normal	Temporoparietal	Solitary	Right	Nil
5.	Wu et al ⁴ 2011	N/A	Normal	Unable to close the left eye	Normal	Normal	CP angle	Solitary	Left	Nil
6.	Patel et al ¹⁵ 2016	N/A	Normal	N/A	N/A	N/A	Temporoparietal	Solitary	Right	Nil
7.	Yamamoto et al ¹⁸ 2017	No	Normal	Normal	Normal	Normal	Temporal	Solitary	Right	Nil
8.	Katsuhara et al ¹³ 2018	No	Normal	Normal	Normal	Normal	Temporal	Solitary	Right	Frontal skull base
9.	Doddamani et al ¹¹ 2018	Yes	Normal	Normal	Right hemiparesis	Normal	Parietal	Solitary	Right	Nil
10.	Michaelson and Connerney ¹⁴ 2020	No	Normal	Normal	Left hand 4/5	N/A	Frontal	Solitary	Right	Nil
11.	Michaelson and Connerney ¹⁴ 2020	N/A	Normal	N/A	Right hemiparesis	N/A	Parasagittal frontal	Solitary	Left	Nil
12.	Present study	No	Right 5 mm, not reacting; left 3 mm reacting to light	Normal	Normal	Normal	Right sellar-parasellar, left clinoid	Multiple	Bilateral	Right parasellar

Abbreviations: CP, cerebellopontine; N/A, not available.

Table 3 Radiological characteristics of the patients

Serial no.	Study ID	Radiological evidence of intra-axial involvement	CT brain plain	Contrast-enhanced CT	T1-weighted	T2-weighted	T1-contrast	Angiography	Radiological diagnosis
1.	Kakita et al ¹² 1992	No	N/A	Homogenous enhancement	N/A	N/A	N/A	N/A	N/A
2.	Wakabayashi et al ¹⁷ 2002	N/A	Mass, calcification	Heterogeneous enhancement	Hypo/Iso	Hyper	Heterogeneous enhancement	Middle meningeal artery blush	N/A
3.	Wakabayashi et al ¹⁷ 2002	N/A	Mass, cyst, calcification	N/A	Hypo/Iso	N/A	Heterogeneous enhancement	Middle meningeal artery blush	N/A
4.	Stavrinou et al ¹⁶ 2010	No	N/A	N/A	N/A	N/A	N/A	N/A	Meningioma
5.	Wu et al ⁴ 2011	No	Mass	Heterogeneous enhancement	Iso	Hyper/Iso	Heterogeneous enhancement	N/A	Petroclival meningioma
6.	Patel et al ¹⁵ 2016	No	N/A	N/A	N/A	N/A	Heterogeneous enhancement	Middle meningeal artery blush	Meningioma
7.	Yamamuro et al ¹⁸ 2017	No	N/A	N/A	Hypo	Hyper	Heterogeneous enhancement	Middle meningeal artery blush	Meningioma
8.	Katsuhara et al ¹³ 2018	No	Mass, edema	N/A	Low	Iso	Heterogeneous enhancement	Middle cerebral artery involved, ICA angiogram normal, ECA showed blush from the middle meningeal artery	Hemangiopericytoma/ Meningioma
9.	Doddamani et al ¹¹ 2018	No	Mass, edema	Heterogeneous enhancement	Hypo/Iso	Hyper/Iso	Heterogeneous enhancement	N/A	N/A
10.	Michaelson and Connerney ¹⁴ 2020	No	Mass, edema	Heterogeneous enhancement	N/A	N/A	Heterogeneous enhancement	N/A	Meningioma
11.	Michaelson and Connerney ¹⁴ 2020	No	N/A	N/A	N/A	N/A	Heterogeneous enhancement	Middle meningeal artery blush	Meningioma
12.	Present study	No	Mass	Homogenous enhancement	Iso/Hypo	Iso/Hyper	Homogenous enhancement	No blush	Meningioma

Abbreviations: CT, computed tomography; ECA, external carotid artery; ICA, internal carotid artery; N/A, not available.

Table 4 Surgery, histopathology, and outcome of patients

Serial no.	Study ID	Operative finding on the demarcation between tumor and brain	Dural adhesion	Vascularity	Extent of resection	Pathological diagnosis	IHC diagnosis	Postoperative radiotherapy	Condition at discharge	Follow-up after discharge	Last follow-up period	Condition, at last, follow-up
1.	Kakita et al ¹² 1992	Surgery not performed, autopsy showed clear demarcation between tumor and brain with a fibrous capsule in between	N/A	N/A	N/A	Glioblastoma	N/A	N/A	Died in hospital	–	–	Died
2.	Wakabayashi et al ¹⁷ 2002	N/A	N/A	N/A	N/A	Glioblastoma	N/A	Yes	No fresh neurological deficits	18 months	18 months	Died
3.	Wakabayashi et al ¹⁷ 2002	N/A	N/A	N/A	N/A	Glioblastoma	N/A	Yes	No fresh neurological deficits	39 months, femur metastasis	51 months	Good
4.	Stavrinou et al ¹⁶ 2010	Clear demarcation between tumor and brain	Present	Moderately	Complete	Glioblastoma	N/A	Yes	No fresh neurological deficits	42 months, recurrence, resurgery	42 months	Good
5.	Wu et al ⁴ 2011	Clear demarcation between tumor and brain	Present	Moderately	Subtotal	Glioblastoma	N/A	No	No fresh neurological deficits	Two months	2 months	Died
6.	Patel et al ¹⁵ 2016	N/A	N/A	Moderately	N/A	Glioblastoma	N/A	Yes	N/A	N/A	N/A	N/A
7.	Yamamuro et al ¹⁸ 2017	Clear demarcation between tumor and brain	Present	Highly vascular	Complete	Glioblastoma	IDH wild and EGFR negative	Yes	No fresh neurological deficits	Six months, recurrence, resurgery	11 months	Died
8.	Katsuhara et al ¹³ 2018	No clear border between the adjacent tumor and brain parenchyma	Present	Highly vascular	Temporal lobectomy was done for complete resection	Glioblastoma	IDH wild GBM Cd-IV originating from the heterotopic glial cluster in the vicinity of Sylvian cistern	Yes	No fresh neurological deficits	Six months, presented with motor weakness, recurrence, and spinal dissemination	10 months	Died
9.	Doddamani et al ¹¹ 2018	No clear border between the adjacent tumor and brain parenchyma	Present	Highly vascular	Complete	Glioblastoma	N/A	Yes	No fresh neurological deficits	N/A	N/A	N/A
10.	Michaelson and Connerney ¹⁴ 2020	No clear border between the adjacent tumor and brain parenchyma	Present	Highly vascular	N/A	Glioblastoma	IDH wild, EGFR amplification, CDKN2A loss, loss of chromosome 10, positive MGMT methylation	Yes	No fresh neurological deficits	30 months	30 months	Good
11.	Michaelson and Connerney ¹⁴ 2020	N/A	N/A	Moderately	N/A	Glioblastoma	N/A	Yes	N/A	N/A	6 months	Died
12.	Present study	No clear border between the adjacent tumor and brain parenchyma	Present	Highly vascular	Subtotal	Glioblastoma	Negative for IDH1(R132H), P53, H3K27M, EMA	Yes	No fresh neurological deficits	Advised for RT and CT	3 months	Died

Abbreviations: CT, computed tomography; EGFR, estimated glomerular filtration rate; EMA, epithelial membrane antigen; GBM, glioblastoma; Gd, gadolinium; IDH, isocitrate dehydrogenase; IHC, immunohistochemistry; IV, intravenous; MGMT, O6-methylguanine-DNA methyltransferase; N/A, not available; RT, radiotherapy.

2.2 × 1.2 × 1.1 cm with homogenous contrast enhancement with no radiological evidence of intra-axial involvement (→ Fig. 2). MR angiogram showed no vessel encasement and no blush from the MMA (→ Fig. 3). A mirror lesion of the same characteristics was found in the left clinoid region of smaller size. The radiological diagnosis was right sellar meningioma with a small lesion in the left clinoid region.

Surgery

The patient underwent right frontotemporal craniotomy, Transylvanian approach and partial decompression of right and left meningioma. The lesion was adherent to the dura, soft to firm in consistency, vascular, suckable, and pinkish fleshy. The lesion was carpeting the internal carotid artery (ICA) vessels with dense attachment. There was no clear plane of demarcation between the lesion and the brain. Due to dense adhesion with the ICA and poor plane of demarcation with a normal brain, partial decompression of the lesion was done. In the same surgical approach, a lesion of the other side was also decompressed. The patient recovered from anesthesia satisfactorily. He had transient delirium on postoperative days 2 to 3, which was managed medically. The rest of the postoperative course was uneventful. At discharge, he was afebrile, conscious, and obeying, with right CN III palsy.

Histopathology and Immunohistochemistry

Histopathological examination of the surgical tissue showed features of a high-grade glioma with fibrillary, gemistocytic, and plump epithelioid cells arranged in the glial fibrillary matrix. Tumor cells showed marked anisonucleosis and frequent mitosis. Microvascular proliferation was prominent. IHC revealed that tumor cells were immunopositive for glial fibrillary acidic protein and vimentin confirming the glial nature of the tumor. The tumor cells were negative for IDH1R132H and had retained expression of ATRX. Tumor cells were negative for P53, H3K27M (for diffuse midline glioma), epithelial membrane antigen (EMA; for ependymoma), and cytokeratin. MIB-1 labeling was 10 to 12%. Hence, the final diagnosis of glioblastoma IDH wild-type was provided. The lesion from the other hemisphere showed similar findings (→ Fig. 4).

Follow-Up

Patient started radiotherapy and chemotherapy, however, expired 3 months later.

Discussion

Reports of glioblastoma as collision tumor with meningioma and extracerebral lesion reflect the mesenchymal location of the malignant glioma cells. Further, there is possibility of multifocal glioblastoma occurring in the pediatric age group with fulminant course and other reports of unusual glioblastoma making glioblastoma an enigmatic entity.^{19,20} We present a case where multicentric glioblastoma in the sellar region looked radiographically as meningioma. To the best of our knowledge, this is the first reported case of

multicentric glioblastoma presenting as meningioma. To the best of our knowledge, 11 cases of glioblastoma as primary extra-axial lesion have been reported in the literature so far.

Sellar Glioblastoma

Sellar gliomas pertain to the pediatric age group as pilocytic astrocytoma or optic pathway hypothalamic glioma, with glioblastoma being rare. Sellar glioma is less likely to cause visual disturbances, growth hormone deficiency, cystic changes, and calcification, instead has primary effects on mental functions and brainstem involvement.⁵ Our patient had a tumor in the sellar and parasellar region and presented with third CN palsy without any visual field deficits. In our study, the first-time presentation of the lesion suggests the de novo formation of glioblastoma. We did not find any description in the literature where sellar glioblastoma has presented as primarily extra-axial tumor mimicking meningioma. Along with the suprasellar and pineal regions, the sella turcica is a special place that can produce uncommon pathological diagnoses. There have been several reports where the lesions in the sella turcica are challenging to diagnose and masquerades the appearance of commonly occurring pituitary adenoma including meningioma and schwannoma.²¹

Primary Intracranial Leptomeningeal Glioblastoma

Bailey first described primary leptomeningeal glioma (PLG) in 1936 as glioma in subdural or extramedullary locations with no connection between the tumor and brain parenchyma.^{22,23} The earliest record of glioblastoma as extracerebral neoplasm was in 1963 and were solitary intracranial extra-axial tumors.²⁴ Nonavailability of advanced neuroimaging would have limited the accurate preoperative diagnosis of these lesions, as intra-axial or extra-axial. Also, there was no dural invasion or invasion of the bone, and the tumors did not mimic meningioma. In our case, the patient had a lesion in the region of dorsum sella bilaterally and appeared extra-axial on preoperative imaging. Though metastasis is not commonly encountered with glioblastoma, still there could be cranial and spinal meningeal metastasis seen with the glioblastoma when the patient's complaints are not explained by the primary lesion.²⁵ However, the meningeal metastasis is different from the primary leptomeningeal glioblastoma in pathology, natural history, course, and outcome.

Pathogenesis of PLG

PLG develop due to the malignant transformation of leptomeningeal neuroglial cells.²⁶ This ectopic neuroglial tissue is seen in 1% of normal individuals and is usually associated with aberrant migration of neuroepithelial derivatives, and transformation could result in malignant glioma.²⁷ Malignant transformation presents as diffuse disease or leptomeningeal carcinomatosis.¹³ Intracranial and intraspinal gliomas arising within the leptomeninges are mostly diffuse astrocytoma (resulting in a clinical picture of gliomatosis cerebri), ependymoma, or oligodendroglioma with glioblastoma being rare.²⁶ PLG is distinct from other

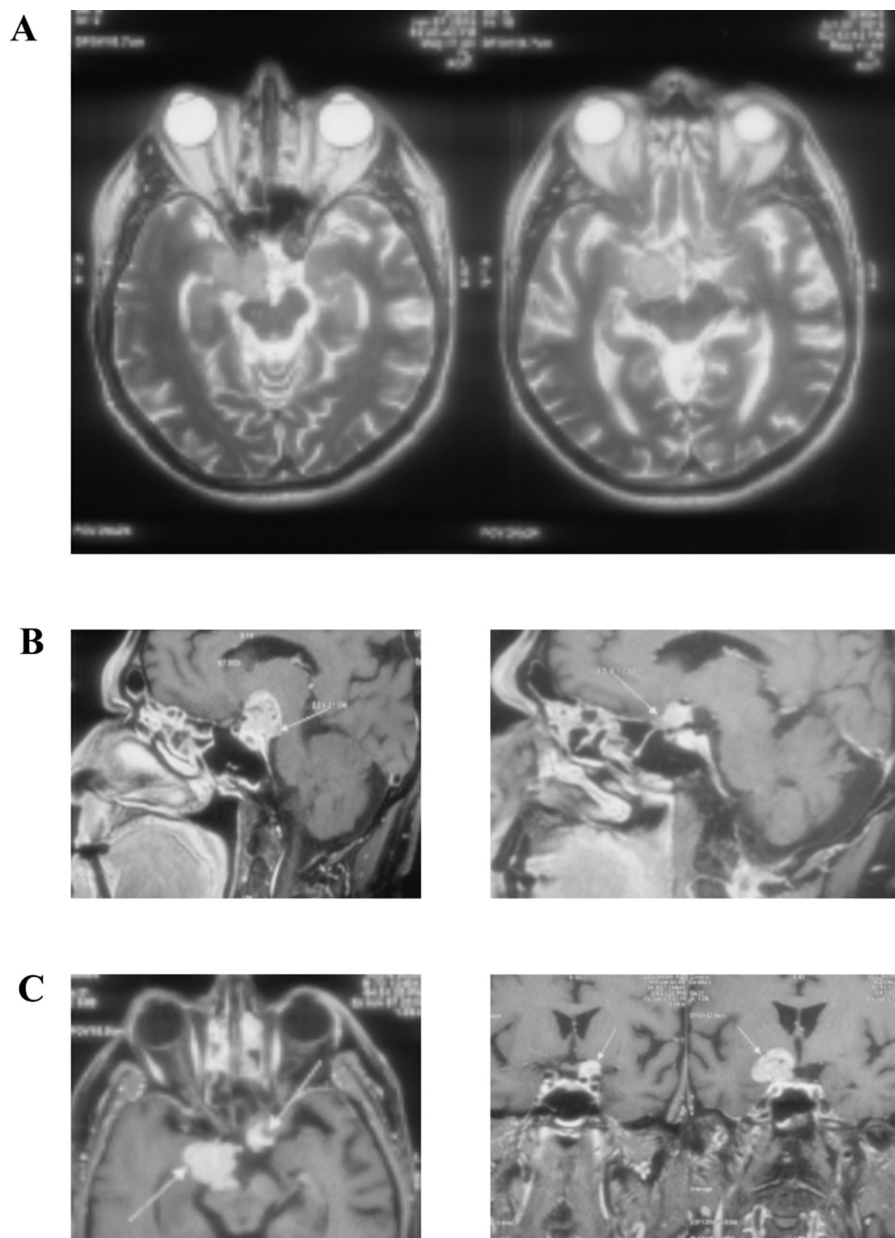


Fig. 2 Magnetic resonance imaging (MRI) brain plain and contrast showed a right sellar/suprasellar lesion, T1 hypointense and T2 hyperintense (A) near the dorsum sella extending to the medial temporal region, and cerebral peduncle of size $2.2 \times 1.2 \times 1.1$ cm with homogenous contrast enhancement (B) with no radiological evidence of intra-axial involvement (C).

intracranial gliomas as the ultrastructural examination of PLG revealed basal lamina and laminin on the surface of astrocytes and around the cytoplasm and cell processes.¹² This suggests that heterotopic astrocytes in PLG can generate basal lamina and mount mesenchymal reaction (unlike parenchymal glioma) similar to the superficial astrocytes and astrocytes found in pleomorphic xanthoastrocytoma and desmoplastic infantile ganglioglioma.¹² Another hypothesis is the development of glioblastoma from the CN.¹¹ Glioblastoma in our patient arose from the neoplastic transformation of neuroglia within the leptomeninges or from the CN. In most of the reported cases of extra-axial glioblastoma, IDH was negative. Our patient was negative for IDH1(R132H), P53, H3K27M, and EMA staining.

Clinical Features of Extra-Axial Glioblastoma

The majority of the patients (including ours) were in the fifth to seventh decade of life except a case reported by Doddamani et al¹¹ (17 years) and Wakabayashi et al¹⁷ (33 years). Most of the cases of extra-axial glioblastoma present with features of headache, nausea, vomiting, seizures, and motor deficits due to compression over the brain (– Tables 1 and 2). In our case, the patient presented with headache in the frontotemporal location suggesting dural stretch headache and third CN palsy due to direct involvement of the third CN in the parasellar region. Most patients have short-lasting symptoms ranging from few weeks to 2 months, and our patient had symptoms for 4 months.

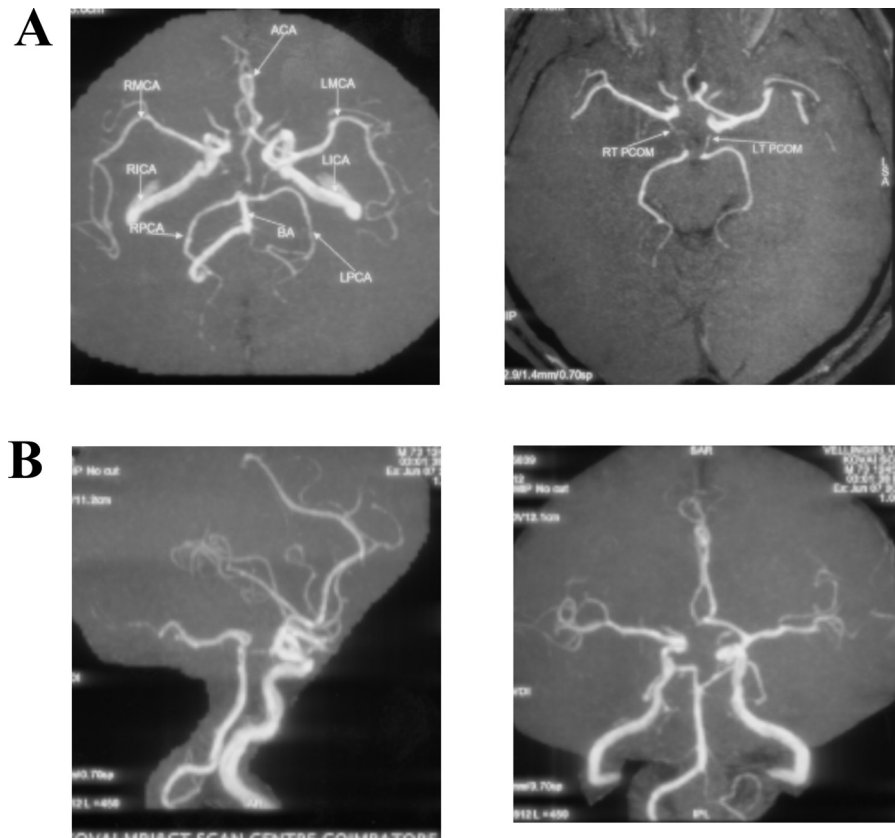


Fig. 3 Magnetic resonance (MR) angiogram showed no vessel encasement and no blush from the middle meningeal artery.

Radiological Features of Extra-Axial Glioblastoma

CT and MRI pattern of leptomeningeal extra-axial glioma depends on the pathological characteristics and malignancy of the tumor.¹³ Most reported cases of extra-axial glioblastoma show visualization of mass on plain CT and enhancement on contrast CT scan. MRI characteristics include T1 isointense and T2 hyperintense, with the homogenous enhancement of T1-gadolinium (Gd) enhanced in most cases (►Table 3).¹³ However, a report exists of ring-like enhancement, central cystic changes, and areas of calcification, and it is suggested that careful and deliberately detailed evaluation of preoperative imaging may reveal the intra-axial component of these neoplasms.¹⁷ Our patient had neuroimaging findings similar to the published reports. The features to differentiate extra-axial lesion like meningioma from intra-axial lesion like glioblastoma are well described. The dural tail sign described in 1989 is a classical feature characteristic of meningioma; however, extra-axial glioblastoma is reported to have a dural tail sign on MRI.^{14,16,28} A high signal intensity at 3.8 ppm on 3T-proton MRI can reliably differentiate between the meningioma (present) and glioblastoma.²⁹

Surgical Findings of Extra-Axial Glioblastoma

Surgical Findings

Three cases^{4,16,18} had clear tumor–brain demarcation and five^{11,13,14} (including our case) did not have clear tumor–brain demarcation. The tumor was vascular and adherent to the dura in where adhesion and vascularity was mentioned. In

our case, we found small vessels into the tumor from the dura when the dura was lifted. Complete excision was obtained in three cases. In three cases, including ours, subtotal excision was done due to dense adhesions and poor tumor–brain interface. Details of surgical findings are shown in ►Table 4.

Prognosis

Glioblastoma portends a poor prognosis, and reports suggest that PLG has a much poorer prognosis with maximum survival of 6 months, even with surgical and adjuvant therapy. In our study, the maximum follow-up period was 51 months (►Table 4). Two patients with follow-up at 42 and 51 months had a good functional outcome. Though other patients died earlier, our review suggests that the prognosis of PLG may not be worse than classical glioblastoma. However, more research with large-scale studies needs to be conducted to accurately understand the outcome and prognosis of extra-axial glioblastoma.

Unique Features in the Present Case

Several novel findings were found in this study as the first case of glioblastoma in the sellar region mimicking an extra-axial lesion with third nerve palsy in the absence of visual field defects. The unique features are glioblastoma at the skull base in a bilaterally symmetrical location presenting in a septuagenarian individual with minimal neurological deficits. In our case, the tumor's extracerebral position, well-defined contour, and invasion of the dura mater were similar to meningioma. In the sellar spectrum of disease and

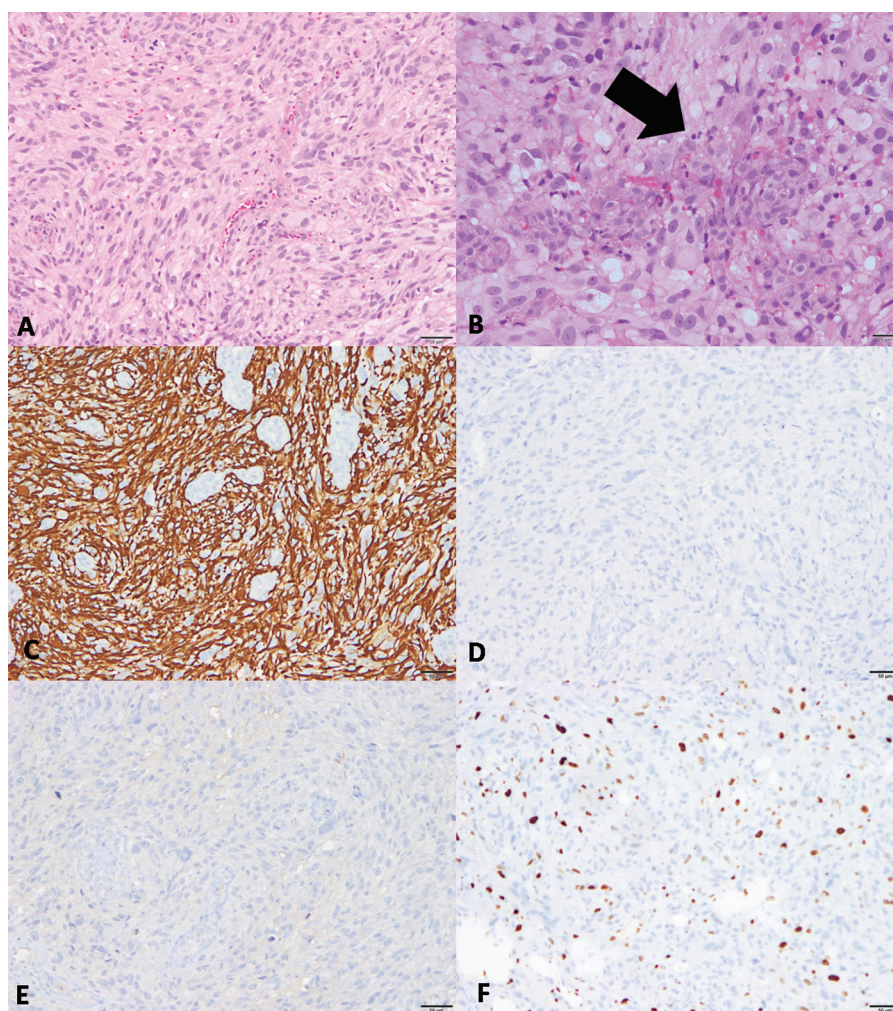


Fig. 4 Photomicrographs show a highly cellular glial neoplasm with increased mitosis (A, hematoxylin and eosin [H&E]) and microvascular proliferation (B, H&E). The cells are diffusely positive for glial fibrillary acidic protein (GFAP) (C) and negative for IDH1R132H (D) and BRAFV600E (E). There is a high proliferation (F, Ki67). Magnification = scale bar.

other extra-axial places that resemble meningiomas, this might be an uncommon differential diagnosis. Operating neurosurgeons should be aware of PLG, and preoperative diagnosis can be aided by MR spectroscopy and MRI characteristics such as T1 isointense, T2 hyperintense, and the homogeneous augmentation of T1-Gd.

Limitations

One of the limitations is the less number of cases. All variables were not reported in all studies. Nonuniform reporting of surgical and radiological findings and outcomes limits the study. IDH and IHC were not reported in all cases. Inadequate follow-up of the reported cases is a significant limitation.

Conclusion

Extra-axial/primary-intracranial-leptomeningeal-glioblastoma is a tumor subtype with specific clinical/radiological features, extent of resection, and outcomes. As glioblastoma prognosis differs significantly from meningioma, extra-axial glioblastoma's identification is essential for decision-making

and prognostication. There is an early trend suggesting that PLG prognosis may not be worse than classic glioblastoma.

Informed Consent

Patient's relatives gave the consent for the inclusion of the patient's details in the manuscript and the consent is available to the corresponding author.

Conflict of Interest

None declared.

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