Spinal glioblastoma metastases

- Intramedullary Glioblastoma as One of Multiple Radiation-Induced Neoplasms
- Glioblastoma mimicking autoimmune meningitis in an adult: A complex diagnostic challenge
- Concordance of Extent of Resection Between Intraoperative Ultrasound and Postoperative MRI in Brain and Spine Tumor Resection
- Molecular profile and clinical outcome of adult primary spinal cord glioblastoma: a systematic review
- Symptomatic spinal metastasis of a supratentorial glioblastoma in a pediatric patient: a case report and comprehensive review of the literature
- Successful treatment of pediatric patients with high-grade gliomas featuring leptomeningeal metastases by targeting BRAF V600E mutations with dabrafenib plus trametinib: two illustrative cases
- Leptomeningeal Dissemination Complicated With Acute Tetraplegia From a Supratentorial Multicentric Isocitrate Dehydrogenase (IDH)-Wildtype Glioblastoma: A Case Report
- Spinal and cervical nodal metastases in a patient with glioblastoma

Epidemiology

Spinal glioblastoma metastases are rare but clinically significant, indicating advanced disease and a shift in tumor biology toward dissemination. Below is an epidemiological summary:

 Incidence & Frequency Overall frequency of extracranial metastases in GBM: <2%

Spinal metastases specifically: 0.9–1.5% of GBM cases

Among those with leptomeningeal spread, ~60–80% have spinal involvement (mostly leptomeningeal, less often intramedullary or epidural)

 Trends Increased detection in recent years due to:

Prolonged survival with standard treatment (Stupp protocol)

Advanced imaging (MRI spine)

More frequent surveillance in long-term survivors

May be underreported due to:

Short survival limiting spread

Low clinical suspicion in late-stage patients

Lack of routine spinal imaging

 Patient Characteristics Age: Most patients > 30 years, median around 40–50 years

Sex: No significant gender predilection

The ability of supratentorial GBM to metastasize along CSF pathways to the spinal cord was first described in 1931 [1].

A review of literature by Erlich et al. in 1978 revealed only 14 well documented cases of spinal subarachnoid seeding [2].

After a stereotactic biopsy with stable intracranial disease, has only been reported in two cases. Traversing the lateral ventricle at the time of biopsy contributed to cerebrospinal fluid seeding with tumor cells and subsequent development of spinal disease [3].

Autopsy series suggest that approximately 25% of patients with intracranial glioblastoma have evidence of spinal subarachnoid seeding, although the exact incidence is not known because postmortem examination of the spine is not routinely performed [4] [5].

The incidence is higher (of up to 60%) for infratentorial GBM [6].

Although the spread of supratentorial glioblastoma multiforme to the brain stem and spine has been extensively described in published autopsy series, information on the diagnosis, treatment, and subsequent clinical course of patients manifesting symptoms of glioblastomatous dissemination ante mortem remains scant.

They may spread along compact fiber pathways such as corpus callosum, optic irradiation, anterior commisure, and fornix or via cerebrospinal fluid (CSF) pathways. However, when GBM is under apparent control, spinal metastases are clinically rarely detected. Although involvement of the spinal cord (SC) has been noted with increasing frequency in recent years, literature provides only a few well documented cases [7].

The number of cases of spinal metastasis from primary intracranial GBM seems to be increasing. This might be due to improved diagnostic tools like CT and MRI, prolonged survival time due to improved therapy, or due to changes in the biological properties of tumors as a result of surgery, radiotherapy, and chemotherapy.

Intramedullary

Intramedullary spinal metastases are still rarer with only six cases reported till 2008 [8].

Metastases from glioblastoma multiforme are rare for a number of reasons: the cerebrum does not have a lymphatic system; the intra-cranial sinuses are enclosed in a dense dural membrane, which makes penetration by tumour cells difficult; intracerebral veins are thin walled and would probably collapse from compression before they could be penetrated by an expanding tumour; and the immunological response of the host organ to neuroglial tumour cells may prevent their growth outside the central nervous system [9].

Glioblastoma metastases in the neuroaxis occur in approximately 20% of Glioblastoma patients, [10] which may relate to overexpression of glial fibrillary acidic protein [11].

Eighteen percent of Glioblastoma grow in transplanted organs, [12] [13]. indicating their metastatic potential.

Classification

By Anatomical Location

- **Leptomeningeal metastases**
  - Most frequent form
  - Dissemination via cerebrospinal fluid (CSF)
  - Involves spinal leptomeninges and nerve roots
- **Intramedullary metastases**
  - Rare (<0.1% of GBMs)
  - Tumor infiltrates the spinal cord parenchyma
  - Often mimics primary spinal cord glioma
- **Epidural metastases / Extradural metastases**
  - Extremely rare
  - Occurs via direct extension or venous spread (Batson's plexus)
  - May compress the thecal sac and spinal cord

By Route of Dissemination

- **CSF seeding (drop metastases)**
  - Most common route
  - Tumor cells migrate from the ventricles to spinal subarachnoid space
- **Hematogenous spread**
  - Very rare
  - Usually involves extradural space or bone
- **Direct invasion**
  - In cases with posterior fossa tumors breaching dura
- **Surgical tract dissemination**
  - Tumor cells seeded during surgery or via shunt systems

By Pathological Characteristics

- **Classic IDH-wildtype GBM**
  - Most common in spinal metastases
  - Often aggressive, therapy-resistant
- **H3K27M-negative midline GBM**

    - May still disseminate through CSF if near aqueduct or fourth ventricle

- **MGMT status** and other markers
    - Not directly predictive of spinal spread but may impact response to therapy

By Clinical Presentation

- **Asymptomatic (incidental findings)**
    - Detected on MRI during follow-up
- **Pain syndromes**
    - Axial spine pain, radicular pain (lumbar or sacral)
- **Myelopathy**
    - Weakness, sensory deficits, bladder/bowel dysfunction
- **Cauda equina syndrome**
    - Seen in lower spinal leptomeningeal disease

Summary

Spinal metastases from GBM are rare but increasingly recognized. Classification by **location**, **route of spread**, **histology**, and **clinical syndrome** facilitates earlier detection, appropriate imaging, and timely palliative or surgical intervention.

Spinal leptomeningeal metastasis (SLM)

see Spinal leptomeningeal metastasis

Treatment Options

see also Glioblastoma treatment.

A. Surgical Resection Indicated in:

Solitary, resectable lesions

Mass effect causing cord compression

Preserved functional status (ECOG 0–2)

Goals: debulking, histologic confirmation, symptom relief

B. Radiotherapy Focal Radiotherapy (IMRT/SBRT):

For localized lesions

Useful post-surgery or in non-surgical candidates

Craniospinal Irradiation:

Rarely used due to toxicity

Considered in selected leptomeningeal spread cases with good performance status

C. Systemic Therapy Temozolomide (TMZ):

Often continued if effective intracranially

Bevacizumab:

For edema and symptom control

Limited data in spinal metastases, but may be considered

Other agents (e.g. lomustine, irinotecan, TTFs):

Limited evidence

Consider in clinical trial settings

D. Tumor Treating Fields (TTF) Not approved for spinal use

Intracranial benefit unclear in disseminated cases

E. Intrathecal Chemotherapy Very limited role

Rarely used due to poor efficacy in solid GBM lesions and risk of toxicity

 3. Investigational Therapies Immunotherapy (checkpoint inhibitors): No proven benefit

Oncolytic viruses / NGS-guided agents: Experimental

Proton therapy: In selected young patients or cases with high-dose constraints

Case series

Fifteen GBM patients with MSD, who were treated and followed up with at the Department of Oncology, Beijing Shijitan Hospital, Capital Medical University from September 2012 to February 2021, were selected for this study. Clinical data, such as demographic characteristics, clinical manifestation, imaging, cerebrospinal fluid (CSF), treatment and prognosis data, were retrospectively analyzed. The time to MSD and overall survival (OS) were estimated using Kaplan-Meier plotting. A univariate analysis was performed using a logarithmic-rank test, and a multivariate analysis was performed using Cox proportional hazards models.

Results: Of the 15 GBM patients with MSD (9 males and 6 females), the primary lesions were located supratentorial region in 12 cases, and subtentorial region in 3 cases. After surgery, the ventricles were open and closed in 7 and 8 cases, respectively. There were 10 cases, 2 cases, 2 cases, and 1 case of MSD in the full spinal cord (FSC), FSC with spinal cord intramedullary infiltration, cervical

spinal cord intramedullary infiltration, and cervical/thoracic MSD, respectively. Whole spinal cord magnetic resonance imaging (MRI) showed dotted-line, nodules, and mixed patterns in 3, 2, and 10 cases, respectively. The average CSF protein level during MSD was 2.49 (range, 0.42-6.68) g/L, and the average CSF d-dimer level was 23,718 (range, 4,056-69,000) ng/L. By the end of the follow-up period, all the patients had died. The median OS of all patients, the median time from surgery to diagnosis of MSD, and the median time after MSD to death was 15.0 (range, 8-52), 10.0 (range, 1-49), and 4.0 (range, 1-14) months, respectively.

Conclusions: MSD is a rare, metastasized type of GBM. The OS after MSD in GBM patients is very short. Whole spinal cord-enhanced MRI may be the best way to determine the range of MSD [14)]

In 11 patients having the signs and symptoms of neuraxis dissemination of supratentorial glioblastoma multiforme. All patients had radiographic documentation of metastases by either contrast-enhanced myelograms or enhanced magnetic resonance imaging scans. Ten presented with spinal involvement, whereas one presented with lower cranial neuropathies secondary to diffuse involvement of the basal cisterns. The mean age of the patients was 38.5 years, and the mean time interval between diagnosis of intracranial disease and diagnosis of metastases was 14.1 months. After diagnosis of tumor spread, subsequent mean survival time was 2.8 months. All patients received additional radiotherapy to the areas of metastasis, but the clinical response to radiotherapy was quite poor. This study confirms previous reports in the literature suggesting that metastases occur in younger patients and in patients with extended survival. The findings suggest that the relatively infrequent clinical incidence of the symptomatic spread of glioblastoma multiforme, as compared with the frequent incidental discovery of such spread at autopsy, may be the result of the limited survival of the affected patients, and not due to the biology of the tumor [15)].

Case reports

A case of a 31-year-old female with glioblastoma who underwent gross total resection followed by standard chemoradiotherapy. For recurrence, she received tumor treating fields and bevacizumab. At 23 months post-surgery, she developed COVID-19 pneumonia treated with dexamethasone, followed by spinal symptoms. MRI revealed L1-L2 lesions, and pathology after lumbar surgery confirmed ECM. Despite further treatment, the patient died of respiratory failure at 28 months. The present case illustrates the aggressive nature of ECM in GBM and the limited efficacy of current therapies in metastatic settings. Surgical resection and chemoradiotherapy remain the mainstay, while emerging treatments may provide hope for recurrent cases. Supportive care plays a critical role in advanced disease stages [16)].

This case report underscores the aggressive and unpredictable behavior of glioblastoma in rare metastatic scenarios. However, it misses critical opportunities for deeper insight, both mechanistically and therapeutically. It reinforces that standard therapies are insufficient in metastatic GBM, but fails to offer innovation or reflection on how such cases can inform future research.

Overall Rating: ★★☆☆☆ (2/5)

Informative but underdeveloped. Appropriate for clinical awareness, but lacks the analytical depth

expected from a high-impact case report.

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