Glioblastoma metastases

- High-frequency irreversible electroporation suppresses invasion and metastasis by targeting SIRT1/2 in highly invasive tumor cells: an in vitro study
- Neuroradiological Evaluation of Anatomo-Morphometric Arcuate Fascicle Modifications According to Different Brain Tumor Histotypes: An Italian Multicentric Study
- Nanotechnology in brain cancer treatment: The role of gold nanoparticles as therapeutic enhancers
- Bioinformatic Analysis of C1GALT1 in Cancer: Insights Into Prognosis, Metastasis and Therapeutic Potential
- Shared decision-making interventions in neuro-oncology practice: a systematic review
- Gyroscopic radiosurgery-based lattice therapy for intracranial tumors: A dosimetric study
- Minimally Invasive and Cost-Effective Access to Deep-Seated Intracranial Lesions Using 19F Peel-Away Sheath Introducer and "Dynamic" Retraction: Technical Note and a Case Series
- Intramedullary Glioblastoma as One of Multiple Radiation-Induced Neoplasms

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Extracranial metastases refer to the spread of GBM beyond the CNS into systemic organs or tissues.

Epidemiology

Reported in < 2% of GBM cases.

True incidence may be underestimated due to:

Short survival times

Lack of systemic imaging or autopsy

Assumption of CNS confinement

Classification

By Anatomical Location

Intracranial

- **Local invasion**: adjacent brain structures, corpus callosum (“butterfly glioma”).
- **Multifocal glioblastoma**: multiple enhancing lesions without clear CSF dissemination.
- **Leptomeningeal dissemination**: involves basal cisterns, sulci, and ventricular lining.
- **Ependymal spread**: along the ventricular surfaces.

Spinal

- **Leptomeningeal spread**: most common form; CSF seeding along the spinal canal.
- **Intramedullary metastasis**: very rare; may mimic a primary spinal cord tumor.
- **Epidural/extradural metastasis**: extremely rare; usually via direct extension or venous plexus (Batson's plexus).

Extraneural (Systemic)

- **Lymph nodes**
- **Lungs and pleura**
- **Bones** (especially vertebrae and pelvis)
- **Liver**
- **Skin and soft tissues**

By Route of Dissemination

- **CSF seeding** – most frequent; explains spinal and leptomeningeal spread.
- **Hematogenous spread** – rare; possible in cases with dural or venous sinus invasion.
- **Surgical tract dissemination** – spread via surgical wounds or shunt systems.
- **Direct invasion** – local extension to dura, skull base, or adjacent tissues.

By Clinical Presentation

- **Asymptomatic** – incidental detection on MRI surveillance.
- **Spinal symptomatic** – back pain, radiculopathy, cauda equina syndrome.
- **Leptomeningeal** – headache, nausea, cranial neuropathies, drop metastases.
- **Systemic** – lymphadenopathy, bone pain, pulmonary symptoms.

Summary

Glioblastoma metastases are rare but clinically significant. They can be classified by:

- **Anatomical location** (intracranial, spinal, systemic)
- **Dissemination route** (CSF, blood, direct, surgical)
- **Molecular subtype**
- **Clinical pattern**

A systematic approach to classification helps improve recognition, diagnosis, and multidisciplinary management.

Common Sites of Metastasis

Lungs

Lymph nodes

Liver

Bones

Less frequent: spleen, skin, adrenal glands

It occur most often in the lungs and pleura (60% of patients) but also in the regional lymph nodes (51%), bones (31%), and liver (22%) [1) 2)].

To date, the cause of the GBM metastatic spread still remains under discussion. It probably develops at the time of intracranial progression following a surgical procedure. According to other hypothesis, the metastases are a consequence of spontaneous tumour transdural extension or haematogenous dissemination [3)].

Spinal glioblastoma metastasis

Spinal glioblastoma metastases.

Case reports

A 45-year-old man presented with history of diplopia and gait disturbance. Magnetic resonance imaging showed a left cerebellar space-occupying lesion. The histopathology was consistent with glioblastoma. The patient underwent adjuvant chemoradiation. A year later, he presented with seizures, worsening headache, neck stiffness, and low back pain. Imaging showed metastasis to the S1/S2 region of the spinal canal. A 29-year-old man presented with episodic headaches associated with nausea, vomiting, neck stiffness, and imbalance while walking. Computed tomography of the brain showed a hypodense lesion involving the left midbrain, pons, and left middle cerebellar peduncle, causing fourth ventricular pressure with obstructive hydrocephalus. A navigation-guided biopsy of the brainstem lesion confirmed the diagnosis of glioblastoma World Health Organization grade IV, isocitrate dehydrogenase 1 (R132 H) and H3K27M negative. Isocitrate dehydrogenase gene sequencing was suggested. The patient was referred for chemoradiation. During treatment, he worsened neurologically and developed axial neck and back pain. Neuraxis screening showed disseminated leptomeningeal spread, which was confirmed on dural biopsy [4)].

A young patient with multiple visceral and osseous metastases occurred after 4 years after first diagnosis of GBM. The strangeness as well as the rarity of this event does not allow to identify an effective treatment for GBM metastases, making the management of this ominous tumor an even greater challenge [5)].

1)
Slowik F, Balogh I (1980) Extracranial spreading of glioblastoma multiforme. Zentralbl Neurochir 41:57–68.

2)
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Grah JJ, Katalinic D, Stern-Padovan R, Paladino J, Santek F, Juretic A, Zarkovic K, Plestina S, Supe M. Leptomeningeal and intramedullary metastases of glioblastoma multiforme in a patient reoperated during adjuvant radiochemotherapy. World J Surg Oncol. 2013 Mar 5;11:55. doi:10.1186/1477-7819-11-55. PubMed PMID: 23496844; PubMed Central PMCID: PMC3599050.
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Pande A, Rajaraman N, Sadiya N, Patil S, Pandian S, Adhithyan R, Rajendran B, Jalali R, Ghosh S. Spinal Drop Metastasis of Glioblastoma-Two Case Reports, Clinicopathologic Features, Current Modalities of Evaluation, and Treatment with a Review of the Literature. World Neurosurg. 2021 Feb;146:261-269. doi: 10.1016/j.wneu.2020.10.023. Epub 2020 Nov 5. PMID: 33161132.
5)
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