

Intracranial metastases

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Epidemiology

Intracranial metastases may be either parenchymal ($\approx 75\%$) or may involve the leptomeninges in [carcinomatous meningitis](#). 80% of solitary metastases are located in the cerebral [hemispheres](#). The highest incidence of parenchymal mets is posterior to the [Sylvian fissure](#) near the junction of temporal, parietal, and occipital lobes (presumably due to embolic spread to terminal MCA branches. Many tend to arise at the gray/white-matter interface. The cerebellum is a common site of intracranial Mets and is the location in 16% of cases of solitary brain mets. It is the most common p-fossa tumor in adults, thus "a solitary lesion in the posterior fossa of an adult is considered a metastasis until proven otherwise." Spread to the posterior fossa may be via the spinal epidural venous plexus (Batson's plexus) and the vertebral veins.

Brain metastases for the [EGFR mutation](#)-positive group were more frequently located in the left [cerebellum](#), left [cuneus](#), left [precuneus](#), and right [precentral gyrus](#). In the [ALK mutation](#)-positive group, brain metastases were more frequently located in the right [middle occipital gyrus](#), right posterior [cingulate](#), right [precuneus](#), right [precentral gyrus](#), and right [parietal lobe](#). In the [KRAS mutation](#)-positive patient group, brain metastases were more frequently located in the posterior left cerebellum. The study showed differential spatial distribution of brain metastases in patients with [Non-Small Cell Lung Cancer](#) according to their [mutation](#) status. Information regarding the distribution of brain metastases is clinically relevant as it could be helpful to guide treatment planning for [targeted therapy](#), and for predicting prognosis ¹⁾.

Classification

[Intracranial metastases classification](#)

Evaluation

Deciding which of the following tests are needed to evaluate a patient with [multiple intracranial lesions](#) must be individualized for the appropriate clinical setting.

1. cardiac echo: to R/O SBE that could shed septic emboli

2. “[Intracranial metastases](#) workup” including:

a) CT of chest/abdomen/pelvis with and without contrast: has become a relatively standard part of the metastatic workup. It has largely supplanted CXR, lower GI (barium enema) and IVP.

Rationale:

- Chest: R/O primary bronchogenic Ca or pulmonary metastases of another Ca. Can demonstrate mediastinal lymphadenopathy. Also to R/O pulmonary abscess that could shed septic emboli

- Assesses for possible primary lesions: e.g. kidneys, GI, prostate

- Evaluates for metastases to liver, adrenal, and even spine

b) mammogram in women

c) [PSA](#) in men

Biomarkers

Up to 14% of patients are diagnosed with BMs of unknown primary, which are commonly characterized by an early and aggressive metastatic spread. It is important to discover novel biomarkers for early identification of BM origin, allowing better management of patients with this disease. Our study focused on microRNAs (MicroRNAs), which are very stable in frozen native and FFPE tissues and have been shown to be sensitive and specific diagnostic biomarkers of cancer. We aimed to identify MicroRNAs with significantly different expressions in the five most frequent groups of BMs and develop a diagnostic classifier capable of sensitive and specific classification of BMs.

Materials and methods: Total RNA enriched for MicroRNAs was isolated using the mirVana MicroRNA Isolation Kit from 71 fresh-frozen histopathologically confirmed BM tissues originating in 5 cancer types. Sequencing libraries were prepared using the QIAseq MicroRNA Library Kit and sequenced on the NextSeq 500 platform. MicroRNA expression was further validated by RT-qPCR.

Results: Differential analysis identified 373 MicroRNAs with a significantly different expressions between 5 BM groups ($p < 0.001$). A classifier model was developed based on the expression of 6 MicroRNAs (hsa-miR-141-3p, hsa-miR-141-5p, hsa-miR-146a-5p, hsa-miR-194-5p, hsa-miR-200b-3p, and hsa-miR-365b-5p) with the ability to correctly classify 91.5% of samples. Subsequent validation confirmed both significantly different expressions of selected MicroRNAs in 5 BM groups as well as their diagnostic potential.

These is the first to analyze MicroRNA expression in various types of BMs using small RNA sequencing to develop a diagnostic classifier and, thus, to help stratify BMs of unknown primary. The presented results confirm the importance of studying the dysregulated expression of MicroRNAs in BMs and the

diagnostic potential of the validated 6-MicroRNA signature ²⁾.

Differential diagnosis

see [Intracranial metastases differential diagnosis](#).

Treatment

see [Intracranial metastases treatment](#).

Outcome

see [Brain metastases outcome](#)

Case series

A retrospective case series including patients who underwent resection of cranial metastases from March 2014 to April 2021 at a single center. This identified 112 patients who underwent 124 resections. The median age was 65 years old (24-84) and the most frequent primary cancers were nonsmall cell lung cancer (56%), breast adenocarcinoma (13%), melanoma (6%), and colorectal adenocarcinoma (6%). Postoperative MRI with contrast was performed within 48 hours in 56% of patients and radiation treatment was administered in 41%. GraphPad Prism 9.2.0 was used for the survival analysis.

At the time of data collection, 23% were still alive with a median follow-up of 1070 days (68-2484). The 30- and 90-day, and 1- and 5-year overall survival rates were 93%, 83%, 35%, and 17%, respectively. The most common causes of death within 90 days were as follows: unknown (32%), systemic or intracranial disease progression (26%), and pneumonia (21%). Age and extent of neurosurgical resection were associated with overall survival ($P < 0.05$). Patients aged >70 had a median survival of 5.4 months compared with 9.7, 11.4, and 11.4 for patients <50 , 50-59, and 60-69, respectively. Gross-total resection achieved an overall survival of 11.8 months whereas the sub-total, debulking, and unclear extent of resection led to a median survival of 5.7, 7.0, and 9.0 months, respectively.

Age and extent of resection are potential predictors of long-term survival ³⁾.

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³⁾

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