Introduction: Meningiomas constitute 15% to 18% of all primary intracranial and intraspinal tumors. The World Health Organization classifies meningiomas into benign (Grade I), atypical (Grade II) and anaplastic/malignant (Grade III)[1,34,]. Extracranial meningioma metastases (EMM) occur very rarely (in approximately 0.1% of intracranial meningioma patients) and therefore clinicians do not include them in their differential diagnosis[30,48,52].
Methods: We searched the following mesh terms in PubMed, used in diverse combinations: "metastatic, meningioma, extracranial, malignant, systematic, systemic, disseminated". We screened 230 studies and we selected 101 studies-,matching all selection criteria and exclusion criteria.
Results: Metastases are found most commonly in the lung followed by liver, lymph nodes, and bones [1,24,36,51,53,65,69,74,76,101]. They almost always occur in anaplastic meningiomas (grade III) and much more rarely in atypical meningiomas (grade II)[71]. Three modes of dissemination are known: Via blood vessels, lymphatics or Cerebrospinal fluid[100]. Patients with distant metastases may present with local symptoms or systemic symptoms caused by paraneoplastic syndromes. The diagnosis of a metastatic tumor can be supported radiologically (CT, MRI) by the interval increase in the size of the lesion, as well as with high Fluor-Desoxy-Glucose uptake of lesions at other sites on the PET-CT scan. An octreotide scan may assist in making the diagnosis. The somatostatin receptors are commonly expressed in meningiomas, and enable visualization with a radiolabeled somatostatin analogue identifying metastatic sites. Extracranial metastasis of malignant meningioma and its clinical, radiological and pathological features are not well-characterised. In addition, metastatic malignant meningioma needs to be distinguished from soft tissue sarcomas and metastatic carcinomas that express epithelial antigens [2,33,40].
Conclusions: We conducted this study to describe the most significant risk factors, diagnostic characteristics and treatment options. EMM is a very rare phenomenon and should be included in the differential diagnosis.

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SEMI-SITTIG POSITION IS ASSOCIATED WITH WORSE OUTCOME AND LONGER HOSPITALISATION THAN PRONE OR SUPINE POSITION FOR RESECTION OF BRAIN METASTASES LOCATED IN THE POSTERIOR FOSSA

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Background: Resection of brain metastases in the posterior fossa (PF) are either performed in the prone, supine or the semi-setting position. Comparative data is missing.
Methods: A retrospective comparative analysis from January 2018 to December 2020 in two neurosurgical departments was performed. All patients with brain metastases located in the PF were included. Groups A, B and C consisted of patients following resection in the semi-sitting, prone and supine position, respectively. Comparative analysis was conducted with regards of morbidity and mortality.
Results: 60 patients were identified (30 patients from each center). 42% were female. The median age was 67 year (range 36-83 years). Group A, B and C included 30, 11 and 19 patients, respectively. Surgical times were similar between group A (167 min [range 89-329 min]) and B (184 min [range 139-285 min]) but definitely shorter in group C (139 min [range 44-260 min]) ($p=0.05$). Median anaesthesia times remained similar in the A [268 min, range 170-465 min] and B group [273 min, range 200-354 min], but were also significantly shorter in the C group [201 min, range 105-363 min] ($p=0.001$). Interestingly the mean Karnofsky index deteriorated significantly in the A group ($p=0.005$). Based on complication rates we experienced siginificantly more deaths (4 patients) and severe postoperative complications in group A ($p<0.0001$). Moreover patients treated in group A (24 days, [range 4-75 days]) had a more prolonged hospital stay compared to the other two groups (group B - 15 days, [range 4-30 days]; group C - 14 days [range 5-29 days]).
Conclusion: The semi-setting position is associated with worse clinical outcome and prolonged hospital stay for patients with brain metastases in the PF.

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IMMUNOPHENOTYPING OF TUMOR-INFILTRATING T CELLS IN PRIMARY CNS LYMPHOMA

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Background: Primary CNS lymphoma represents a malignant disease with dismal prognosis. Standard of care is high dose chemotherapy and radiation. However, this combination cannot be applied to the elderly and fragile population. Immunotherapy holds great promise to be effective in these patients. This study therefore aims to explore the phenotype of tumor-infiltrating lymphocytes (TIL) in order to analyze the potential for immune checkpoint inhibition.
Methods: We performed ex vivo multicolor flow-cytometry on surgical specimens of nine patients with intracerebral lymphoma, including seven with primary CNS lymphoma after isolation of TILs following standard protocols. Data was analyzed using a Fortessa LSR flow cytometer and Diva software. The study was approved by the local ethics committee (PV4904).
Results: Our ex vivo phenotyping demonstrated a predominant infiltration of CD8+ T cells, which outnumber CD4+ T cells by a ratio of 2:1 ($p<0.01$). Regulatory T cells (Tregs) were not increased in the tumor microenvironment and the NK cell frequency was reduced compared to the peripheral blood. While CD4+ T helper cells displayed significantly increased surface expression of multiple activation and checkpoint markers, including TIGIT, PD-1, Tim3 and CD57, cytotoxic CD8+ T cells predominantly expressed only TIGIT and PD-1. On average 70% and 80% of CD8+ T cells expressed PD-1 and TIGIT, respectively, compared to 35% and 60% of PD-1 and TIGIT on CD4+ T cells ($p<0.05$). CD8+ T cells furthermore showed an increased expression of CD39 and a simultaneous downregulation of CD73, both ectoenzyms involved in the modulation of intratumoral ATP, thereby indicating a metabolic immune modulation by the tumor.
Conclusion: Taken together, our study demonstrates a strong infiltration of cytotoxic CD8+ T cells into cerebral lymphoma, which potentially can be disinhibited using checkpoint immunotherapy. Our profiling suggests that PD-1 and TIGIT present appealing targets for such kind of immune disinhibition.

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CLINICAL DETERMINANTS IMPACTING OVERALL SURVIVAL OF PATIENTS WITH OPERABLE BRAIN METASTASES FROM NON-SMALL CELL LUNG CANCER

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Background: The overall incidence of brain metastases (BM) continues to rise due to improved treatment of extracranial tumor manifestations and subsequent prolonged survival. Although the mortality from lung cancer has declined sharply over the past 10 years, over 10% of all patients with lung cancer still develop BM within the first two years. Diagnosis of BM usually results in death within less than 12 months. Thus, the occurrence of cerebral metastases remains a major challenge in modern neuro-oncology.
Methods: We performed a retrospective analysis on 264 patients undergoing surgical resection for BM from lung-cancer from 2014 to 2019. Overall survival was correlated to age, gender, number and size of BM, localization, symptoms, mass edema index and previous therapy (initial diagnosis, after chemotherapy, after immunotherapy). Statistical analysis was performed using SPSS.
Results: Overall survival from surgery was 11.5 months (15.3 SD). Overall survival from the initial diagnosis of lung cancer was 23.2 months (27.3 SD). 57.2% of patients presented with BM at initial diagnosis. The histology was adeno- (82.4%), squamous- (9,5%), neuro-endocrine-carcinoma (4.9%) and not further specifiable (3.2%). A significant dismal prognosis in overall survival from brain surgery was found for age (^{3}60 years), gender (male), size (^{3}7cm^3), number of BM (^{3}2) and singular vs. solitary BM. History of smoking or localization (infra-