Abstract Title: Clinical and disease characteristics of metastatic uveal melanoma patients who develop symptomatic brain metastases

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Research Summary Overview

Metastatic uveal melanoma (mUM) is an advanced ocular malignancy characterized by a hepatotropic pattern of spread. As the incidence of brain metastases (BM) in mUM patients has been thought to be low, routine CNS surveillance has not been recommended. Notably, no formal assessment of BM incidence in mUM has to date been published to support this clinical practice. We aimed to determine the true rate of BM in mUM and to clarify the clinical and genomic risk factors associated with BM patients through a collaborative multicenter, retrospective research effort.

Methods

Data collected from 1,847 consecutive mUM patients in databases across four NCI-designated comprehensive cancer centers from 2006-2020 were retrospectively analyzed to identify patients with BM. Brain imaging in most cases were performed due to onset of neurological symptoms and not for routine surveillance. An analysis of demographics, therapies, gene expression profile, tumor next generation sequencing (NGS) data, time to metastasis (brain or other), and survival in the BM cohort was completed.

Results

137 out of 1,847 (7.4%) mUM patients were identified with BM. The median age at time of UM diagnosis was 53 (range: 18-77). 58.9% of cases occurred in females. 92.6% arose in the choroid. The median time to any metastasis was 38.5 months (range: 1-369.5). The most common initial metastatic site was liver (86.6%) followed by bones (15.1%) and lungs (11.0%). 2/1274 (0.2%) patients had BM at time of metastatic diagnosis. The median time to BM from first metastasis was 16.6 months (range: 0-115.5). Median survival after a diagnosis of BM was 5.5 months (range: 0.4-67.2). The median number of organs involved at time of BM diagnosis was 3 (range: 1-9), with 62.3% having an elevated LDH. Prior to diagnosis of BM, mUM patients had received a median of 4 lines of therapy (range: 0-10), with 65.8% of patients having received immunotherapy. DecisionDX-UM profiling was completed on 12 patients: 9-Class 2, 2-Class 1B, and 1-Class 1A. NGS and cytogenetic data were available for 19 and 18 patients, respectively. *BAP1* and *SF3B1* mutations were detected in 65.1% and 27.3% of cases. Monosomy 3 was present in 77.8% of cases and 8q amplifications in 61.1%. The most common non-*GNAQ/GNA11* mutations were in MET (21.1%), CDK2 (15.8%), and CDKN2A (15.8%).

Conclusion:

BM was identified in 7.4% of mUM cases, typically late in the disease course, and was associated with high disease burden and a median survival of under 6 months once diagnosed. As the majority of patients in this cohort were symptomatic, the incidence of asymptomatic BM remains unknown. These data suggest the use of routine brain imaging in all mUM patients at risk for developing BM for early detection. Intervention with locoregional therapies may potentially improve patient survival and prevent a reduced quality of life from symptomatic brain disease.