Intramedullary Spinal Cord Tumors: Exomic Sequencing and Outcomes After Resection

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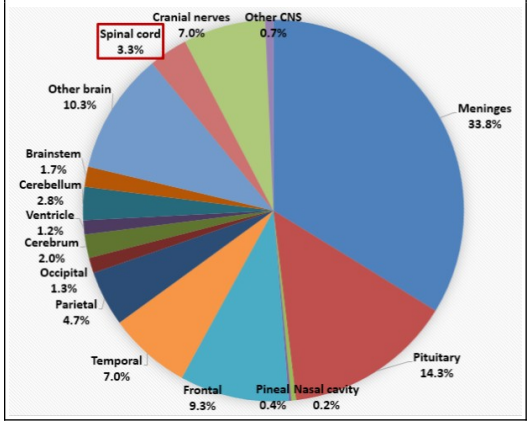
Relative incidence of CNS tumors by location



Introduction

IMSCTs are a rare and heterogeneous group of primary spinal tumors for which management remains controversial. Additionally, due to the rarity of these lesions, little is known about the genetics and molecular pathogenesis. The present study aims to 1) identify prognostic factors for progression-free survival (PFS) and overall survival (OS), 2) assess long-term neurologic outcomes after surgical resection, and 3) perform exomic sequencing of these tumors.

Methods

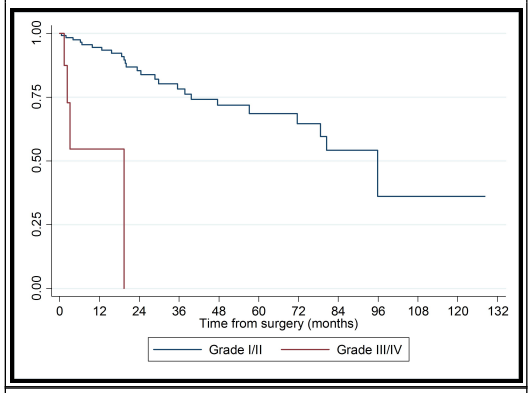
We retrospectively reviewed information for 231 patients with IMSCTs, the largest cohort assembled to date, who underwent surgical resection of their tumors at our institution between 1996 and 2014. 191 out of 231 (82.7%) patients had clinical follow-up data and the mean duration of follow-up was 31.7 ± 34.7 mo. Exomic sequencing of 33 tumors with available pathologic samples was also performed.

Results

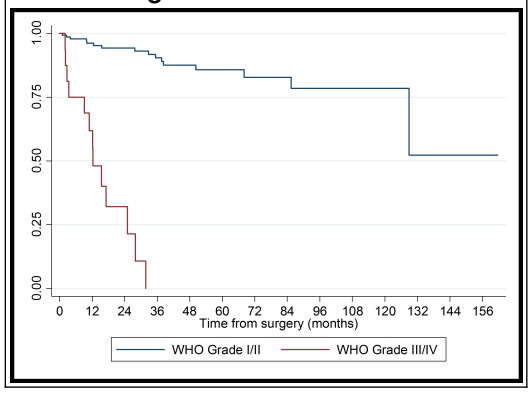
231 patients with IMSCTs underwent surgical resection at a mean age of 33.6 ± 19.2 years. The majority of patients were adults, with 64 (27.7%) pediatric patients. Ependymomas were the most common histologic subtype, observed in 112 (48.5%) cases, followed by astrocytomas (81, 35.1%), hemangioblastomas (21, 9.1%), gangliogliomas (13, 5.6%), and oligodendrogliomas (1, 0.4%). Out of 217 cases, 19 (8.8%) were WHO grade III or IV tumors. In 85 (36.8%) cases, gross total resection (GTR) was achieved and was associated with low-grade tumors (OR 0.10, 95% CI 0.13 – 0.83, p = 0.033).

The median PFS was 95.8 mo (95% CI 71.6 mo -) and was independently predicted by previous surgical resection (HR 3.68, 95% CI 1.70 – 7.94, p = 0.001), ependymomas (HR 0.29, 95% CI 0.13 – 0.67, p = 0.004), and low-grade tumors (HR 10.1, 95% CI 2.88 – 35.44, p < 0.001). The median OS was 128.9 mo (95% CI 128.3 mo -) and was associated with ependymomas (HR 0.17, 95% CI 0.04 – 0.61, p = 0.007) and low-grade tumors (HR 13.1, 95% CI 5.08 – 33.71, p < 0.001). The strongest predictor of long-term neurologic outcomes was preoperative functional status; predictors of motor status included preoperative motor status (p < 0.001), and the duration of preoperative symptoms (p = 0.009).

IMSCT grade and progression-free survival



IMSCT grade and overall survival



For the 33 sequenced tumors, the histologic subtype included ependymoma in 15 (48.5%) cases, astrocytoma in 13 (39.4%) (pilocytic astrocytoma in 4, diffuse in 5, anaplastic in 2, and glioblastoma in 2), hemangioblastoma in 1 (3.0%), oligodendroglioma in 1 (3.0%), and ganglioglioma in 2 (6.1%). Upon genetic analysis of the tumors, 5 out of 15 (33.3%) ependymomas displayed mutations in NF2. No recurrent mutations were found in the other histologic types.

Conclusions

Tumor histology is the strongest predictor of PFS and OS; low-grade lesions including ependymomas, hemangioblastomas, and gangliogliomas are associated with high rates of GTR and improved outcomes. Astrocytomas, and high-grade astrocytomas in particular, are associated with lower rates of GTR. Treatment of IMSCTs must take into consideration functional neurologic status, as functional outcomes appear dependent on preoperative neurologic status, and warrants early treatment of these tumors. Our data confirms the role of NF2 in ependymomas, but suggests that intraspinal tumors are genetically distinct from their intracranial counterparts, and may arise from a divergent disease process.

References

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