J Pathol. 2023 Apr 28. doi: 10.1002/path.6084. Online ahead of print.

Mutational landscape of primary spinal cord astrocytoma

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PMID: 37114614 DOI: 10.1002/path.6084

Abstract

Primary spinal cord astrocytoma (SCA) is a rare disease. Knowledge about the molecular profiles of SCAs mostly comes from intracranial glioma; the pattern of genetic alterations of SCAs is not well understood. Herein, we describe genome-sequencing analyses of primary SCAs, aiming to characterize the mutational landscape of primary SCAs. We utilized whole exome sequencing (WES) to analyze somatic nucleotide variants (SNVs) and copy number variants (CNVs) among 51 primary SCAs. Driver genes were searched using four algorithms. GISTIC2 was used to detect significant CNVs. Additionally, recurrently mutated pathways were also summarized. A total of 12 driver genes were identified. Of those, H3F3A (47.1%), TP53 (29.4%), NF1 (19.6%), ATRX (17.6%), and PPM1D (17.6%) were the most frequently mutated genes. Furthermore, three novel driver genes seldom reported in glioma were identified: HNRNPC, SYNE1, and RBM10. Several germline mutations, including three variants (SLC16A8 rs2235573, LMF1 rs3751667, FAM20C rs774848096) that were associated with risk of brain glioma, were frequently observed in SCAs. Moreover, 12q14.1 (13.7%) encompassing the oncogene CDK4 was recurrently amplified and negatively affected patient prognosis. Besides frequently mutated RTK/RAS pathway and PI3K pathway, the cell cycle pathway controlling the phosphorylation of retinoblastoma protein (RB) was mutated in 39.2% of patients. Overall, a considerable degree of the somatic mutation landscape is shared between SCAs and brainstem glioma. Our work provides a key insight into the molecular profiling of primary SCAs, which might represent candidate drug targets and complement the molecular atlas of glioma. © 2023 The Pathological Society of Great Britain and Ireland.

Keywords: astrocytoma; genomic profiling; glioma; mutational landscape; rare disease; spinal cord.