Diffuse Midline H3 K27-Altered Gliomas in the Spinal Cord: A Systematic Review

Mohammad Faizan Khan[1], Jennifer Manyu Wong[2], Bradley Estes[3], Christian Ogasawara[4], Giuseppe E. Umana[5], Paolo Palmisciano[6], Gina Watanabe[2]

[1]Indiana University School of Medicine, Indianapolis, IN; [2]John A. Burns School of Medicine, University of Hawai'i, Honolulu, HI, USA; [3]University of Kansas School of Medicine, Kansas City, KS, USA; [4]Department of Neurosurgery, University of Texas Medical Branch, Galveston, TX, USA; [5]Department of Neurosurgery, Trauma Center, Gamma Knife Center, Cannizzaro Hospital, Catania, Italy; [6]Department of Neurosurgery, University of Cincinnati College of Medicine, Cincinnati, OH, USA

Background: Gliomas account for 80-90% of all intramedullary spinal cord tumors (IMSCTs). Though rare compared to brain tumors, spinal cord gliomas can cause significant morbidity and mortality. Diffuse midline gliomas (DMGs) with H3 K27M-mutation, first introduced in the 2016 WHO classification, are high-grade tumors with aggressive behavior and poor prognosis. The 2021 updated WHO classification renamed them "diffuse midline glioma, H3 K27-altered" to include other molecular changes. Limited single-institution data on spinal cord DMGs (DMG-SCs) hinder comprehensive understanding and optimal treatment protocols. In this review, we summarize clinical and molecular features, management strategies, and survival impact in patients with DMG-SCs.

Project Methods: A systematic review was performed following the (PRISMA) guidelines. PubMed, Ovid EMBASE, Scopus, and Web of Science were searched. Clinical characteristics, treatment protocols, and outcomes were analyzed.

Results: A total of 26 studies with 259 patients were included. Most patients were male (63%), diagnosed at a mean age of 32 years (range, 4-72), and tumors were predominately located in the cervical (32%) or thoracic (43%) regions of the spinal cord. Primary management included surgical resection (97%), radiotherapy (78%), and chemotherapy (62%). Most common combination of treatment included surgical resection, radiotherapy, and chemotherapy (47%). The mean overall and progression free survival were 25 (range, 0.1-48) and 14 (range, 0.1-25) months, respectively. Gene alterations included p53 mutation (61%), loss of ATRX (46%), Olig-2 positive (100%), and GFAP positive (80%). The mean Ki-67/MIB-1 was 23% (12-40%).

Conclusion/Impact: DMG-SCs affect mostly the adult population and appear to resemble adult DMGs in terms of molecular features, management, and prognosis.