











Infrared Thermography – A Novel Tool in the Surgical Treatment of H3 K27M-Altered Diffuse Midline Spinal Cord Glioma: Technical and Case Report

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Abstract

Diffuse midline gliomas (DMGs), H3K27-altered, are rare and aggressive tumors primarily affecting children, though adult cases occur. These gliomas present significant surgical challenges, and novel techniques are needed to improve outcomes. We present the case of a 53-year-old male with a solid expansive lesion located at T12 to L1, who presented with bilateral thigh pain, loss of sphincter control, and increased urinary frequency. Initial magnetic resonance imaging suggested an ependymoma; however, tumor resection followed by immunohistochemical analysis confirmed a diagnosis of diffuse midline glioma, H3K27-altered. The patient underwent a successful two-level lumbar laminectomy with a microsurgical gross total resection. An innovative technique of intraoperative infrared thermography mapping was employed, representing a novel approach for this rare tumor. The patient remains alive at the time of the present publication.

Keywords

- ▶ glioma
- ▶ thermography
- ▶ surgical oncology
- ▶ spinal cord neoplasms

Introduction

Diffuse midline gliomas (DMGs), H3K27-altered, are rare tumors that predominantly affect children and adolescents, with fewer cases observed in middle-aged and elderly individuals. This condition does not exhibit a significant sex difference. Infratentorial tumors of this type are frequently associated with motor and sensory abnormalities, ataxia, and other neurological symptoms. Despite advancements in surgical techniques, radiotherapy, and chemotherapy, the

prognosis for patients with H3K27-altered gliomas remains poor.¹ Recent innovations, such as infrared thermography (IRT), present promising enhancements for the surgical management of malignant tumors. Infrared thermography is a noninvasive technique that captures infrared radiation emitted from the surface of tissues, generating thermal images that reflect underlying physiological states. Tumors often exhibit thermal asymmetries relative to surrounding tissues due to differences in metabolic activity, vascular density, and perfusion. In neurosurgical settings, these

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thermal profiles can potentially assist in intraoperative delineation of tumor margins, enabling more precise resections and reducing the risk of neurological sequelae. However, to date, no published reports have specifically addressed the use of IRT for spinal cord gliomas. The present case report aims to explore the intraoperative application of IRT in an adult patient with new DMG, H3K27-altered, and to evaluate its potential benefits and implications for refining surgical practices in this challenging context. The present study was submitted to and approved by the Ethics Committee of Hospital Luxemburgo/Fundação Mário Penna/Associação Mário Penna, state of Minas Gerais, Brazil, under submission number CAAE: 50919521.0.0000.5121. Informed consent was obtained from the patient involved in the study, 3 months before surgery.

Clinical Case Description

A 53-year-old male patient presented with progressive bilateral thigh pain, complete loss of sphincter control, increased urinary frequency, and incontinence. Magnetic resonance imaging (MRI) performed in August 2022 identified an expansile lesion at the conus medullaris, measuring $\sim 2.5 \times 1.7 \times 1.4$ cm, with a heterogeneous appearance suggesting ependymoma. Resection of the spinal tumor, involving a laminectomy of T12-L1, was performed in October 2022, with intraoperative findings suggesting complete resection, but postoperative MRI revealed residual tumor. Initial surgical findings suggested a low-grade glioma; however, subsequent immunohistochemistry (IHC) revealed atypical glial proliferation consistent with a high-grade glioma, along with negativity for IDH1, R132H, and TP53 mutations, indicating a diagnosis of glioblastoma, IDH wild-type, WHO Grade IV. The patient underwent radiotherapy (54 Gy over 30 sessions) and 12 cycles of temozolomide chemotherapy. Following treatment, there was a deterioration in neurological function, resulting in paraplegia and loss of sphincter control. Immunohistochemistry performed in February 2023 confirmed an H3 K27M+ glioma. The diagnosis of DMG, H3K27-altered was given. Follow-up MRIs showed initial swelling and cystic/necrotic changes, with varying lesion sizes over time. This imaging also revealed degenerative changes in the lumbar spine, including spondylosis and disc protrusions. No brain lesions were detected, indicating the glioma remained confined to the spinal cord. In April 2024, a reoperation to the tumor was undertaken, involving a two-level lumbar laminectomy with a microsurgical gross-total resection. The procedure was guided by intraoperative ultrasound and infrared thermography, with the latter performed using a 76,800-pixel forward looking infrared (FLIR) machine (—Fig. 1).

Discussion

Diffuse midline gliomas with histone H3 lysine 27-to-methionine mutations (H3 K27M-mutant) were identified as a distinct category in the 2016 WHO classification of central nervous system tumors.² These highly aggressive brain tumors predominantly affect children and adolescents, although they

can also occur in middle-aged and elderly individuals. Typically found in midline regions such as the thalamus, brainstem, or spinal cord, these tumors are classified as WHO grade IV, indicating a poor prognosis regardless of their histological characteristics. In adults, prognosis may vary depending on tumor location and spatially regulated gene expression.^{2,3} Despite available treatments like surgical resection, radiotherapy, and chemotherapy, patient outcomes remain bleak.

Imaging plays a crucial role in diagnosing H3 K27M-mutant gliomas. Magnetic resonance imaging is the preferred modality, revealing heterogeneous masses with irregular, poorly defined margins. These tumors typically show mixed signal intensity on T1- and T2-weighted images due to a combination of solid tumor tissue, necrosis, and cystic areas, with significant, irregular enhancement patterns on contrast-enhanced MRI. Peritumoral edema and mass effects causing spinal cord compression are common findings. Ultrasound, though less frequently used, can provide valuable intraoperative information, showing echogenic masses with irregular margins indicative of aggressive tumors and assessing the extent of resection post-operatively.² Surgical interventions such as gross total resection (GTR) are optimal, but the H3 K27M mutation's role in prognosis and treatment remains a subject of ongoing research. The infiltrative nature of these tumors makes it challenging to distinguish tumor margins from normal tissue, thereby highlighting an opportunity for the potential use of IRT.

No clinical trials have evaluated the advantage of IRT in accessing DMGs, H3K27-altered, leaving a gap in understanding its full potential.^{4,5} The surgical approach to DMGs, H3K27-altered largely depends on selecting the safest and most direct access to the lesion, with a technique that should be safe, efficient, easy to perform, and exhibit high sensitivity and specificity. Infrared thermography is a non-contact diagnostic tool that provides real-time functional information about the tumor.^{4,5} Although IRT has been utilized in the surgical management of malignant brain tumors, specific reports on primary spinal cord glioblastoma (PSC GBM) are lacking. Generally, malignant gliomas present with lower temperatures relative to the surrounding normal tissue, due to reduced metabolism, perifocal edema, and decreased density of tumor microvessels, as seen in our images.⁴

The utility of IRT for predicting resection extent and acute ischemia has been underestimated. In our case, IRT mapping effectively identified the tumor's location, thereby improving the surgical approach. Thermal imaging, captured using a FLIR thermal camera and direct observation during the surgical procedure, was employed. Comparative analysis of thermal and surgical images of the thoracolumbar spine demonstrated a clear correlation between heat distribution and tumor presence. Thermal imaging provides valuable supplementary insights into metabolic activity and inflammation, thereby enhancing surgical planning and clinical management. The present case highlights the importance of integrating innovative technologies like IRT in the management of rare and complex spinal cord tumors, underscoring its potential to improve surgical precision and patient outcomes.

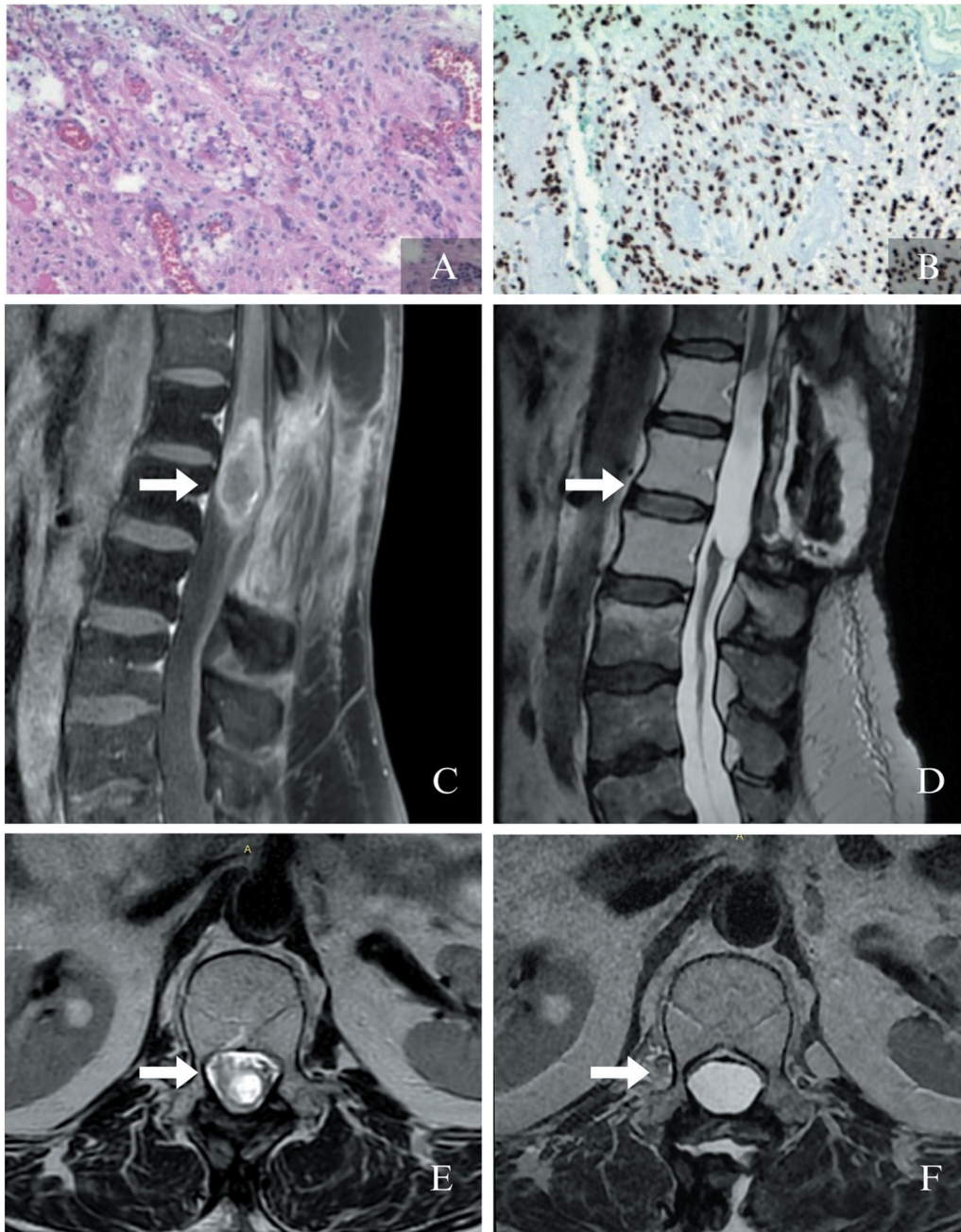


Fig. 1 Pre- and postoperative imaging. Notes: (A) The histological sections display a glial neoplasm with high cellularity. The astrocytic cells exhibit moderate atypias, necrosis, and foci of microvascular proliferation. There are suggestive foci of reactive areas post-treatment. (B) The immunohistochemical study showed positivity for the H3.3 K27M antibody with partial (“mosaic”) loss of the trimethylated form H3K27me3. These findings together corroborate the diagnosis of H3 K27M-positive glioma. Diffuse midline glioma, H3 K27-altered (grade 4, WHO 2021) is a diagnostic possibility from a morphological and immunohistochemical standpoint. (C) Sagittal T1-weighted magnetic resonance imaging (MRI) with postvenous contrast fat suppression, showing intradural and intramedullary oval-shaped contrasting expansile lesion at the thoracolumbar transition (white arrow). The tumor exhibits poorly defined margins and exerts considerable mass effect, compressing and displacing the spinal cord. (D) Sagittal MRI image without postsurgical changes, showing normal alignment and signal intensity of the spinal cord. The vertebral bodies and intervertebral discs appear intact, with no evidence of residual or enhancing lesions. (E) Axial T2-weighted MRI showing a hyperintense expansile lesion (white arrow) within the spinal canal, consistent with a tumor. The lesion is causing significant compression and displacement of the surrounding spinal structures, leading to a reduction in the available space within the canal. (F) Axial T2-weighted MRI postsurgery, demonstrating complete gross resection of the tumor. The spinal canal now appears decompressed with restored alignment, and there is no visible residual or enhancing lesion.

Although the application of IRT in high-grade gliomas remains scarcely documented, there is growing evidence of its use in tumors such as breast carcinoma, melanoma, and thyroid nodules. These studies suggest that thermal imaging may serve as an adjunct in detecting tumor margins or

perfusional abnormalities. Nonetheless, the technique presents limitations, including its sensitivity to ambient conditions, lack of standardized protocols, and the need for quantitative analysis methods, which currently hinder its broader clinical implementation. Future multicenter

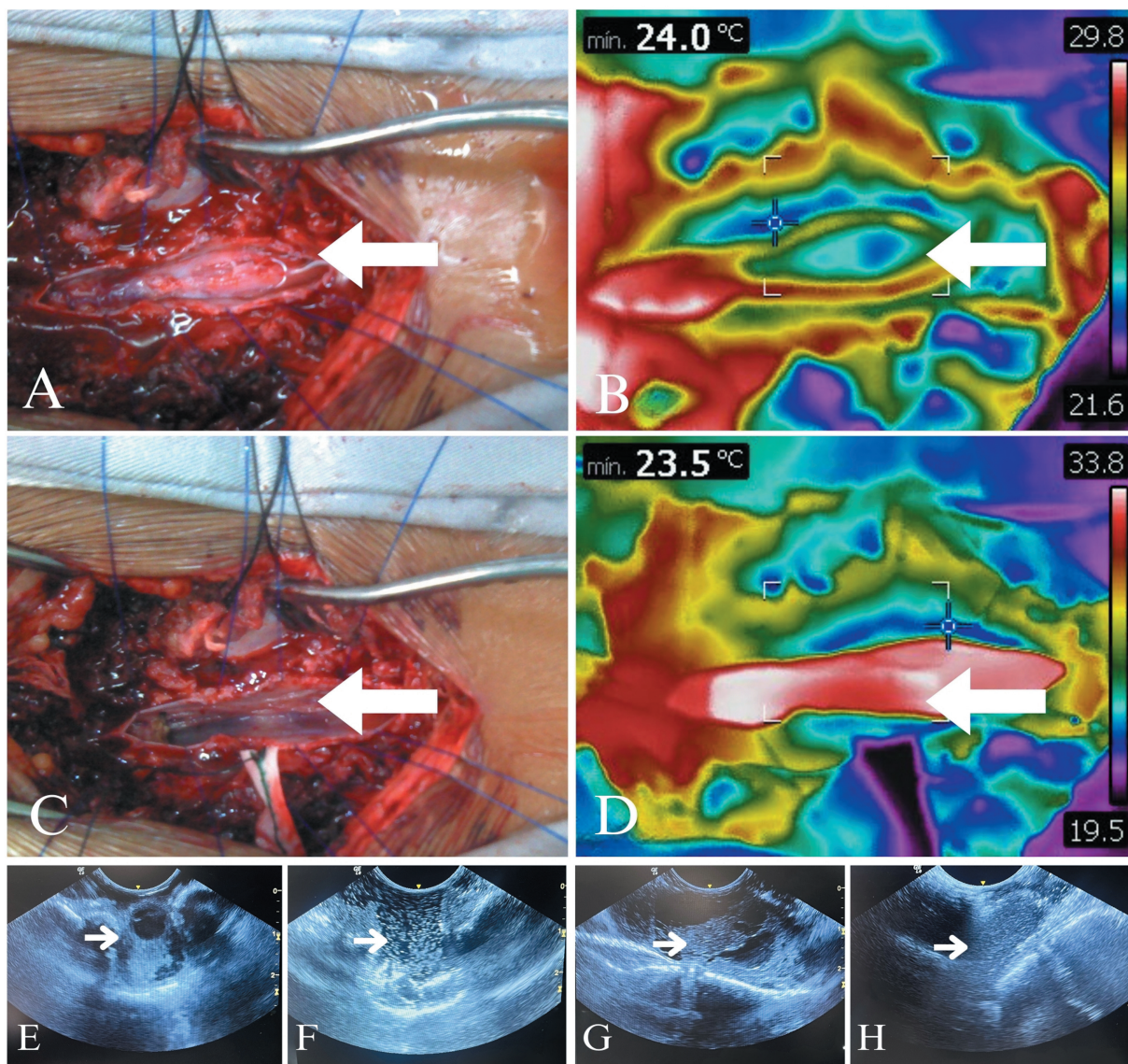


Fig. 2 Intraoperative imaging, ultrasound, and thermal mapping. Notes: (A) Intraoperative view of the spinal cord with the exposed surgical field and visible tumor (arrow), showing detailed anatomical structures and tumor infiltration for resection planning. (B) Intraoperative thermal image using a forward looking infrared (FLIR) camera, showing a cooler region (arrow) corresponding to the tumor due to reduced metabolic activity and perfusion (necrotic region), aiding in tumor margin delineation. (C) Intraoperative view after gross total resection (GTR) of the tumor, with the surgical site indicated (arrow), showing the remaining spinal cord and surrounding tissues. (D) Intraoperative thermal image showing normalized temperature in the resected area, indicating restored metabolic activity and blood flow. (E) Intraoperative axial ultrasound shows an echogenic mass with irregular margins and mass effect. (G) Intraoperative sagittal ultrasound shows a pronounced echogenic mass with significant spinal cord compression. (F) Intraoperative axial ultrasound shows reduced mass and normalized spinal canal signal after tumor resection. (H) Intraoperative sagittal ultrasound shows a substantial reduction in mass and improved spinal canal appearance.

prospective studies are necessary to confirm the reproducibility and effectiveness of IRT in the surgical treatment of rare diffuse midline gliomas and further investigations should focus on the standardization of IRT protocols and the development of quantitative metrics to enhance tumor visualization and surgical guidance and aim to correlate intraoperative thermal findings with histopathological analysis, particularly at the tumor margins, to assess diagnostic accuracy. Direct comparison with other intraoperative adjuncts, such as fluorescence-guided resection or intraoperative MRI, would be instrumental in defining the specific advantages and limitations of infrared thermography (►Fig. 2).

Conclusion

The initial presentation and progression of the case herein described diverged markedly from those typically reported in the literature, particularly with the patient's age. Infrared thermography demonstrated a significant role in the present case and shows potential applications; however, further validation is needed, because there is a lack of extensive research, necessitating further studies to evaluate its efficacy. H3 K27M+ glioma has been less frequently addressed in medical literature, resulting in a need for more data to support standardized guidelines. Improvement in the understanding of this pathology, registration, and cooperation among multiple centers are essential.

Authors' Contributions

GFSQ: conceptualization, data curation, formal analysis, funding acquisition, investigation, methodology, project administration, resources, software, supervision, validation, visualization, writing – original draft, writing – review & editing; BMD, AACD, CCMPC, DMS, AASS, LSO: data curation, investigation, methodology, writing – review & editing; LRS, MMF, LAWH: supervision, validation, resources.

Conflict of Interests

The authors have no conflict of interests to declare.

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