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Multicentric low-grade glioma: A systematic review of a rare neuro-oncological disease

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Highlights

- Multicentric Low-grade gliomas show high long-term survival: 87 % (children) and 85 % (adults).
- Maximum safe resection is the preferred treatment, with re-resection as needed.
- Postoperative chemo/radiotherapy did not significantly affect progression-free survival.

- Molecular markers may improve prognosis assessment for multicentric LGGs.

Abstract

Introduction

Multicentric and multifocal gliomas are rare and mainly described in high-grade gliomas, however, they have rarely been reported with LGG in about 2–10 % of all cases. This study aims to identify the reported multicentric low-grade gliomas (mLGGs) in literature and review their pathologies, management, and outcomes.

Methods

A systematic search using a pre-defined search strategy was conducted across three databases (PubMed, Cochrane Library, and Scopus). Following the PRISMA guidelines, relevant articles were selected. The data including demographic details, clinical presentations, lesion locations, pathology, neurosurgical interventions, extent of resection, adjuvant therapies, and survival outcomes were reported.

Results

We identified 36 patients across 17 studies. Presenting symptoms varied, with seizures (27.7 %) and headaches (22.2 %) being the most common. Typical imaging features involve hypo- to isotense signals on T1-weighted images and hyperintensity on T2-weighted images, with MR spectroscopy aiding in differentiation. Histological consistency across tumor sites was observed in 29 cases, with some variability in a few. Survival was 66.6 % among patients, and initial reports in the 1960s indicated high mortality due to intracranial pressure shifts. Adjuvant therapies included chemotherapy (14 patients) and radiotherapy (9 patients), though many cases lacked complete therapy data. Although chemotherapy and radiotherapy lacked a significant impact on progression-free survival, early, extensive resection remains advocated, with a mean progression-free survival of 30.14 months.

Conclusion

Most of the current evidence surrounding mLGG consists of case reports with few retrospective case series. Early, extensive resection appears to be the most effective approach for managing mLGG, while adjuvant therapies have limited impact on progression-free survival, highlighting the need for more comprehensive molecular profiling to guide treatment. Further research into standardized protocols for adjuvant therapies and long-term outcomes is essential to optimize survival and improve management of unresectable or recurrent cases.

Introduction

Central Nervous System (CNS) tumors occur in 24.71 per 100,000 population [31]. Gliomas are the most common among CNS tumors [29] and Low-grade gliomas (LGG) constitute roughly 15 % of all gliomas diagnosed annually [6]. These are slow-growing, primary brain tumors in young adults with a prolonged clinical course and natural history[40]. Most patients present with seizures (60 %–88 %) and relatively intact neurological function[35]. Prompt diagnosis and maximum safe resection have shown survival ranges from 5.6 to 13.3 years, depending on specific histology[7]. Patients with high-risk factors are often deferred to radiation and chemotherapy.

Multicentric and multifocal glioma is a rare entity that is mainly described in high-grade gliomas (HGG)[22], however, it has rarely been reported with LGG. The incidence is 2–10 % collected through various series[4]. The working definition was primarily defined by Batzdorf and Malamud as multifocal refers to tumor cells spreading through established pathways, such as commissural fibers and cerebrospinal fluid, and Multicentric refers to lesions in different brain areas with no macroscopic or microscopic continuity5, 46.

The rarity of such cases in the reported literature has equally made it difficult for any consensus to be made regarding diagnosis, management, need for intervention, and follow-up protocols. There is debate amongst various authors, with some advocating for stereotactic biopsy for the diagnosis while others have pushed for more aggressive maximal resection and even multiple craniotomies if necessary[32]. Hasaneen and colleagues recommend multiple craniotomies for select multifocal/multicentric gliomas as survival is equivalent to that of patients undergoing solitary lesion surgery, without increase in complications[14]. The tendency of low-grade gliomas for malignant transformation, has also prompted many authors to go for extensive surgical resection wherever possible[43]. However, this cannot account for inaccessible lesions and role of medical therapies such as Whole brain radiotherapy with concurrent temozolomide that have shown good results with progression-free survival and overall survival[20].

Multifocal and multicentric gliomas present a unique management challenge. With a wide array of available treatment options and evolving understanding of disease progression that differentiates it from other LGG, it has become imperative to prioritize practices and approaches for better outcome. This study aims to identify the reported multicentric low-grade gliomas (mLGGs) in literature and review their pathologies, management, and outcomes.

Section snippets

Search strategy and article selection

A systematic search for all publications describing patients with the search strategy

“(Multimodal OR multicentric) AND (low-grade AND glioma* OR LGG OR glioma*)” was conducted across 3 databases including PubMed, Cochrane Library, and Scopus to identify all eligible articles. …

Inclusion and exclusion criteria

The inclusion criteria consisted of case reports, series, and observational studies reprting patients with multicentric or multimodal LGGs.

Only clinical articles limited to medicine and neuroscience were added. Reviews, …

Results

We recorded data for a total of 36 patients across 17 studies that we considered in our analysis. In our study there were 38.9 % females and 61.1 % males. In terms of handedness, 19.4 % patients had a right handedness, 2.8 % had a left handedness, and for 77.8 % patients, this information was unavailable. The presenting complaints among the patients varied significantly. Seizures were reported in 27.7 % of cases, while 22.22 % of patients experienced headaches. Reduced vision and blindness were …

Discussion

Effective management of brain tumors requires understanding their natural history and treatment response. With an overall survival rate of about 87 % at 20 years in population studies, low-grade gliomas in children are linked to long-term survival and a low incidence of tumor-related morbidity in adulthood[3]. In comparison, low-grade gliomas in adults are associated with an overall survival of 85 % and median progression-free survival of 34 % at 10 years. In contrast, the overall survival rate …

Conclusion

Most of the current evidence surrounding mLGG consists of case reports with few retrospective case series. Our findings suggest benefits with maximally safe resection in same-hemispheric lesions, with re-resection as required, and with good outcomes, as seen by few centers. However, the overall prognosis of this disease remains uncertain. Molecular investigations may help identify key markers correlating with prognosis in this disease. …

CRediT authorship contribution statement

Enam Syed Ather: Supervision, Validation. **Aziz Hafiza Fatima:** Conceptualization. **Shamim Muhammad Shahzad:** Conceptualization. **Bajwa Muhammad Hamza:** Conceptualization, Methodology, Writing – original draft. **Tariq Rabeet:** Methodology, Writing – original draft, Writing – review & editing. **Hussain Nowal:** Methodology, Writing – original draft, Writing – review & editing. …

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Recommended articles

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Multicentric Low-Grade Gliomas

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