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# Low-grade gliomas presenting with hemorrhage: Are intratumoral blood products associated with malignant transformation?


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## Highlights

- Case Report: 50-year-old female diagnosed with a hemorrhage stemming from a WHO grade 2, IDH-mutant astrocytoma.
- Systematic review revealed 16 patients with low-grade gliomas that presented acutely as hemorrhage.
- Hemorrhage in low-grade gliomas may indicate malignant transformation due to the increased microvascular abnormalities.

## Abstract

### Objective

Gliomas are the most common primary tumor in the central nervous system (CNS), with low-grade gliomas (LGG) comprising more than 5 percent of all adult primary CNS tumors. While glioblastoma, the most malignant glioma subtype, is known to present with hemorrhage, LGGs rarely present with hemorrhage. This systematic review investigates LGGs that present as hemorrhage and provides an illustrative case presentation in order to evaluate trends and outcomes for this pathology.

### Methods

A systematic review of the literature was performed to evaluate presentation, treatment, and outcomes for patients with LGG that present as intracranial hemorrhage. Articles included were case series describing surgical approach; literature reviews were excluded. Variables evaluated included presenting symptoms, imaging results, and postoperative outcomes.

### Results

The initial screen yielded 1373 articles. Fourteen articles, published between 1977 and 2023, met inclusion criteria. Sixteen (16) patients were identified with LGG that presented initially as hemorrhage. The most common tumors were pilocytic astrocytoma (6/16), subependymoma (4/16), and ependymoma (2/16). The most common presenting symptoms were headaches (9/11) and impaired consciousness (9/11). Eleven patients underwent gross total resection of the tumor, while four patients received partial resection. Outcomes included two mortalities and one recurrence after six months; the thirteen remaining patients had no recurrence at final reported follow-up.

### Conclusion

LGGs presenting with hemorrhage are associated with more severe initial symptoms. Though

very uncommon, it is imperative to recognize the possibility of an underlying low-grade neoplasm in the setting of hemorrhage. Such early identification can lead to expeditious surgical intervention which can alleviate symptoms, lead to diagnosis, and ultimately trigger adjuvant treatment that has the potential to prolong survival. Continued research on the underlying pathophysiology of these hemorrhagic low-grade tumors is needed to further stratify risk in these populations.

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## Introduction

Gliomas are the most common primary tumors of the central nervous system (CNS), accounting for 80% of all malignant primary brain tumors [1], [2], [3]. Per the World Health Organization (WHO) classification of CNS tumors, grade 1 tumors are well-circumscribed, slow-growing tumors that may be curable if completely resected [1], [4]; this group includes pilocytic astrocytomas and subependymomas [3]. Grade 2 gliomas, such as astrocytomas and oligodendrogliomas, are the more common infiltrating gliomas [1], [3]. The grade 3 group, including anaplastic oligodendrogliomas, anaplastic astrocytomas, and anaplastic ependymomas, have an intermediate clinical course, while the grade 4 glioblastoma is the most aggressive [4].

Low-grade gliomas (LGG) consist of WHO grades 1 and 2 tumors and make up 6.4% of all adult primary CNS tumors [2]. Presentation of gliomas is dependent on pathology as well as location. Seizures are common in patients with oligodendrogliomas and other infiltrating lesions, as they tend to invade the cortex [5]. Patients can also present with nonspecific findings such as headache, vertigo, and lethargy [5], [6]. Early suspicion and identification of LGG is critical, as expeditious treatment is a significant prognostic factor. Hemorrhage within a low-grade glioma is rare but appears to be associated with poor outcomes [7]. In general, intracranial hemorrhage occurs at a rate of 3.7%–7.2% in gliomas as a whole and more so in high-grade gliomas (HGG) compared to LGG [8]. It is important to understand the characteristics associated with hemorrhagic gliomas to improve accuracy and speed of diagnosis for relevant patients.

The pathogenesis of hemorrhages in LGG is widely unknown. In HGG, hemorrhagic onset is attributed to necrosis of the blood vessels and increased neovascular proliferation [8]. Especially in glioblastoma, hemorrhage originates from new vessels that traverse necrotic areas or invasion of large vessels by the tumor, leading to weakening and rupturing of vessel walls [9]. Though the pathogenesis is unclear, it is plausible that growth of the tumor into nearby vasculature can lead to hemorrhage. In a similar fashion, the pathogenesis of seizures is linked to invasion into surrounding normal tissue and release of excitatory neurotransmitters [10], [11]. Moreover, changes in seizure control after a period with no or controlled seizures is associated with tumor progression [12]. While more evidence is needed, the pathogenesis of hemorrhage in LGG may arise from invasion of the tumor and changes to the chemistry of the peritumoral tissue.

The presence of hemorrhage can be a complicating factor for identifying an underlying glioma given the tendency of hemorrhage to obscure detection on both computed tomography (CT) and magnetic resonance imaging (MRI). In this paper, we present a case of a grade 2 astrocytoma presenting with intratumoral hemorrhage as well as a systematic review of the literature to

elucidate patterns in the presentation and pathology of LGG that present as hemorrhage.

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## Section snippets

### Methods

A query of the Pubmed and Embase databases was performed on 5/31/2023 in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA)17 guidelines. Search terms (glioma OR astrocytoma OR oligodendroglioma OR “glioma”[MESH] OR “astrocytoma”[MESH] OR “oligodendroglioma”[MESH]) AND (hemorrhage OR bleed OR hematoma) AND (acute) were used. There was no limitation for time of publication. Duplicate articles were removed and inclusion and exclusion criteria were ...

### Case report

A 50-year-old female presented with rapidly progressive confusion and behavioral changes over the course of one day. She then became progressively lethargic with episodes of emesis and incontinence. Her husband brought her to an outside hospital (OSH) for evaluation where workup included a CT scan of the head showing an acute large right frontal intracranial hemorrhage with some extension into the ventricles. The patient was transferred to our facility for further evaluation and management.

On ...

### Discussion

Low-grade gliomas, WHO grades 1 and 2, are slow-growing tumors that present with clinical signs and symptoms related to compression of nearby structures [14]. Early detection of these tumors allows for prompt management to improve symptoms (especially seizure activity), obtain pathologic tissue for diagnosis, and reduce the likelihood of malignant transformation. The most common presenting symptoms for LGG include seizures, headache, and vertigo [14], [15]. Intracranial hemorrhage occurs at a ...

### Limitations

The goal of this systematic review was to summarize common characteristics of LGG presenting as acute hemorrhage and investigate whether such hemorrhage is a poor prognostic sign. The first limitation is the small sample size; although hemorrhage in LGG is fundamentally rare, the small sample size makes it difficult to generalize findings. Further, due to the large range of follow-up durations and heterogeneity in reporting, it is not possible to comment on outcomes as they relate to long-term ...

## Conclusion

Low-grade gliomas (LGG) infrequently present with acute intracranial hemorrhage. Exacerbation of subacute symptoms leading to sudden neurologic decline may be indicative of hemorrhage within LGG. Furthermore, the hemorrhage often presents within the tumoral margins on imaging though spread outside of the tumor is not uncommon. Locating these neoplasms can be challenging in the face of hemorrhage since this often obscures the tumor on imaging. Specific imaging characteristics, such as vasogenic ...

## CRedit authorship contribution statement

**Aarti Kishore Jain:** Writing – review & editing, Writing – original draft, Methodology, Data curation. **Sima Vazquez:** Writing – review & editing, Methodology, Data curation. **Sabrina Zeller:** Writing – review & editing. **Eris Spirollari:** Writing – review & editing. **Simon J Hanft:** Writing – review & editing, Conceptualization. ...

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. ...

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