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Clinical Study

Clinical attributes and surgical outcomes of angiocentric gliomas

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ABSTRACT

Angiocentric gliomas (AG) are exceedingly rare low-grade neoplasms which often present in the form of intractable epilepsy within younger patients. The current study extensively reviews all reported cases which were pathologically verified as AG in the literature to analyze clinical attributes and surgical outcomes of this neoplasm. There were 88 patients with AG reported in the literature consisting mostly of pediatric cases. The sex distribution consisted of 45 males and 36 females with the remaining seven cases not documenting sex. The average age of initial diagnosis was 16 years with almost half of all diagnosed patients being within the first decade of life. In cases where extent of resection was reported, gross total resection (GTR) was achieved in 54 patients, subtotal resection (STR) in 16, and biopsy only in three. Post-operative complications were transient and only occurred in three patients with no reports of death following surgery. Only five cases reported tumor recurrence on follow-up. Eight patients had seizure recurrence post-operatively and GTR offered improved rates of seizure control when compared to STR ($p = 0.0005$). Nearly half of the cases of AG are diagnosed within the first decade of life and they usually manifest with intractable seizures. GTR appears to offer better seizure control in the post-operative period. Surgical resection is the mainstay therapy for AG as post-operative complications and tumor recurrence remain uncommon. Since the number of reported cases is limited, future studies with longer follow-up periods will help elaborate more long-term outcomes.

1. Introduction

Angiocentric gliomas (AG) are rare entities, which usually manifest superficially with a predilection for fronto-parietal and temporal lobes. AG are considered World Health Organization (WHO) grade I due to their indolent nature. Gross total resection (GTR) tends to be curative, resulting in regression of epileptogenic events. A hallmark of these lesions is that they almost inevitably present with a history of intractable seizures in childhood and young adults. Epileptogenic events are common presenting symptoms for patients harboring AG lesions.

Indolent and slow growing lesions, such as low-grade gliomas, tend to be more epileptogenic in nature. High-grade gliomas with a rapid growth rate tend to present with symptoms related to increased intracranial pressure, as opposed to seizure-related symptoms [1]. In contrast, tumors classified as low-grade more frequently present with seizures which may be due to the development of functional changes attributed to the indolent growth rate [2]. Additionally, lesions which are superficially located in the frontal and temporal lobes are prone to present with seizures compared to deep-seated neoplasms [1]. AG were initially reported in 2002 by Wang et al. as "angiocentric bipolar astrocytoma", and then further refined by two independent subsequent reports by Wang et al. and Lellouch et al. in 2005 [3–5]. They were ultimately classified in 2007 by the WHO as "other neuroepithelial tumors" [6]. Given the rarity of these neoplasms, published clinical experience has been limited to small case series and case reports. Consequently, potential clinical parameters which may influence patient outcome remains poorly elucidated. The present study identified all patients with AG reported in the literature to further elaborate on the clinical features and operative outcomes of AG to optimize management of these rare tumors.

2. Methods

2.1. Literature search

A broad literature search was conducted on 26 August 2015. This search included published case reports, case series, and

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abstracts. Medline (OVID/PubMed), Scopus, Embase and Web of Science databases were searched utilizing the keywords "angiocentric" AND "glioma". In order to refine the results, a limitation for English-only manuscripts was imposed on the search. All relevant articles were screened and our inclusion criteria consisted of including articles that sufficiently stratified each individual patient with the diagnosis of interest. The reference lists from acquired articles were also searched in order to identify any additional relevant publications not included in the original literature search. Studies with limited patient data, or data that could not be disaggregated were excluded from the analysis.

2.2. Data collection and statistics

The following variables were collected by three researchers (L.A., W.C., J.D.): age of diagnosis, interim period from onset of symptoms to clinical presentation, sex, tumor location, tumor size, presenting symptoms, radiological findings, histopathological findings, Ki-67/MIB-1 proliferation index, extent of resection, adjuvant therapy, seizure recurrence, tumor recurrence, clinical findings on last follow-up, and overall survival. Length of time between onset of symptoms and diagnosis following surgery was inclusive of onset of seizure disorder. Analysis of categorical data was performed with Fisher's exact t-test. All tests were two-tailed, with $p < 0.05$ considered statistically significant.

3. Results

3.1. Demographics

Thirty-nine articles, comprising a total of 88 patients with AG, met inclusion criteria and were included in our analysis (Table 1). Fifty-one percent were males (n = 45), and 40% females (n = 36). Sex was not documented in seven patients (9%). Excluding one case which noted age as "childhood", the age range of initial diagnosis spanned from 2 to 79 years with an average age of 16 years. Nearly half of the reported patients fell between the age range of 1–10 years old (Fig. 1).

3.2. Presentation

The time interval from the initial onset of symptoms (which we deemed as the age when a seizure disorder first began) to diagnosis was reported in only 44 patients, ranging from acute presentations to 38 years with a mean of 6 years. Out of the 88 patients, 86% (n = 76) presented with a history of seizures. The next most commonly reported symptoms were headache (8%) and visual impairment (8%). Presenting symptoms are summarized in Table 2. There were no reported cases of incidental tumor discovery.

3.3. Tumor features

Tumor size was reported in 30 cases which ranged from 1 to 8 cm in largest diameter, and the mean was 3.1 cm. The most commonly reported location of AG was the temporal region (39%), closely followed by the frontal lobar region (30%) (Table 3).

3.4. Histology

Typical immunohistochemical staining for these lesions demonstrate immunoreactivity for glial fibrillary acidic protein (GFAP), vimentin, epithelial membrane antigen (EMA), and S-100. The EMA stains paranuclear or intercellular regions which leads to the appearance of a "dot-like" pattern. Other positive stains include podoplanin, epidermal growth factor receptor, and CD34.

The presence of mitoses was reported in 13 cases, but reporting was not uniformly quantitative. Seven cases noted that mitotic figures were "rare". Another case reported mitotic activity as being one per/50 high-power fields and the remaining three cases ranged from 1 to 6 per/10 high-power fields. Sixty-five cases provided a numerical MIB-1/Ki-67 proliferation index value for the resected initial tumors which ranged from <1% to 12%. There were two cases demonstrating 12% on MIB-1 staining; one of these cases recurred 12 years later and the recurrent lesion had an index of 22% [7]. Four cases reported the index as being "low" and the remaining cases did not report a proliferation index.

3.5. Imaging

Reported imaging characteristics are very heterogeneous for AG. Reports on CT scan have thus far been poorly documented in the literature. From the sparse number of reports noting a description of the CT scan, it appears that the lesion ranges from a hypodense to hyperdense, or heterogeneous appearance [8–10]. On MRI, most AG were hyperintense on T2-weighted imaging and were largely non-enhancing after administration of gadolinium with the exception of three cases. Two of these cases demonstrated a mild irregular internal enhancement while the other noted patchy peripheral enhancement [8,9,11]. T1-weighted imaging was highly variable with some cases demonstrating a hypointense, isointense, or hyperintense appearance. Other features reported included peripheral cortical "rimlike" hyperintensity surrounding the tumor on T1-weighted imaging [5,9,12,13], stalk-like extension to the ventricle on T2-weighted and fluid-attenuated inversion recovery imaging [5,12], and associated calcifications in five cases [12,14–17].

3.6. Treatment

Surgery was the mainstay treatment with 61.4% (n = 54) of patients undergoing GTR, 18.2% (n = 16) patients undergoing STR, 3.4% (n = 3) undergoing biopsy, and 17% (n = 15) of cases not documenting extent of resection (EOR). Post-operative complications were reported in three cases (4%) [18–20], comprising transient hemiparesis, meningitis, and right-sided hemianopsia. There were no deaths reported post-operatively. There were five reported cases (5.6%) of recurrence from the 88 patients accrued (Fig. 2). Time to recurrence after initial surgical intervention ranged from 6 months to 12 years. Follow-up was reported in 83 patients with an average of 36 months (median of 24 months) after initial surgery.

Three of the recurrent cases underwent GTR, one underwent STR, and EOR was not reported in one patient. Of the three patients who underwent biopsy, two received adjuvant radiotherapy (RT) and did not have recurrences at last follow-up, ranging from 5 to 24 months. Mean follow-up for these patients was 15 months. Mean length of follow-up following GTR and STR was 35 months (median 18.5 months) and 32 months (median 24 months), respectively.

In nearly all cases, surgery was the primary and sole treatment modality. Only a sparse number of cases (5.6%; n = 5) underwent RT and only one case underwent chemotherapy after initial resection. Only 5.5% (n = 3) of patients who underwent GTR received RT, while 67% (n = 2) of the patients who underwent biopsy without subsequent surgical intervention did. None of the patients who underwent STR received adjuvant treatment with radiation. Out of the five patients who underwent radiation, only one suffered a recurrence after a period of 6 months [8].