Journal of Clinical Neuroscience 21 (2014) 1310–1314

Contents lists available at ScienceDirect

Journal of Clinical Neuroscience

journal homepage: www.elsevier.com/locate/jocn

Clinical Study

Primary intracranial haemangiopericytoma: Comparison of survival outcomes and metastatic potential in WHO grade II and III variants

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ARTICLE INFO

Article history:
Received 18 May 2013
Accepted 13 November 2013

Keywords:
Grade
Haemangiopericytoma
High grade
Local recurrence
Low grade
Metastasis

ABSTRACT

Primary intracranial haemangiopericytomas (HPC) are rare, highly vascular tumours with a high propensity for local recurrence and distant metastasis. Optimal treatment includes maximal surgical resection followed by adjuvant radiotherapy. In 2007, new histopathological grading criteria were introduced to differentiate between high grade (World Health Organization [WHO] grade III) and low grade (WHO grade II) tumours. Given the rarity of this tumour, there is a paucity of information regarding the prognostic significance of histological grade. We conducted a retrospective review of our 20 year experience in treating 27 patients with HPC at our institution. Statistical analysis to compare overall survival, local recurrence rate and metastatic potential between the two grades were conducted using Kaplan–Meier analysis. The estimated median survival for grade II HPC was 216 months and for grade III tumours was 142 months. On multivariate analysis, grade II tumours were associated with better survival than grade III lesions (hazard ratio = 0.16, 95% confidence interval 0.26–0.95; $p = 0.044$). During the study period, 33% of grade III tumours developed local recurrence compared to 21% of grade II tumours. Metastases were found in 36% of grade II patients and 25% of grade III patients. There was no significant statistical difference in local recurrence rate and metastasis between the two grades. Higher histological grading in HPC is associated with worse overall survival. However based on our series higher histological grading is not associated with higher local recurrence or distant metastatic rates.

1. Introduction

Primary intracranial haemangiopericytomas (HPC) are rare, highly vascular tumours with a high propensity for local recurrence and distant metastasis [1]. They originate from pericytes around capillaries and account for less than 1% of all intracranial tumours [2]. They share a common arachnoidal location with meningiomas [1]. Establishing a preoperative diagnosis can be challenging, as most radiological features are similar to those typically associated with meningiomas [3]. Optimal treatment includes maximal surgical resection followed by adjuvant radiotherapy [1,2]. Despite this, previous studies have reported local recurrence rates between 30% to 90% and a 15 year risk of peripheral metastasis approaching nearly 50% [1,4,5]. The role of chemotherapy is limited with HPC, but has been indicated in the treatment of peripheral metastatic disease [4].

HPC were previously classified as "angioblastic meningiomas". Its unique characteristics led the World Health Organization (WHO) to reclassify HPC as a separate entity in 1993. In 2007, new histopathological grading criteria were introduced to differentiate between high grade (WHO grade III) and low grade (WHO grade II) tumours. This concept was adopted from a large series on meningeal HPC published by Mena et al. in 1991 [6]. Given the rarity of this tumour and the recent introduction of the WHO grading scheme, there is very little information regarding the prognostic significance of histological grade and rationale for long term monitoring. In this paper, the authors report their 20 year experience in treating 27 patients with HPC at our institution. This paper aims to provide a long term comparative analysis and experience in both grade II and grade III intracranial HPC.

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http://dx.doi.org/10.1016/j.jocn.2013.11.026
0967-5868/

2. Methods

Patients diagnosed with HPC between 1989 and 2011 were identified by performing a computer search of a prospectively maintained database within the Department of Neurosurgery at Sir Charles Gairdner Hospital, Australia. Histopathology reports were verified to confirm the diagnosis of HPC. Relevant clinical, surgical and radiological data were collected by retrospective chart review. Information recorded included details of surgical treatment, adjuvant therapy, postoperative complications, local or distant recurrence, and peripheral metastasis at most recent follow-up. Extent of resection was quantified as gross total resection (GTR) or subtotal resection. Extent of tumour resection was established from operative notes and was defined as "gross total" after verification with available postoperative imaging (CT scan or MRI). Where there was insufficient information to confirm the extent of resection, it was documented as "unable to quantify".

HPC diagnosed prior to 2007 were not graded. Based on the WHO 2007 classification guidelines tumours with anaplastic features were designated as grade III. Features of anaplasia include high mitotic activity (more than five mitoses per 10 high power fields) and/or necrosis, plus at least two of haemorrhage, moderate to high nuclear atypia, and cellularity [7]. For the purposes of this study, all pathology slides were independently reviewed by an experienced neuropathologist (P.R.) who was blinded to the clinical and survival data of individual patients.

Overall survival was calculated from the time of initial surgery to death or the date of last known post-treatment follow-up. Histopathology grading was unable to be performed in one patient, hence they were excluded from survival and comparative analysis. Local recurrence was defined as unequivocal evidence supporting tumour growth in the postoperative site on imaging. Peripheral metastasis was deemed to be present if symptomatic lesions in extra-central nervous system sites were confirmed by imaging studies. Neuroaxis metastasis denoted new tumour development in the brain or spine distant from the primary operative site.

Statistical analysis of overall survival was conducted using the Kaplan–Meier product-limit method with confidence interval (CI) at 95% and the significant p value was set below 0.05. A Cox proportional hazards regression analysis was conducted to determine the factors associated with cause-specific survival. The chance for interaction between variables was further checked using a backward stepwise regression. Statistical analysis was conducted using the Statistics Package for the Social Sciences version 20 (SPSS, Chicago, IL, USA).

3. Results

A total of 27 patients with HPC were treated at our institution from 1989 to 2011. The median age of the 12 men and 15 women was 42 years (range 25–82 years). Supratentorial tumours were the most common, accounting for 76% of all cases. Most of these lesions (42%) were found in a parasagittal location. Posterior fossa and spine locations accounted for 12% and 4% of tumours, respectively. Two patients (7.4%) underwent preoperative cerebral angiogram and embolisation of arterial feeders prior to surgery due to radiological features of hypervascularity on MRI.

Pathological diagnosis of HPC was made by identifying typical features such as branching "staghorn" vasculature, widespread staining for reticulin and absence of staining for epithelial membrane antigen [1,8]. Based on WHO 2007 criteria, 12 (44.4%) patients were assessed as grade III and 14 patients (52%) were classified as having grade II HPC.

3.1. Treatment

All patients underwent surgical resection. In total, 23 patients (85%) achieved GTR and two patients (7.5%) had subtotal resection. The extent of resection was unable to be quantified from operative notes in two patients. These two patients had their surgery at least 18 years ago and postoperative imaging data were not available. Early in the surgical series, one patient died in the early postoperative period due to severe blood loss. This patient was excluded from subsequent statistical analysis of data. One patient underwent a two stage procedure to achieve GTR after severe blood loss was encountered during the first stage of surgery. A cerebral angiogram was undertaken and arterial feeders were embolised prior to the subsequent surgery to excise the residual disease (estimated to be 30% of original tumour volume).

Early external beam radiotherapy to the peri-resection zone (dose ranges 48 to 60 Gy) was administered to 63% (17/27) of patients following initial surgery. Two patients who had early external beam radiotherapy also received stereotactic radiosurgery for a subsequent small recurrence. In the remaining patients, 50% (5/10) who had not received radiotherapy treatment following their initial surgery subsequently received adjuvant radiotherapy for the first recurrence after surgery.

3.2. Survival

Patients were followed up by both the neurosurgical and radiation oncology teams in their respective clinics. All patients were seen within 3 months of surgery and had regular clinic visits with either annual or bi-annual follow-up brain imaging performed. Eleven patients (including one early postoperative death) died during the follow-up period. The median overall survival for all patients was 216 months (Fig. 1). The overall survival rates at 5, 10, 15 and 20 years were 79%, 56%, 44% and 22%, respectively. The estimated median survival for grade II HPC was 216 months and for grade III HPC was 142 months (Fig. 2). On multivariate analysis, grade II tumours were associated with better survival than grade III lesions (hazard ratio [HR] = 0.16, 95% CI 0.26–0.95; $p = 0.044$) (Fig. 2, Table 1). Patient age did not impact survival, but male sex was associated with better survival (HR = 0.097, 95% CI 0.013–0.73; $p = 0.023$) (Fig. 2, Table 1). Neither the presence of peripheral metastasis nor local recurrence was significantly associated with poorer survival rates. Treatment variables such as GTR and adjuvant radiotherapy were also not associated with better survival.

3.3. Local recurrence

The local recurrence rate in our series was 28% (7/25) at a median follow-up period of 172.5 months (14.4 years). The 5, 10 and 15 year recurrence rates were 20%, 54% and 77%, respectively. In the study period, 55.6% (5/9) of patients who did not receive early adjuvant radiotherapy developed local recurrence. By comparison, only 12.5% (2/16) of patients who received adjuvant radiotherapy developed local recurrence. On multivariate analysis, early adjuvant radiotherapy following the first surgery was associated with reduction in local recurrence (HR = 0.071, 95% CI 0.007–0.70; $p = 0.023$). During the study period, 33% of grade III tumours developed local recurrence compared to 21% of grade II tumours. However, a higher histological grade was not statistically associated with increased risk of local recurrence ($p = 0.52$).

3.4. Metastasis

In this series, 32% (8/25) of patients developed symptomatic peripheral metastasis during a median follow-up period of 204.6 months. Neuroaxis metastasis was noted in 12% (3/25) of