



Clinical Study

Bifocal germinomas in the pineal region and hypothalamo-neurohypophyseal axis: Primary or metastasis?



Hui Zhang, Song-Tao Qi*, Jun Fan, Lu-Xiong Fang, Bing-Hui Qiu, Yi Liu, Xiao-Yu Qiu

Department of Neurosurgery, Nanfang Hospital, Southern Medical University, Guangzhou 510515, China

ARTICLE INFO

Article history:

Received 4 March 2016

Accepted 4 June 2016

Keywords:

Bifocal germinomas

Differential diagnosis

Hypothalamo-neurohypophyseal axis

MRI

Pineal region

ABSTRACT

Whether bifocal germinomas (BFGs) synchronously presenting within the pineal region and the hypothalamo-neurohypophyseal axis (HNA) are primary germinomas of dual-origin remains to be elucidated. We analyzed MRI images and clinical features of 95 neurohypophyseal germinomas and 21 BFG patients and developed a tentative definition of the BFGs. We found dual-primary BFGs (true BFGs) do exist. The fundamental difference between primary and metastatic HNA germinomas was the direction of tumor growth. For a true BFG, the primary HNA tumor grew from the neurohypophysis toward the hypothalamus and almost invaded the whole pituitary stalk. For a false BFG (primary pineal germinoma with HNA metastasis), the metastatic HNA tumor first appeared at the third ventricular floor (TVF), grew toward the neurohypophysis, but commonly did not invade the inferior pituitary stalk. Compared to false BFGs, true BFGs commonly had diabetes insipidus as the first symptom, dysfunction of the anterior pituitary, no high-intensity MRI signal at the posterior pituitary, a larger extension of the HNA tumor, and fewer numbers of remote lesions from cerebrospinal fluid seeding. Accordingly, 12.8% (12/96) of our germinoma patients had true BFGs, and of these, 58.3% (7/12) were free of remote metastases and warranted treatment with limited radiotherapy. True BFGs with remote metastases and all false BFGs should be treated with craniospinal irradiation. We provided evidence for the diagnosis of true BFGs that is useful for radiotherapy strategy, suggesting that the existence of metastasis to other locations is not a diagnostic criterion for a true BFG.

© 2016 Elsevier Ltd. All rights reserved.

1. Introduction

Intracranial germ cell tumors (iGCTs) frequently present as synchronous pineal region (PR) and hypothalamo-neurohypophyseal axis (HNA) tumors, with an incidence of 2–41% [1]. These tumors, primarily germinomas, are categorized as bifocal germinomas (BFGs) [2]. Although the primary treatment strategy for BFGs, craniospinal irradiation (CSI), has excellent long-term disease control, it can have adverse effects [3]. For non-metastatic germinomas, local irradiation plus full ventricular irradiation has been recommended to minimize adverse effects [4]. Whether BFGs constitute metastatic or primary tumors is unclear; consequently, the proper treatment for BFGs remains controversial [3,5–7].

Cuccia and Alderete defined suprasellar/pineal bifocal germ cell tumors (SPBTs) as a group of iGCTs that lacked seeding between tumors or to distant sites and suggested that spinal radiotherapy was unnecessary [5]. Weksberg et al. divided BFGs into two groups: tumors without metastases to other locations (group 1)

versus tumors with metastases to other locations (group 2) [6]. They found that limited radiotherapy for group 1 tumors was associated with spinal failures. Phi et al. [7] believed that bifocal GCTs may result from metastatic spread of suprasellar or pineal GCTs and recommended CSI for bifocal GCTs. The above-mentioned authors did not provide criteria to further differentiate HNA tumors as primary or metastatic, and the definitions of bifocal GCTs were contradictory.

Several important issues remain regarding BFGs including: (1) whether any dual-origin primary BFGs exist; (2) if bifocal tumors of the PR and HNA are dual-origin primary tumors; and (3) if dual-origin primary BFGs are associated with metastases to other locations. During the endoscopic surgical treatment of a patient with BFGs, we found that the HNA tumor was located outside the ependyma of the third ventricular floor (TVF), which excluded the possibility of metastasis of the HNA tumor from the pineal region tumor and confirmed the case as a true BFG. Meanwhile, we observed two other BFGs whose HNA tumors were obviously different from neurohypophyseal germinomas on MRI. If HNA tumors are primary, they should have the same MRI features and initial clinical symptoms as neurohypophyseal germinomas [8].

* Corresponding author. Tel./fax: +86 02061641806.

E-mail address: zhanghuinf@163.com (S.-T. Qi).

Therefore, we conducted a systematic literature review of neurohypophyseal germinomas and a retrospective analysis of intracranial germinoma (IGM) patients from our institution and used the analyses to develop a tentative definition of BFGs.

2. Materials and methods

2.1. Systematic literature review

PubMed was searched for English-language, original articles published from January 1990 to December 2014, using the following terms or combinations: (“infundibulum” OR “stalk” OR “hypothalamus” OR “neurohypophysis” OR “posterior pituitary” OR “posterior lobe” OR “suprasellar” OR “intrasellar”) AND (“germinoma” OR “germinomas”). Each study was required to contain a minimum of three neurohypophyseal germinomas and to also indicate the locations of the tumors involving the following regions: the intrasellar/posterior lobe/pituitary stalk (PS)/neurohypophysis and the TVF/third ventricle/hypothalamus.

The search was expanded based on the citations of the identified articles. The following data were collected and pooled together from all patients: the ratio of high intensity signal (HIS) on T1-weighted MRI within the posterior pituitary, the presence of diabetes insipidus on the first visit, the frequency of anterior pituitary hormone deficiencies (APHDs), and the extension of tumor and the incidence of thickened PS.

2.2. Retrospective analysis of patients from our institution

Approval for this study was obtained from our institutional ethics committee. Data from 96 IGM patients treated at our hospital from March 2005 to March 2014 were retrospectively analyzed.

2.2.1. Inclusion criteria for the intracranial germinoma group

Inclusion criteria for the IGM group were: (1) pathologically confirmed diagnosis of IGM; (2) serum alpha-fetoprotein (AFP) level <8.1 ng/mL [9]; (3) pretreatment MRI and/or CT scan showing no hemorrhage [10] or teratoma component [11] within the tumor; (4) serum β -human chorionic gonadotropin (β -hCG) level <100 mIU/mL [12]; (5) diagnostic radiotherapy at a dose of 20 Gy to the tumor area followed by MRI indicating a >50% decrease in the tumor size [13]; and (6) after radiotherapy, any residual tumor had resolved during follow-up. Patients must fulfill both criteria (1) and (2) for a pathological diagnosis of IGM. For a clinical diagnosis of IGM, patients must fulfill criteria (2), (3), (4), (5) and (6).

Information regarding gender, age at diagnosis, clinical presentation, and associated neurologic deficits was extracted from the medical records. The pretreatment levels of serum and cerebrospinal fluid (CSF) β -hCG/AFP and anterior pituitary hormones were collected.

We defined multiple IGMs involving both the HNA and the PR with or without metastasis to other locations as BFGs.

The 96 patients had the following tumors: 21 BFGs with serum pretreatment β -hCG levels <50 mIU/mL; 22 neurohypophysis germinomas (three with at least one metastasis to a non-PR region); 48 PR germinomas (eight with at least one metastasis to a non-HNA region); four germinomas involving the basal ganglia; and one cerebellar germinoma.

2.2.2. MRI analysis of bifocal germinoma patients

All patients had an enhanced MRI of the full central nervous system (CNS). Patient 19 was found to have a metastasis in the spinal subarachnoid space. Two neurosurgeons with expertise in neuroimaging (J. F. and B-H. Q.) separately analyzed the MRI data in a double-blind manner using the “straight line measurement” tool

of the JW-PACS Software© (Southern Medical University Network Center, Guangzhou, China). Under 4 \times magnification of either the coronal or sagittal MRI slices, the minimum diameter (mm) of the PS, the HIS on T1-weighted MRI within the posterior pituitary, the size of the PR or HNA tumor, and the total number of CNS tumors were recorded. A senior neurosurgeon (L-X. F.) independently judged the extension of tumor within the HNA and the shape of the neurohypophyseal axis (NA). All data were transferred to H. Z. and Y. L. for statistical analyses under the guidance of S-T. Q. The data from the 22 neurohypophyseal germinomas were collected and pooled with the data from the literature search.

2.2.3. Treatment strategies for 21 patients with bifocal germinomas

One patient with obstructive hydrocephalus underwent endoscopic partial HNA tumor resection plus third ventriculostomy. The remaining patients were diagnosed clinically as having BFGs. All 21 patients were treated with CSI.

2.2.4. Criteria for determining metastatic hypothalamoneurohypophyseal axis tumors (false bifocal germinomas)

It was assumed that the HNA tumors meeting one of the following conditions were metastatic tumors (false BFGs): (1) the inferior PS was <3.0 mm (normally, the maximum size of the smallest part of the PS is 3.0 mm) [14], with or without obvious superior PS thickening, indicating that the inferior PS was not involved; and (2) HIS within the posterior pituitary was present on T1W MRI.

2.3. Statistical analysis

The 21 BFG patients were categorized as true or false BFGs based on conditions previously described. All continuous data were expressed as mean \pm standard deviation (SD). Chi-squared test and phi coefficient analyses were used to analyze the relationships between categorical variables of true versus false BFGs. Student's t-test was performed to compare differences in continuous data between true versus false BFGs. Multivariate logistic regression was utilized to determine potentially predictive variables for BFGs, while controlling for other variables. A *P* value <0.05 was considered statistically significant. All analyses were performed using IBM SPSS Version 20 (SPSS Statistics V20, IBM Corporation, Armonk, New York, USA).

3. Results

3.1. Analysis of neurohypophyseal germinoma features

A total of 95 neurohypophyseal germinomas were included in this study: 73 patients from 12 relevant studies [8,14–24] identified by the literature search, and 22 patients from our institution (Table 1).

Of these 95 neurohypophyseal germinomas, 72 patients had MRI analysis of the posterior pituitary; none presented with HIS. Cranial MRIs of the 95 patients showed that, except for two intrasellar neurohypophyseal germinomas, all others had thickening of the entire PS, including thickening of the inferior PS, due to tumor. In 90/95 (94.7%) patients, the presenting symptom was diabetes insipidus. Three patients without diabetes insipidus were associated with pan-hypopituitarism, and the other two patients lacked symptom data. Detailed analyses of all patients, including clinical symptoms and the MRI findings, are shown in Table 1.

3.2. Differentiation between true and false bifocal germinomas

A patient received endoscopic surgery for partial resection of an HNA germinoma and third ventriculostomy due to obstructive

Download English Version:

<https://daneshyari.com/en/article/5629872>

Download Persian Version:

<https://daneshyari.com/article/5629872>

[Daneshyari.com](https://daneshyari.com)