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Clinical course and management of intracranial meningiomas in neurofibromatosis type 2 patients

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ABSTRACT

Objective: The aim of this study is to evaluate our surgical experience with intracranial meningiomas in NF2 patients and provide knowledge of the natural history of these lesions.
Methods: We included in the natural growth study patients with the diagnosis of NF2 who harbored intracranial meningiomas and were observed for at least 1 year. Tumors that were resected before achieving long-term follow-up were excluded from this analysis.
Results: We found 118 intracranial meningiomas in 34 patients in our series. 8 meningiomas in 7 patients were symptomatic. It was found that with an increase in tumor volume, brain edema and with the tumor location at the skull base, meningiomas are more likely to be symptomatic. Univariate analysis revealed that tumor growth was associated with a younger age at the onset of NF2-related symptoms, greater initial tumor volume, brain edema and with the presence of intracranial non-vestibular schwannoma. Multivariate analysis showed that the probability of tumor growth is associated with prolonged follow-up time. De novo meningiomas exhibited a significantly higher growth rate than other meningiomas. These tumors were more frequent in patients with intracranial non-vestibular schwannoma and with increasing length of meningioma observation.
Conclusion: Meningiomas occur in about half NF2 patients. Many of them exhibit slow growth and long remain asymptomatic, however, those associated with early onset of NF2 symptoms and other features of the disease severity should be monitored in case of clinical and radiological progression that may require surgical treatment.

1. Introduction

Neurofibromatosis type 2 is an autosomal dominant syndrome predisposing to multiple benign tumors of the central and peripheral nervous system. The hallmark of this disease is the development of bilateral vestibular schwannomas, which occurs in 90–95% of patients [1–3]. Meningiomas are the second most frequent tumor type in NF2. They are often multiple [1–3] and occur in about half of these patients [4]. They develop at a younger age than their counterparts with sporadic cases of meningiomas [2,3,5]. In the pediatric age

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group meningiomas are often the first sign of NF2 [6]. Furthermore NF2 is diagnosed in 10–29% of children presenting with meningioma [7–10]. Meningiomas associated with NF2 frequently show aggressive features on pathological examination [11,12]. A higher proliferative potential of NF2 meningiomas, however, is observed in tumors requiring surgery while remaining slow-growing lesions are probably less aggressive nature [13]. Meningiomas in NF2 patients are associated with disease severity as risk of mortality is 2.5-fold greater in people with meningiomas compared to those without such lesions [14].

Yet little is known about long-term natural history of meningiomas in NF2 patients. Data about meningioma surgery in NF2 are sparse in the literature. Knowledge of meningiomas behavior in NF2 patients should be determined for their optimal management, including timing of surgical treatment. The aim of this study is to evaluate our surgical experience with intracranial meningiomas in NF2 patients and provide knowledge of natural history of these lesions. We sought to define whether meningiomas are a major problem in the treatment of patients with NF2, and whether we can safely observe meningiomas in these patients. We assessed clinical characteristics, new tumor development, surgical outcome and growth patterns of meningiomas in NF2 patients with long-term clinical and radiographic follow-up. Furthermore we compare NF2 patients with intracranial meningiomas to those without to identify differences between the two patient subgroups.

2. Materials and methods

2.1. Patient population

Thirty four patients with neurofibromatosis type 2, as defined on the basis of the modified National Institute of Health (NIH) Consensus Panel Criteria [15], were surgically treated at our institution between 1998 and 2014. We have retrospectively reviewed the clinical records, neuroimaging studies, and follow-up data of the treated patients. Among 34 patients, 13 had no intracranial meningiomas and 21 had one or multiple intracranial meningiomas. We included in the natural growth study patients with the diagnosis of NF2 who harbored intracranial meningiomas and were observed for at least 1 year. Tumors that were resected before achieving long-term follow-up were excluded from this analysis. Two meningiomas were resected at another institution and were not included in the study. Another 3 tumors were excluded from growth rate analysis given their short follow-up before resection. A total of 118 meningiomas in 21 patients met the inclusion criteria and were suitable for growth rate analysis. Resected tumors were graded according to the WHO 2000 and the WHO 2007 [16] grading scheme. All patients had a clinical examination and brain MRI study performed at least once a year.

2.2. Tumor measurements.

The T1-weighted multiplanar images with gadolinium enhancement were used for volume measuring. Tumor volumes were determined manually using the 3-diameters technique $V = (D_1 \times D_2 \times D_3)/2$ [17]. Multilobulated tumors were divided into individual compartments and tumor volumes of these components were then summed. 3D MRI sequences for the calculation of exact changes in tumor's volumes were not available. Tumors with no increase in its tumor volume were defined as stable. Tumor growth was defined as an increase in tumor size over a measurement interval. Tumor growth rate was calculated as: (final volume − initial volume)/follow-up interval. Tumor quiescence was defined as no tumor growth over 1-year interval. De novo meningiomas were defined as tumors that were undetectable on the previous imaging.

2.3. Factors affecting tumor growth rate

Clinical and radiological features that might be related to meningioma growth were recorded: age at first symptoms of NF2, sex, length of observation, tumor volume at diagnosis, peritumoral edema, skull-base tumor location, number of intracranial meningiomas and presence of non-vestibular schwannomas and spinal tumors.

2.4. Statistical analysis

Statistical analyses were performed in STATISTICA version 10.0 (StatSoft Inc., 2011). Quantitative variables were characterized by the arithmetic mean, standard deviation, median, minimum and maximum values and 95% CI (confidence interval). Statistical significance of differences between the two groups was analyzed with *t*-Student-test or Mann–Whitney *U*-test. Statistical significance of differences between more than two groups was tested by an *F* test (ANOVA) or Kruskal–Wallis test. In the case of two variables associated model *t*-Student-test or Wilcoxon-test were used. Chi-square tests were used for categorical variables. Statistical significance was presumed $p = 0.05$.

3. Results

3.1. Patient and tumor characteristics

There were 19 women and 15 men in the entire cohort of NF2 patients. Characteristics of the patients and the comparison between NF2 patients with intracranial meningiomas and those without the lesions are given in Table 1. Among the 21 patients with meningiomas spinal ependymomas and non-vestibular schwannomas were more frequently observed. We found 118 intracranial meningiomas in 21 patients in our series (mean 5.2 ± 3.9 tumors/patient, range 1–16 tumors). 16 (76.2%) patients had multiple meningiomas. The most common locations of meningioma were convexity (37.3%), parasagittal and falx region (29.7%), and the skull base (27.1%). In 5 patients extensive tumor growth was observed along the parasagittal and falx region and convexity. MRI revealed adjacent parenchymal edema in 8 tumors (7%). 8 meningiomas in 7 patients were symptomatic. In 3 cases these tumors produced the first symptoms of the disease. In the other 5 cases meningiomas became symptomatic during the follow-up interval. In a univariate analysis, it was found that with an