3D Volumetric Measurement of Neurofibromatosis Type 2-Associated Meningiomas: Association Between Tumor Location and Growth Rate

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■ OBJECTIVE: **Treatment of meningiomas in neurofibromatosis type II (NF2) patients is challenging because the natural history of these tumors is unclear. More insight in tumor growth and factors predicting growth may contribute to a better clinical management. In this study, growth characteristics of supratentorial NF-related meningiomas were examined and the association between tumor growth rate and location was evaluated.**

■ METHODS: **In all NF2 patients followed up at the VU University Medical Center, who underwent a minimum of 3 consecutive scans, tumor volumes were assessed by using 3D volumetric measurement (Brainlab, Feldkirchen, Germany). Growth patterns were visually analyzed. To assess the association between tumor growth rate and tumor location, the meningiomas were divided in 3 groups on the basis of their location: skull base, convexity, and "other." Univariable and multivariable logistic regression models were built.**

■ RESULTS: **Twenty-one patients (13 females) with a mean (standard deviation) follow-up period of 5.55 (2.48) years and a total of 210 meningiomas were included in the analyses. Tumors followed different growth patterns and did not increase in size simultaneously within 1 patient. Skull base meningiomas had a significantly higher absolute growth rate compared with convexity (β = 0.91, 95% confidence interval [CI] 0.08–1.73) and "other" (β = 1.07, 95% CI 0.27–1.86) and a significantly higher relative growth rate on both linear and geometric growth rate compared with "other" (β = 90.73, 95% CI 5.50–175.95 and β = 18.63, 95% CI 2.94–34.31, respectively) on multivariable logistic regression.**

■ CONCLUSION: **Within a single patient, NF2-related meningiomas follow different growth patterns. Skull base meningiomas grow faster compared with other locations. Yearly magnetic resonance imaging scans and timely treatment of skull base meningiomas should be considered.**

INTRODUCTION

Neurofibromatosis type II (NF2) is an autosomal dominant disorder resulting from inactivating mutations of the NF2 tumor suppressor gene on chromosome 22. Affected individuals have a predisposition to develop several spinal and intracranial neoplasms including schwannomas, meningiomas, ependymomas, and astrocytomas (6). This heritable disorder has a birth incidence of 1 in 33,000 and a disease prevalence of 1 in 56,161 (13).

Meningiomas occur in more than 50% of the NF2 patients and are generally multiple (15, 21). The occurrence of meningiomas in these patients is associated with increased morbidity and mortality compared with NF2 patients without meningiomas (2, 6, 7).

Treatment of NF2-associated meningiomas includes watchful waiting, surgery, stereotactic radiosurgery, and radiotherapy (20, 28). The vast majority of patients require surgery, which is the core intervention in the case of significantly growing and/or symptomatic meningiomas (9, 15). Multiple sessions of surgery are commonly necessary during the life of an NF2 patient because meningiomas often recur and new meningiomas develop.

Key words
- Meningioma
- Neurofibromatosis type II
- Oncology
- Tumor growth
- Volumetric analysis

Abbreviations and Acronyms
CI: Confidence interval
GR: Growth rate
IQR: Interquartile range
MRI: Magnetic resonance imaging
NF2: Neurofibromatosis type II
VUmc: VU University Medical Center

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Citation: World Neurosurg. (2015) 84, 4:1062-1069.
http://dx.doi.org/10.1016/j.wneu.2015.05.068

Journal homepage: www.WORLDNEUROSURGERY.org

Available online: www.sciencedirect.com

Therefore scheduling of treatment (surgery or radiotherapy) is important. A wait-and-scan approach delays the risks involved in treatment. However, in the case of a fast-growing tumor, delay of intervention may cause symptoms that might not be reversible and limit the treatment options.

The presence of meningiomas is related to higher morbidity and mortality risk. Treatment is challenging, and optimal management has not yet been established. More insight is necessary in tumor growth and factors predicting growth. Only one study identified factors that might be associated with increased tumor growth of NF-related meningiomas: younger age at onset and female gender (11). However, because the meningiomas also appear to behave differently within individuals, other factors seem to be involved. In incidental (non-NF2) meningiomas the curve of growth can be linear, exponential, or S-shaped, and a relation between location and growth velocity was suggested (16, 17, 23). Additional knowledge about the relation between growth and tumor location may contribute to a better clinical management and treatment planning.

Therefore the aim of this study is to examine the growth patterns and growth rates of NF-related meningiomas and to evaluate the association between tumor growth rate and location.

MATERIAL AND METHODS

Patient Selection

All NF2 patients with supratentorial meningiomas, who were followed up at the VU University Medical Center (VUmc) from June 1997 to August 2012, were retrospectively selected for this study. NF2 was diagnosed on the basis of clinical criteria (8).

Data Collection

Age, gender, number of intracranial operations, radiotherapy, time of follow-up, and cause and date of death were collected through chart review. The VUmc radiology digital archive was systematically checked for brain magnetic resonance imaging (MRI) of the NF2 patients. All available imaging data of MRI-T1 contrast-enhanced brain scans were included until time of death or last follow-up. Last follow-up could be due to end of data collection (2008–2012), resection, follow-up at another institution, or merging of tumors; in some cases the meningiomas grew into each other during follow-up and volumes after merging were not used. Tumors with only 1 scan were excluded from the study.

Tumor Volumes

Tumor volumes were calculated using BrainLABsoftware (iPlan Cranial 2.6.1) by manually marking the contours of the tumor on each MRI. Localization of the tumor was determined on magnetic resonance images (SE) and confirmed by an experienced neurosurgeon (SP) or radiologist (ES).

Locations of meningiomas were defined as convexity, falx, parasagittal, tentorial, ventricle, intraorbital, orbit roof, sellar, olfactory groove, sphenoid wing, petrous ridge, and temporal fossa (**Figure 1**).

To avoid the inclusion of volumes of residual or recurrent tumors, the follow-up of a tumor stopped in case of surgical debulking/resection or radiotherapy. Thus volumes of residual or recurrent tumors were not included.

Determination of Growth Pattern and Rate

The tumor volumes were plotted against a time scale to explore growth patterns with the aim of MATLAB (version 7.14.0; the Mathworks, Natick, Massachusetts, USA). Only data of tumors with a minimum of 3 consecutive scans were used because growth patterns cannot be explored on the basis of 2 time points. Growth curves were visually analyzed (SE) and divided in exponential, linear, S-curved, and other/saltatory growth. For the analysis of growth rate, data of tumors with a minimum of 2 consecutive scans were used. Absolute growth rate (cm^3/year) was calculated using the following formula: (latest tumor size in cm^3—initial tumor size in cm^3)/interval of follow-up in years.

In the literature a commonly used formula for relative growth rate is based on the assumption that the tumors grow geometrically (17, 22, 29). However, because literature indicates that not all of the NF2-related meningiomas show a similar pattern (11, 22, 29), both a formula for annual linear growth and a formula based on the assumption that the tumors grow geometrically were used to calculate the relative growth rate. Thus relative growth rate

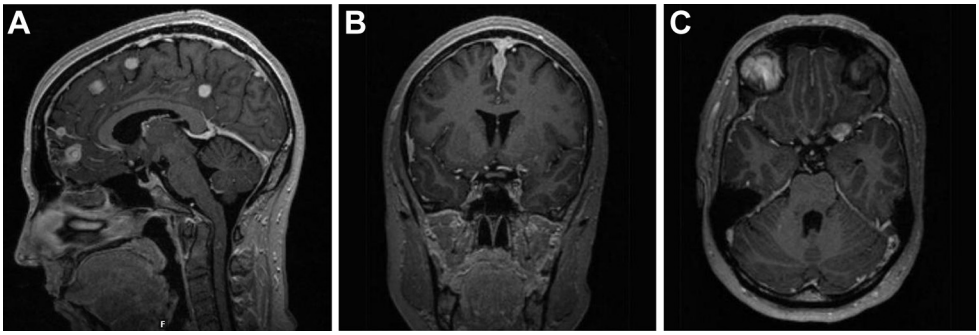

Figure 1. (**A**) Sagittal magnetic resonance imaging (MRI) showing multiple meningiomas at the falx and parasagittal. (**B**) Coronal MRI showing a meningioma at the falx and convexity. (**C**) Axial MRI showing a meningioma at the left sphenoid wing.