Nervous system: Meningioma

Anne Marie Capodano

Laboratoire de Cytogénétique Oncologique, Hôpital de la Timone, 264 rue Saint Pierre, 13005 Marseille, France (AMC)

Published in Atlas Database: July 2000
Online updated version: http://AtlasGeneticsOncology.org/Tumors/MeningiomaID5014.html
DOI: 10.4267/2042/37654
This work is licensed under a Creative Commons Attribution-Noncommercial-No Derivative Works 2.0 France Licence.
© 2000 Atlas of Genetics and Cytogenetics in Oncology and Haematology

Classification

Clinics and pathology

Disease
Meningiomas are tumors arising from cells of the meningeal covering of the brain and spinal cord. These tumors are generally slow growing masses. Neurological signs and symptoms appear by compression of adjacent structures.

Etiology
Meningiomas are known to be induced by radiation with an average time interval to tumor appearance of 20-35 years. The majority of patients with radio-induced meningiomas have received irradiation for tinea capitis or for primary brain tumor.

Epidemiology
Meningiomas account for 15-25% of primary intracranial and intraspinal neoplasms, with an annual incidence of approximately 6 per 100,000 individuals. Meningiomas are often multiple in patients with neurofibromatosis type 2 (NF2). Sporadic meningiomas may also be multiple. Meningiomas are most common during the sixth and seventh decade of life, but can occur in both children and in the elderly. There is a marked high frequency in females.
Histological features of a fibroblastic meningioma - Anne Marie Capodano.

**Clinics**
The vast majority of meningiomas arise within the intracranial, orbital, and intravertebral cavities.

**Pathology**
According to the World Health Classification (WHO 1993), the tumors are defined as Meningothelial meningioma, Fibroblastic meningioma, Transitional meningioma, Psammomatous meningioma, Angiomatous meningioma, Chordoid meningioma, and are classified according to increased degrees of anaplasia in grades I, II and III.

90% of meningiomas are slowly growing benign tumors that histologically correspond to grade I according WHO classification.

6-8% of meningiomas are designated as atypical meningiomas: WHO grade II. These tumors show a tendency for local recurrence even after complete resection.

2-3% of meningiomas exhibit histological signs of malignancy: these tumors are classified as anaplastic malignant meningiomas of WHO grade III. They have a high risk for local recurrence and metastasis.

**Treatment**
The treatment consists of total surgical resection of tumor.

**Prognosis**
The major evolution is recurrence. The tumor grade provides the most useful predictor of recurrence.

Benign meningiomas have a recurrence rate of about 7-20%. Atypical meningiomas recur in 29-38% of cases, and anaplastic meningiomas in 50-78% of cases. So, proliferation indices have been used to predict recurrence and survival.

**Cytogenetics**

**Cytogenetics Morphological**
Meningiomas were among the first solid tumors recognized as having cytogenetic alterations.

The most consistent change reported in benign meningiomas is partial (del(22)(q12)) or total deletion of chromosome 22. Loss of chromosome 22 more often occurs in meningiomas grade I.

Other karyotypic abnormalities, associated or not with monosomy 22, are seen in grade II (atypical meningiomas), and grade III (anaplastic meningiomas). The most frequent abnormalities changes are deletion of the short arm of chromosome 1, partial or complete loss of chromosome 10, and loss of chromosome 14. Unstable chromosome alterations including rings, dicentrics and telomeric associations, have been observed.

A statistical correlation between fibroblastic type and some chromosome abnormalities (monosomy 22 and telomeric associations), was reported. Studies support a postulated role of chromosome 22 as the primary event in the development of the majority of the meningiomas.
**Genes involved and proteins**

**Note**
Allelic losses: Molecular genetic findings using polymorphic DNA markers, confirmed that half of meningiomas have allelic loss of band q12 on chromosome 22. Atypical and anaplastic meningiomas often show allelic losses of chromosomal arms 1p, 9q, 10q, 14q, and 17p. LOH of chromosome 14 was the most frequent abnormality in atypical meningiomas: for this reason it is considered to be a step of malignant progression.

**NF2**

**Location**
22q12

**DNA / RNA**
Tumor suppressor gene.

**Protein**
Called merlin or schwannomin.

**Germinal mutations**
In neurofibromatosis type 2 patients.

**Somatic mutations**
Mutations in the NF2 gene are detected in approximately 60% of sporadic meningiomas. The majority of mutations are small insertions, deletions or non-sens mutations that affect splice sites. The common effect of such mutations is a truncated merlin protein. The frequency of NF2 gene mutations varies according to the meningiomas types. Few mutations of NF2 gene were observed in meningothelial meningiomas: only 25% of cases. 70-80% of fibroblastic and transitional meningiomas carry NF2 gene mutations.

Mutations and allelic loss events are also found in other tumors (schwannomas) and in neurofibromatosis type 2 tumours.

**Note**
LOH studies on chromosome 22 have also detected losses of genetic material outside the NF2 region. NF2 is likely to be the major tumor suppressor gene of meningiomas, but other genes localized in other loci on chromosome 22 are probably involved.

Another candidate gene on chromosome 22 is MN1 which has been implicated in a case of translocation in a meningioma.

PTEN mutations, a gene localized in 10q23, were described in anaplastic meningiomas.

Rare mutations were reported on the CDKN2A gene.

**References**


Lindblom A, Rutledge M, Collins VP, Nordenskjöld M, Dumanski JP. Chromosomal deletions in anaplastic meningiomas suggest multiple regions outside chromosome 22 as important in tumor progression. Int J Cancer. 1994 Feb 1;56(3):354-7

Lekanne Deprez RH, Riehm PH, Groen NA, Warringa UL, van Biezen NA, Molijn AC, Bootsma D, de Jong PJ, Menon AG, Kley NA. Cloning and characterization of MN1, a gene from chromosome 22q11, which is disrupted by a balanced translocation in a meningioma. Oncogene. 1995 Apr 20;10(8):1521-8


This article should be referenced as such: