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Solid Tumour Section

Mini Review

Nervous system: Meningioma

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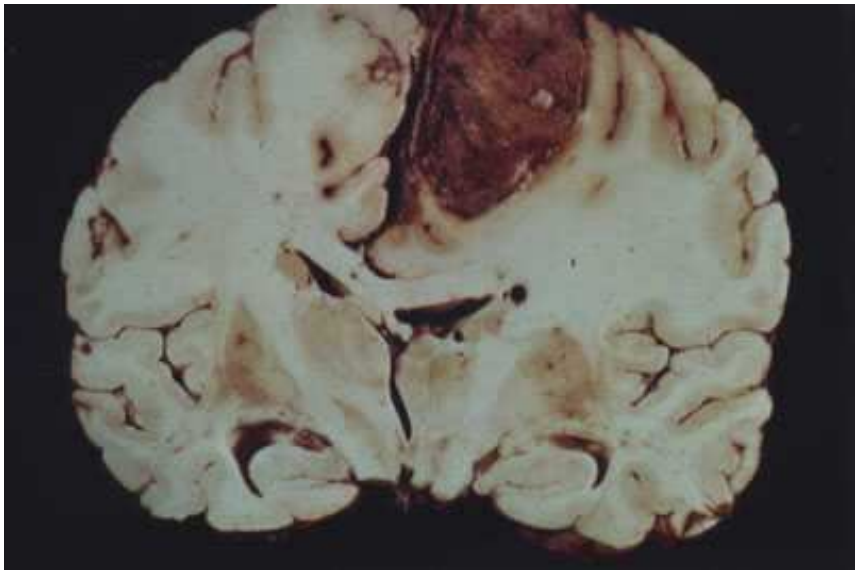
Classification



Macroscopic aspect of a parassagital meningioma - Anne Marie Capodano.

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

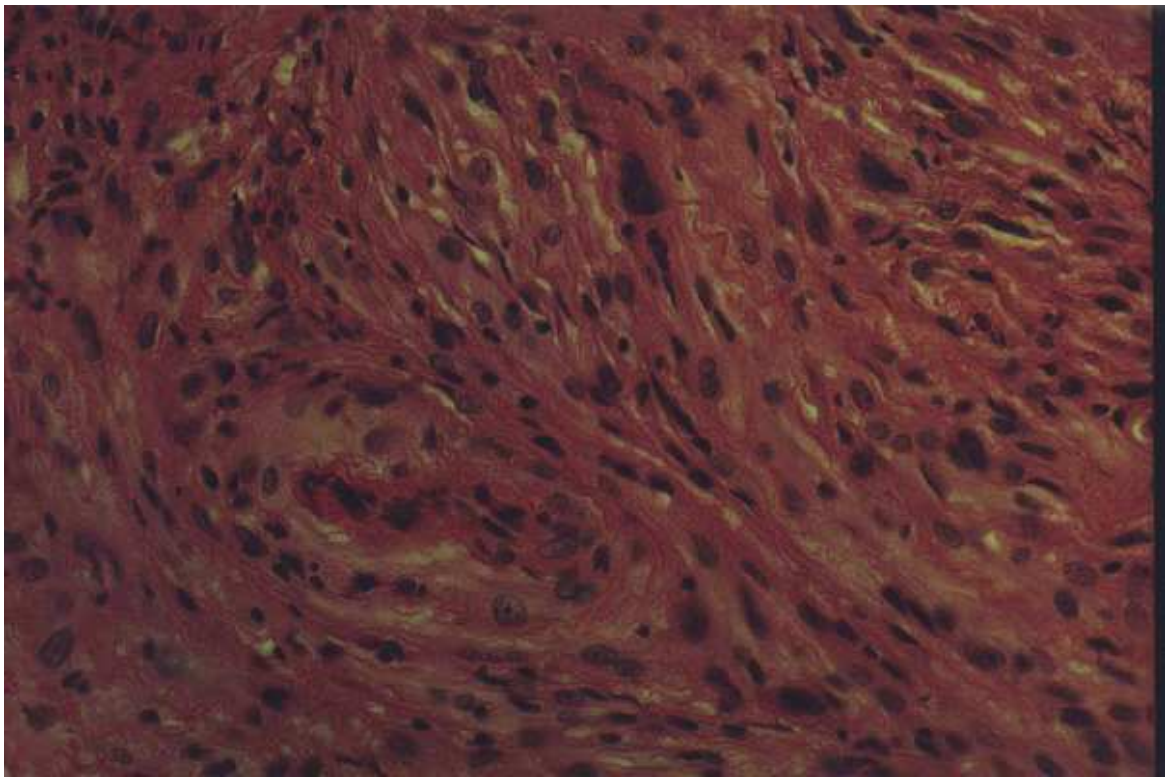
Meningiomas are known to be induced by radiation with an average time interval to tumor appearence of 20-35 years. The majority of patients with radio-induced meningiomas have received irradiation for tinea capitis or for primary brain tumor.

Epidemiology

Meningiomas account for 15-25% of primary intracranial and intraspinal neoplasms, with an annual incidence of approximatively 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 childrens 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 Meningiothelial meningioma, Fibroblastic meningioma, Transitional meningioma, Psamommatous 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 tendancy for local recurrence even after complete resection.

2-3% of meningiomas exibit 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

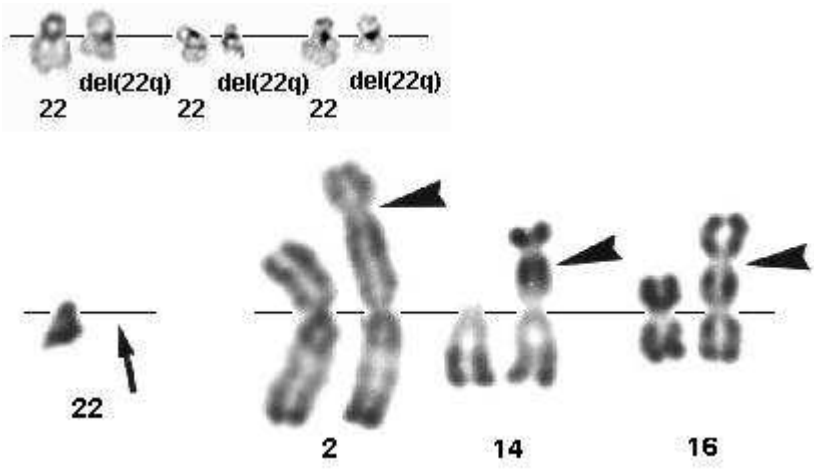
Cytogenetics Morphological

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 developpement of the majority of the meningiomas.



Top: del(22q) (G-banding) - Courtesy G. Reza Hafez, Eric B. Johnson, Sara Morrison-Delap Cytogenetics at the Waisman Center; bottom: partial karyotype of a fibroblatic meningioma cell; there was hypoploidy (39,XX), a monosommy 22 (arrow), and tas (arrowheads) - Courtesy Anne Marie Capodano.

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 aproximatively in 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 wich 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

Mark J, Levan G, Mitelman F. Identification by fluorescence of the G chromosome lost in human meningomas. Hereditas. 1972;71(1):163-8

Zulch KJ. International histological classification of tumors. Histological types of tumors of the central nervous system. Genova, World Health Organization,1979; 40-52.

Yamada K, Kondo T, Yoschioka M, Oami H. Cytogenetic studies in 20 human brain tumors : association of n22 chromosome abnormalities with tumors of the brain. Cancer Genet Cytogenet. 1980;2:293-307.

Zankl H, Zang KD. Correlation between clinical and cytogenetical data in 180 meningiomas. Cancer Genet Cytogenet. 1980;2:1346-51.

Tedeschi F, Fragnito C, Brizzi R, Lechi A, Trabattoni G, Pietrini V. On the pathology of meningiomas. A study of 412 cases. Acta Neuropathol Suppl. 1981;7:119-21

Rouleau GA, Wertelecki W, Haines JL, Hobbs WJ, Trofatter JA, Seizinger BR, Martuza RL, Superneau DW, Conneally PM, Gusella JF. Genetic linkage of bilateral acoustic neurofibromatosis to a DNA marker on chromosome 22. Nature. 1987 Sep 17-23;329(6136):246-8

Seizinger BR, de la Monte S, Atkins L, Gusella JF, Martuza RL. Molecular genetic approach to human meningioma: loss of genes on chromosome 22. Proc Natl Acad Sci U S A. 1987 Aug;84(15):5419-23

Russell DS, Rubinstein LJ. - Pathology of Tumors of the Nervous System, 1989; 5th edition, London.

Dumanski JP, Rouleau GA, Nordenskjöld M, Collins VP. Molecular genetic analysis of chromosome 22 in 81 cases of meningioma. Cancer Res. 1990 Sep 15;50(18):5863-7

Maier H, Ofner D, Hittmair A, Kitz K, Budka H. Classic, atypical, and anaplastic meningioma: three histopathological subtypes of clinical relevance. J Neurosurg. 1992 Oct;77(4):616-23

Vagner-Capodano AM, Grisoli F, Gambarelli D, Figarella D, Pellissier JF. Telomeric association of chromosomes in human meningiomas. Ann Genet. 1992;35(2):69-74

Rey JA, Bello MJ, de Campos JM, Vaquero J, Kusak ME, Sarasa JL, Pestaña A. Abnormalities of chromosome 22 in human brain tumors determined by combined cytogenetic and molecular genetic approaches. Cancer Genet Cytogenet. 1993 Mar;66(1):1-10

Lekanne Deprez RH, Bianchi AB, Groen NA, Seizinger BR, Hagemeijer A, van Drunen E, Bootsma D, Koper JW, Avezaat CJ, Kley N. Frequent NF2 gene transcript mutations in sporadic meningiomas and vestibular schwannomas. Am J Hum Genet. 1994 Jun;54(6):1022-9

Lindblom A, Ruttledge 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, Riegman 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

Lekanne Deprez RH, Riegman PH, van Drunen E, Warringa UL, Groen NA, Stefanko SZ, Koper JW, Avezaat CJ, Mulder PG, Zwarthoff EC. Cytogenetic, molecular genetic and pathological analyses in 126 meningiomas. J Neuropathol Exp Neurol. 1995 Mar;54(2):224-35

Louis DN, Ramesh V, Gusella JF. Neuropathology and molecular genetics of neurofibromatosis 2 and related tumors. Brain Pathol. 1995 Apr;5(2):163-72

Papi L, De Vitis LR, Vitelli F, Ammannati F, Mennonna P, Montali E, Bigozzi U. Somatic mutations in the neurofibromatosis type 2 gene in sporadic meningiomas. Hum Genet. 1995 Mar;95(3):347-51

Wellenreuther R, Kraus JA, Lenartz D, Menon AG, Schramm J, Louis DN, Ramesh V, Gusella JF, Wiestler OD, von Deimling A. Analysis of the neurofibromatosis 2 gene reveals molecular variants of meningioma. Am J Pathol. 1995 Apr;146(4):827-32

Ono Y, Ueki K, Joseph JT, Louis DN. Homozygous deletions of the CDKN2/p16 gene in dural hemangiopericytomas. Acta Neuropathol. 1996;91(3):221-5

Kleihues P, Cavenee WK. Tumours of the Nervous System. Pathology and Genetics. 1997.

Weber RG, Boström J, Wolter M, Baudis M, Collins VP, Reifenberger G, Lichter P. Analysis of genomic alterations in benign, atypical, and anaplastic meningiomas: toward a genetic model of meningioma progression. Proc Natl Acad Sci U S A. 1997 Dec 23;94(26):14719-24

Zattara-Cannoni H, Gambarelli D, Dufour H, Figarella D, Vollot F, Grisoli F, Vagner-Capodano AM. Contribution of cytogenetics and FISH in the diagnosis of meningiomas. A study of 189 tumors. Ann Genet. 1998;41(3):164-75

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