Atlas of Genetics and Cytogenetics in Oncology and Haematology

OPEN ACCESS JOURNAL AT INIST-CNRS

Solid Tumour Section

Mini Review

Nervous system: Medulloblastoma

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/MedulloblastomaID5065.html
DOI: 10.4267/2042/37653

Clinics and pathology

Disease

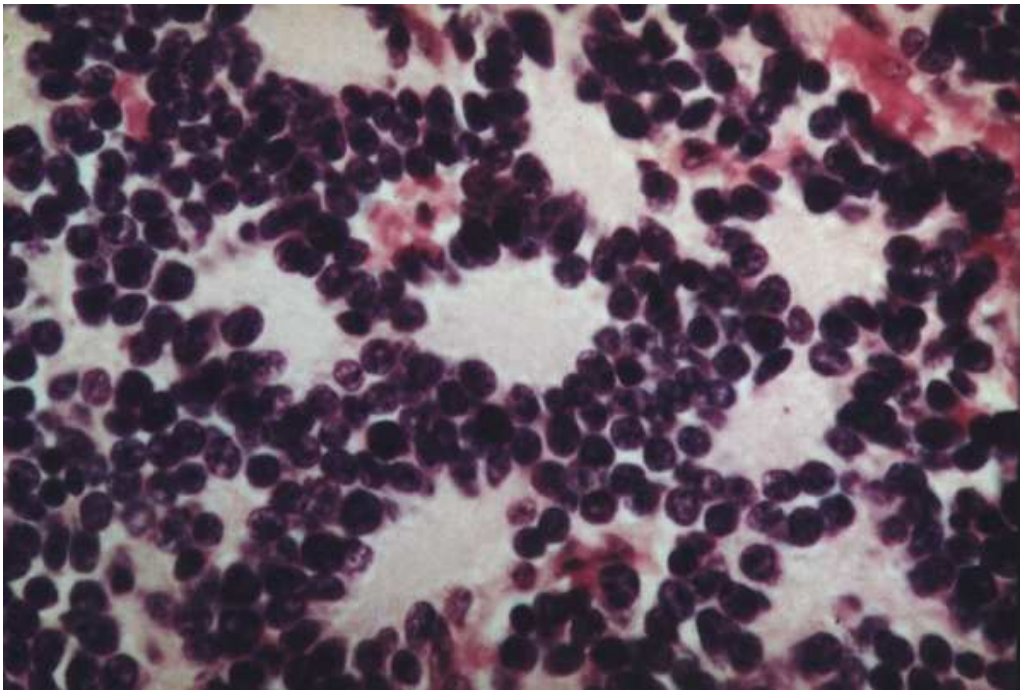
Medulloblastomas are malignant invasive embryonal tumours of the cerebellum with a tendency to metastasize in the central nervous system (CNS). This tumor is more frequently found in children.

Epidemiology

It represents 10 at 20 % of brain tumours and 30 % of tumours localized in posterior fossa; annual incidence is 0,5 per 100000 children; peak of occurrence at 7 years.

Pathology

Belongs to the primitive neurectodermal tumours (PNET): highly malignant embryonal tumours of the CNS with predominant neuronal differentiation. Several variants medulloblastoma are recognized in the OMS classification:
Classic medulloblastoma composed of densely jacked round-cells with round to oval hyperchromatic nuclei.
Desmoplastic medulloblastoma represents a variant with abundant reticulin and collagen.
Large cell medulloblastoma is a rare variant composed of cells with large round nuclei.



Histological features of a typical medulloblastoma: Homer-Wright rosettes - Anne Marie Capodano.

Immuno histo chemistry: Classic medulloblastoma is strongly immuno-reactive for Vimentin. Some tumours are immunoreactive for NSE, Synaptophysine and GSAP.

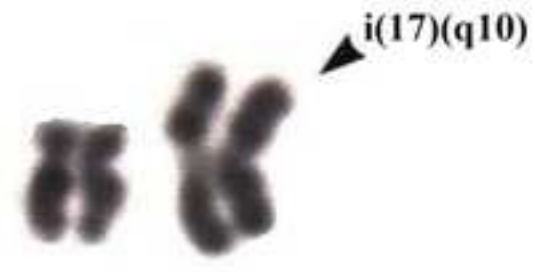
Treatment

The treatment associates total surgical resection and radiotherapy or, according to the age, chemotherapy.

Prognosis

Survival without recurrence is 50 at 70 %; depends on the quality of surgical resection and on the presence of metastases at the time of diagnosis.

Cytogenetics



i(17q) - R-banding.

Cytogenetics Morphological

The most common specific abnormality in medulloblastomas, which is present in approximately 50 % of cases, is isochromosome 17q [i(17q)]. The breakpoint is in the proximal portion of p-arm at 17p11.2, so that the resultant structure is dicentric. In a few cases, partial or complete loss of 17p occurs through interstitial deletion, unbalanced translocation or monosomy 17.

Chromosome 1 is also involved in medulloblastomas. The most frequent abnormalities are unbalanced translocations, deletions and duplications. Rearrangements of chromosome 1 often result in trisomy 1q without loss of the p-arm.

Others less common chromosomal changes are: deletions of 6q, 9q, 10q, 11q, 11p and 16q, monosomy 22 and in rare cases double minutes.

Cytogenetics Molecular

Isochromosome 17q has been observed in interphase nuclei using fluorescence in situ hybridization. This technique is used in particular when only a few metaphases are obtained or when only normal diploid cells are obtained in culture.

Genes involved and proteins

Note

Studies on loss of heterozygosity (LOH) have confirmed loss of portions of 17p in 30-45 % of cases. Some studies showed a correlation between LOH for 17p and a poor response to therapy and shortened survival. Mutations of p53 gene located on 17p13 have been found in only 5-10 % of these tumors.

Expression of PAX5 and PAX6 mRNA was shown in 70 % of medulloblastomas. The precise mechanism by which these genes are involved remains unknown.

Inactivation of PTCH tumor suppressor gene occurs in a subset of medulloblastomas.

References

Burger PC, Grahmann FC, Bliestle A, Kleihues P. Differentiation in the medulloblastoma. A histological and immunohistochemical study. Acta Neuropathol. 1987;73(2):115-23

Bigner SH, Mark J, Friedman HS, Biegel JA, Bigner DD. Structural chromosomal abnormalities in human medulloblastoma. Cancer Genet Cytogenet. 1988 Jan;30(1):91-101

Biegel JA, Rorke LB, Packer RJ, Sutton LN, Schut L, Bonner K, Emanuel BS. Isochromosome 17q in primitive neuroectodermal tumors of the central nervous system. Genes Chromosomes Cancer. 1989 Nov;1(2):139-47

Bigner SH, Vogelstein B. Cytogenetics and molecular genetics of malignant gliomas and medulloblastoma. Brain Pathol. 1990 Sep;1(1):12-8

Cogen PH, Daneshvar L, Metzger AK, Edwards MS. Deletion mapping of the medulloblastoma locus on chromosome 17p. Genomics. 1990 Oct;8(2):279-85

Giangaspero F, Chieco P, Ceccarelli C, Lisignoli G, Pozzuoli R, Gambacorta M, Rossi G, Burger PC. "Desmoplastic" versus "classic" medulloblastoma: comparison of DNA content, histopathology and differentiation. Virchows Arch A Pathol Anat Histopathol. 1991;418(3):207-14

Nakagawa H, Inazawa J, Misawa S, Tanaka S, Takashima T, Taniwaki M, Abe T, Kashima K. Detection of an i(17q) chromosome by fluorescent in situ hybridization with a chromosome 17 alpha satellite DNA probe. Cancer Genet Cytogenet. 1992 Sep;62(2):140-3

Vagner-Capodano AM, Zattara-Cannoni H, et al. Detection of i(17q) chromosome by fluorescent in situ hybridization (FISH) with interphase nuclei in medulloblastoma. Cancer Genet Cytogenet. 1994 Nov;78(1):1-6

Reardon DA, Michalkiewicz E, Boyett JM, Sublett JE, Entrekin RE, Ragsdale ST, Valentine MB, Behm FG, Li H, Heideman RL, Kun LE, Shapiro DN, Look AT. Extensive genomic abnormalities in childhood medulloblastoma by comparative genomic hybridization. Cancer Res. 1997 Sep 15;57(18):4042-7

Lescop S, Lellouch-Tubiana A, Vassal G, Besnard-Guerin C. Molecular genetic studies of chromosome 11 and chromosome 22q DNA sequences in pediatric medulloblastomas. J Neurooncol. 1999 Sep;44(2):119-27

McLendon RE, Friedman HS, Fuchs HE, Kun LE, Bigner SH. Diagnostic markers in paediatric medulloblastoma: a Paediatric Oncology Group Study. Histopathology. 1999 Feb;34(2):154-62

This article should be referenced as such:

Capodano AM. Nervous system: Medulloblastoma. Atlas Genet Cytogenet Oncol Haematol. 2000; 4(3):147-148.