Atlas of Genetics and Cytogenetics in Oncology and Haematology

OPEN ACCESS JOURNAL AT INIST-CNRS

Solid Tumour Section

Mini Review

Nervous system: Peripheral neuroblastic tumours (Neuroblastoma, Ganglioneuroblastoma, Ganglioneuroma)

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Published in Atlas Database: September 2001

Online updated version : http://AtlasGeneticsOncology.org/Tumors/neurob5002.html
DOI: 10.4267/2042/37818

This article is an update of: Kaneko Y, Couturier J, Satgé D. Neuroblastoma. Atlas Genet Cytogenet Oncol Haematol 1998;2(2):63-64

Classification

Note

Belongs to the group of 'small blue round cell' tumours of the children, and differential diagnosis with primitive neurectodermal tumours (PNET), lymphoma, Ewing's tumour, and rhabdomyosarcoma may be difficult.

Clinics and pathology

Disease

Tumour of the sympathetic nervous system: medulloadrenal gland (50%), abdominal (25%), thoracic (15%), cervical or pelvic paraspinal ganglia; metastatic at diagnosis in 60% of cases (lymph nodes, bones and bone marrow, liver, skin).

Embryonic origin

Neural crest cells.

Etiology

Unknown; possible excess in neurofibromatosis type I, Wiedemann-Beckwith syndrome, and maternal exposure to phenyl hydantoin; exceptional familial cases.

Epidemiology

Incidence is 5-10 per million children per year; 10% of cancers in childhood; half cases by the age of 2 years, 90% before 6 years.

Clinics

Presenting signs are according to the localization of the tumoural mass; high catecholamin excretion.

Pathology

Tumours may exhibit various degrees of differentiation:
- Neuroblastoma: undifferentiated cells that may be arranged in rosettes surrounding a fibrillar centre; 2 - Ganglioneuroblastoma: presenting with more fibrillar material and a mixture of the above.

Described with >50% of more mature cells, those found in 3-ganglioneuroma, composed of well differentiated ganglion cells and Schwann cells; a given tumour may contain more and less mature cell areas.
Staging (Evans):
Stage I: confined to the organ or structure of origin,
Stage II: extending beyond the organ, but not crossing the midline (e.g. homolateral lymph nodes may be involved),
Stage III: extending and crossing the midline,
Stage IV: distant metastases,
Stage IVs: stage I or II otherwise in children aged.

Treatment

Surgery and/or radiation therapy, and/or chemotherapy, and with or without myeloablative therapy followed by stem cell transplantation.

Evolution

Spontaneous (and treatment induced) regression or differenciation into benign cells (ganglioneuroma)

occurs rarely in tumors (mainly in infant cases) clinically found and frequently in tumors found by mass screening at 6 months of age.

Prognosis

Prognosis is very poor in most cases (median survival 1 year), myeloablative therapy with stem cell transplantation may benefit stage IV patients 1 year or older; good outcome (90%) only for patients with stage I and II disease; younger patients especially less than 12 months of age have better outcome than older patients; cytogenetic and genetic anomalies are of important prognostic value (see below).

Genetics

Note

Heterogenous disease from the genetic viewpoint; 90% cases exhibit genetic abnormalities. Linkage analysis using 10 families with neuroblastoma mapped the hereditary neuroblastoma locus at 16p12-p13.

Cytogenetics

Cytogenetics Morphological

Two types can be delineated according to ploidy:
Aneuploid tumours (near triploid, pentaploid or hexaploid), with whole chromosome anomalies, often with relative gains of chromosomes 17, 7, 6, relative losses of chromosomes 11, 14, X (molecular cytogenetics: detection with comparative genomic hybridization (CGH); these are low grade tumours, with good prognosis.
Diploid and/or tetraploid tumours, with 1p deletion - minimal critical region being 1p36- in 40% cases, 11q deletion, trisomy or tetrasomy for 17q21-qter (in 90% of high grade tumours), DM or HSR (MYCN amplification); these anomalies are often associated, found in high grade tumours, and bear a grave prognosis. MYCN amplification is associated with 1p deletion and partial 17q polysomy, and is inversely related to 11q deletion.

Genes involved and proteins

MYCN

Location: 2p24

Protein

Nuclear protein; contains a helix-loop-helix and a leucine zipper; transcription factor.

Result of the chromosomal anomaly

Fusion Protein

Oncogenesis

Amplification of MYCN is found in various tumours, in particular neuroblastoma; the level of amplification increases with tumour progression.

To be noted

Note

Urinary mass screening programs for cathecolamine metabolites in several countries could not induce a fall in mortality. Consensus conference recommended discontinuance of the screening under 7 months of age. Screening programs at age 12 months or later are ongoing in some countries.

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This article should be referenced as such:

Kaneko Y. Nervous system: Peripheral neuroblastic tumours (Neuroblastoma, Ganglioneuroblastoma, Ganglioneuroma). Atlas Genet Cytogenet Oncol Haematol. 2002; 6(1):37-39.