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: February 1998

Online updated version is available from: http://AtlasGeneticsOncology.org/Tumors/neurob5002.html
DOI: 10.4267/2042/37421

Identity

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 yr; 10% of cancers in childhood; half cases by the age of 2 yrs, 90% before 6 yrs.

Clinics

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

Pathology

Tumours may exhibit various degrees of differentiation:

1- 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;
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 < 1 yr, with metastases in: liver, skin, bone marrow, but not in the bones.

Treatment

Surgery and/or radiation therapy, and/or chemotherapy.

Evolution

Spontaneous (and treatment induced) regression or differenciation into benign cells (ganglioneuroma) occurs rarely in tumours (mainly in infant cases).

Prognosis

Prognosis is very poor in most cases (median survival 1 yr); good outcome (90%) only for patients with lymph nodes negative for tumour (POG stage A); younger patients 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.

Cytogenetics

Morphological cytogenetics

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 del(1p) - minimal critical region being 1p36- in 40% cases, del(11q), partial trisomy for 17q21-qter (in 90% of high grade tumours), DM or HSR (N-myc amplification); these anomalies are often associated, found in high grade tumours, and bear a grave prognosis.

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

To be noted

Screening programs in several countries could not induce a fall in mortality

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This article should be referenced as such:

Couturier J, Satgé DNervous system: Peripheral neuroblastic tumours (Neuroblastoma, Ganglioneuroblastoma, Ganglioneuroma) Atlas Genet Cytogenet Oncol Haematol.1998;2(2):63-64.