Solid Tumour Section
Mini Review

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

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Classification

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

Clinics and pathology

Disease
Tumour of the sympathetic nervous system: medullodrenal 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 differentiation 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 catecholamine 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.

**References**


This article should be referenced as such: