Atlas
Peripheral Neuroblastic Tumors

International Neuroblastoma
Pathology Committee
Definition of Peripheral Neuroblastic Tumors
Embryology
International Neuroblastoma Pathology Classification
Four Categories of Peripheral Neuroblastic Tumors

1. Neuroblastoma (Schwannian stroma-poor)
2. Ganglioneuroblastoma, Intermixed (Schwannian stroma-rich)
3. Ganglioneuroma (Schwannian stroma-dominant)
4. Ganglioneuroblastoma, Nodular (composite, Schwannian stroma-rich/stroma-dominant and stroma-poor)
Neuroblastoma
(Schwannian stroma-poor)

Undifferentiated subtype
Poorly differentiated subtype
Differentiating subtype
Neuroblastoma
(Schwannian stroma-poor)

Undifferentiated Subtype
Neuroblastoma
(Schwannian stroma-poor)
Poorly differentiated Subtype
Neuroblastoma
(Schwannian stroma-poor)

Transition between Poorly differentiated subtype to Differentiating subtype
Neuroblastoma
(Schwannian stroma-poor)
Differentiating Subtype
Neuroblastoma
(Schwannian stroma-poor)

- Different Cellularity
- Calcification
- Multi-nucleated cells
- Melanin pigment
- Mitosis
- Mitosis-Karyorrhexis
- Apoptosis
Neuroblastoma
(Schwannian stroma-poor)

Transitional to
Ganglioneuroblastoma, Intermixed
(Schwannian stroma-Rich)
Ganglioneuroblastoma, Intermixed (Schwannian stroma-rich)
Ganglioneuroma
(Schwannian stroma-dominant)

Maturing subtype
Mature subtype
Ganglioneuroblastoma, Nodular (composite, Schwannian stroma-rich/stroma-dominant and stroma-poor)
Particular Features of Peripheral Neuroblastic Tumors

Embryonic rest/Neuroblastoma in situ
Stage 4S Disease
Cystic Neuroblastoma
Angiomatoid Neuroblastoma
Neuroblastoma with OMA
Neuroblastoma detected through Mass Screening
Unusual Features of Peripheral Neuroblastic Tumors

- Pleomorphic neuroblastoma
- Focal area of pleomorphic cells
- Fusiform/Spindle cell neuroblastoma
- Diffuse pattern
- Pseudoalveolar (pseudopapillary) pattern
- Nuclear inclusions of cytoplasmic material
- Rhabdoid cells in neuroblastoma
- Prominent vascular proliferation
- Desmoplastic reaction
- Sarcoid reaction
Metastatic Disease
Immunohistochemistry
### Peripheral Neuroblastic Tumors

<table>
<thead>
<tr>
<th>Tumor cell types</th>
<th>Reactive cell types</th>
</tr>
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<tbody>
<tr>
<td><strong>Neuroblasts</strong></td>
<td></td>
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<tr>
<td>Differentiating neuroblasts</td>
<td></td>
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<tr>
<td>Ganglionic cells</td>
<td></td>
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<tr>
<td><strong>Schwann cells</strong></td>
<td></td>
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<tr>
<td>Lymphocytes, if present</td>
<td></td>
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</tbody>
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<table>
<thead>
<tr>
<th>Peripheral Neuroblastic Tumors</th>
<th>CD 44</th>
<th>TrkA</th>
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</thead>
<tbody>
<tr>
<td><strong>Prognostic markers</strong></td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Better Prognosis Tumors</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Poor Prognosis Tumors</td>
<td>-</td>
<td>-</td>
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</table>

### Peripheral Neuroblastic Tumors, differential diagnosis

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>TH</th>
<th>Vimentin</th>
<th>PGP 9.5</th>
<th>CD 45</th>
<th>Desmin</th>
<th>MyoD1/ Myogenin</th>
<th>CD99</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neuroblastoma (Schwannian stroma- poor)</td>
<td>+</td>
<td>+/-</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Ewing's/pPNET</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>-</td>
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<td>+</td>
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<tr>
<td>Rhabdomyosarcoma</td>
<td>-</td>
<td>+/-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Non-Hodgkin Lymphoma (lymphoblastic type)</td>
<td>-</td>
<td>+/-</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>+/-</td>
</tr>
</tbody>
</table>
Genetic Properties

Karyotype
MYCN amplification
Deletion of chromosome 1p
Gain of chromosome 17q
Ganglion cells and Schwann cells
Pathology Checklist
Morphologic Features
(as described in Shimada et al. CANCER 1999;86:349-63)

(I) Tumor Type

Neuroblastoma (Schwannian stroma-poor)-------------------------- I I
Ganglioneuroblastoma, Intermixed (Schwannian stroma-rich)-------- I I
Ganglioneuroma (Schwannian stroma-dominant)--------------------- I I
Ganglioneuroblastoma, Nodular (Composite, Schwannian stroma-rich/stroma-dominant and stroma-poor)--------------------- I I

Primary tumor showing “Ganglioneuroblastoma, Intermixed” or “Ganglioneuroma” appearance with concurrent metastatic nodule(s) of Neuroblastoma is classified as “Ganglioneuroblastoma, Nodular”.

(II) For Neuroblastoma (Schwannian stroma-poor) and stroma-poor portion of the Ganglioneuroblastoma, Nodular*

1) Neuroblastic differentiation
   a) Undifferentiated (Totally undifferentiated, difficult in making the diagnosis by routine H&E examination, alone)------------------- I I
   b) Poorly differentiated (<5% differentiating neuroblasts)------------- I I
   c) Differentiating (>5% differentiating neuroblasts)------------------- I I
   Differentiating neuroblasts = neuroblastic cells having synchronously maturing nucleus and cytoplasm

2) MKI (mitosis-karyorrhexis index)
   a) low (<2% or <100/5,000 cells)----------------------------------- I
   b) intermediate (2-4% or 100-200/5,000 cells)--------------------- I
   c) high (>4% or >200/5,000 cells)----------------------------------- I

*List different histologies, if present, of nodular lesions separately (circle a, b, or c for each morphologic feature; codes, see above):

Nodule 1: neuroblastic differentiation (a, b, c); MKI (a, b, c)
Nodule 2: neuroblastic differentiation (a, b, c); MKI (a, b, c)
Nodule 3: neuroblastic differentiation (a, b, c); MKI (a, b, c)

(III) For Ganglioneuroma (Schwannian stroma-dominant)

1) Neuroblastic maturation towards ganglion cells
   a) Maturing (mixture of completely and incompletely mature ganglion cells)-------- I I
   b) Mature (complete maturation with satellite cells)------------------------------- I I

(IV) Other Findings
Calcification: yes-------------------------------------------------------- I I
no------------------------------------------------------------- I I

Comments: __________________________________________________________
________________________________________________________
________________________________________________________
________________________________________________________

Patient I.D.
Date of Birth
Date of Surgery/Biopsy
International Neuroblastoma Pathology Classification

Schwannian Development

- None to <50%
- ≥50%
  - Grossly visible Nodule(s)

Neuroblastoma (Schwannian stroma-poor)

- Undifferentiated subtype
- Poorly differentiated subtype
- Differentiating subtype

Variant forms*

Microscopic neuroblastic foci (naked neuropil)

- Absent
- Present

Ganglioneuroblastoma, Intermixed (Schwannian stroma-rich)

Ganglioneuroma (Schwannian stroma-dominant)
- Maturing subtype
- Mature subtype

Ganglioneuroblastoma, Nodular (composite, Schwannian stroma-rich/ stroma-dominant and stroma-poor)

mitotic & karyorrhectic cells

- Any age
- ≥200/5,000 cells
- 100-200/5,000 cells
- <100/5,000 cells

- Any age
- ≥1.5 yr
- <1.5 yr

- Any age
- ≥1.5 yr
- <1.5 yr
- ≥5 yr
- <5 yr

FH: favorable histology
UH: unfavorable histology

For variant forms and prognostic evaluation of “Ganglioneuroblastoma, Nodular”, see CANCER 2003;98:2274-81.