NEUROBLASTOMA

Epidemiology:

- Most **common malignancy in infancy** and most common pediatric extracranial solid tumor
- Median age at diagnosis is 18-19 months, with wide age range (e.g., in-utero diagnosis to patients in their 20s)

PRESENTATION

Depends on tumor's location and degree of differentiation (i.e., tumor behaviour ranges from spontaneous cell maturation to rapid metastasis).

Primary Tumor

- **Tumor can originate from any site within the SNS:**
  - Adrenal glands (>50%)
  - Abdominal paraspinal ganglia (24%)
  - Thoracic paraspinal ganglia (20%)
  - Neck (3%)
  - Brain (rarely)
- **Abdominal tumor:**
  - Palpable mass in the flank (hard, non-tender)
  - Distension
  - Abdominal pain
  - Constipation
- **Thoracic/cervical tumor**:
  - Dyspnea
  - Horner syndrome (ptosis, miosis, anhydrosis)
  - Stridor
  - Superior vena cava syndrome
- **Paravertebral tumor:**
  - Pain and numbness
  - Limb weakness
  - Sphincter dysfunction, loss of bowel/bladder function

Metastasis

- Metastasis is common at presentation
- May present with constitutional symptoms (e.g., anorexia, fever, weight loss)

Common sites of metastasis:

- **Bone/Bone Marrow:**
  - Bone pain
  - Limp
  - Pancytopenia
  - Periorbital ecchymoses secondary to orbital bone metastases
- **Liver**
- **Lymph nodes**
- **Skin**:
  - "Blueberry muffin" skin nodules (i.e., purple cutaneous nodules that blanch on palpation)

Paraneoplastic syndromes:

- Catecholamine production → hypertension, palpitations, and diaphoresis
- Vasoactive intestinal peptide production → secretory diarrhea (associated with hypokalemia)
- Opsoclonus myoclonus syndrome, presents as rapid, multidirectional eye movements, myoclonus of limbs or trunk, and/or ataxia

PATHOPHYSIOLOGY

Tumors arising from embryonic neural crest cells that normally form the sympathetic nervous system (SNS) and adrenal medulla

Sporadic (98%)	**Inherited/Familial** (2%)
MYCN amplification = most common somatic genetic mutation	ALK oncogene germline mutation = familial neuroblastoma

MYCN and ALK mutations are associated with aggressive tumor phenotype and poor prognosis

DIAGNOSIS

Laboratory

- ❑ Complete blood cell count with peripheral smear
- ❑ Complete metabolic panel, uric acid
- ❑ Coagulation panel
- ❑ Ferritin and lactate dehydrogenase levels
- ❑ Liver enzyme levels
- ❑ Urine vanillylmandelic acid and homovanillic acid

Radiology

- ❑ Initial: Chest radiograph or ultrasonography
- ❑ Urgent/emergency: CT scan of the chest, abdomen, and pelvis
- ❑ Preferred: MRI of the primary site and chest, abdomen and pelvis
- ❑ Metastatic: I-123 metaiodobenzylguanidine

Pathology

- ❑ Bilateral bone marrow aspirate and biopsy with immunohistochemistry analysis
- ❑ Tumor biopsy with immunohistochemistry analysis and DNA ploidy
- ❑ Segmental chromosomal alteration analysis
- ❑ Fluorescence in situ hybridization and polymerase chain reaction for MYCN and ALK

MANAGEMENT

Treatment, which may be observation only or include combo of surgery, radiotherapy, chemotherapy, autologous stem cell transplant, immunotherapy, is determined by numerous factors including stage, age and histology/genetics.

Staging can be determined by either of the following:

- Prior to treatment initiation, with radiology alone

OR

- After initial surgery, with use of histology

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