Neuroblastoma & Wilms tumor

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Neuroblastoma

- Embryonic cancer of the peripheral sympathetic nervous system with heterogeneous clinical presentation and course.

**Epidemiology:**

- Third most common pediatric cancer.
- 8% of childhood malignancies.
- Most common neoplasm in infants.
- 28%-39% of neonatal malignancies.
- 90% of cases are diagnosed by 5 yr. of age.
- Incidence is slightly higher in boys and in whites.
Most common cancer in children < 1 y.o.
2/3 are in children < 5 y.o.
70% of all patients have mets at dx
One of the small blue round cell tumors
[leukemia, lymphoma, Ewing/PNET, RMS, Wilms, desmoplastic]
Pathology

- Variable degrees of neural differentiation, ranging from undifferentiated small round cells to mature ganglion cells (ganglioneuroblastoma or ganglioneuroma)
- The tumor may resemble other small round cell tumors such as rhabdomyosarcoma, Ewing sarcoma, and non-Hodgkin lymphoma.

Genetics:

- Prognostic importance.
- Amplification of MYCN is strongly associated with advanced tumor stage and poor outcome independent of stage and age.
- Hyperdiploidy confers better prognosis if the child is younger than 1 year of age at diagnosis.
Clinical findings

- Originates in sympathetic NS: paraspinal ganglia or adrenal medulla
- Most common: mass effect sx, bone pain, proptosis/peri orbital ecchymoses from retrobulbar mets
- Can invade neural foramina, ➔ paralysis
- Less commonly: fever, anemia, HTN
- Rarely: VIP secretion ➔ diarrhea, cerebellar ataxia, opsoclonus/myoclonus
Prognostic factors

- **Stage** *(males present later, but o/w male is not worse)*
- **Age** *(<1 y.o. better *except* maybe <6 wks with no skin nodules)*
- **Primary tumor site** *ONLY for stage 3-4 (abd is worse)*
- **Primary tumor size** *(> 100 cm3 is worse)*
- **Shimada criteria**
Prognostic factors, cont.

- **Biology, esp. myc-n but also:**
  - **Good:** hyperdiploidy, proto-oncogene,
  - **Bad:** increased telomerase RNA (hTR), high ferritin, neuron-specific enolase, high LDH, low tumor CD44
  - **NOT** catecholamine levels
Shimada

Favorable

Stroma rich

no

Nodular pattern? yes

Stroma poor

Age < 1.5 y

yes

Age > 5 y

no

MKI < 200?

yes

Differentiated

AND MKI < 200?

no

yes
Diagnosis

- Mass or multiple masses on plain radiograph, CT or MRI.
- HVA and VMA are elevated in 95% of cases.
- Pathological diagnosis by biopsy.
- Cytogenetic.
- NB can be diagnosed without tumor biopsy if neuroblasts are observed in BM and elevated HVA and VMA in urine.
- Evaluation of metastatic disease should include BM aspirate and biopsies, bone scan and MIBG scan.
Staging

1: localized, GTR, & LN’s not involved
2A: as above but no GTR
2B: ipsilateral +LN’s: must Bx contralat LN’s
3: Unresectable tumor crossing midline (edge of vertebral body) +/- regional nodes
   OR bilateral extension/nodes (regional only)
• 4: Disseminated tumor
Treatment and Prognosis

1: > 90%, still good even with local recurrence. Surgery only UNLESS: age > 2y, myc-n amplified, unfavorable histology, +LN

2: 75-90%. Bx/surg, chemo (4-6 mos of CTX/DOX), then definitive surg.

3, <1y: 80%. Surg +/- chemo

3, >1y: 50-70%. Surg + chemo, +/- XRT. & SCT
Rx and Px, cont.

- 4: 10-40%, SCT better than chemo alone
- Recurrent Dz: bad if disseminated; usually disseminated. CNS involvement common, UNLIKE at primary Dx.
WILMS TUMOUR
(NEPHROBLASTOMA)
Right kidney with Wilms’ tumor
DEFINITION

- Wilms Tumour is a malignant tumour of the kidney which arise from embryonal renal cells of the metanephros.
Mesoblastic Nephroma (Neonatal Nephroblastoma):

- Differs from Wilm's tumor in absence of lobulation, necrosis, or hemorrhage.
- Microscopically there is a preponderance of interlacing bundles of spindle cells.
- Excellent Prognosis.
INTRODUCTION

- Accounts for 8% of renal Tumours
- Second commonest solid abdominal Tumour in Infants & early Childhood
- Incidence- 1/200,000 Children. (Not affected by Race or Climate)
- Sex-equal incidence
- Age- occurs before 7 years (very few occur between 7-12 years)
- 80% of Patients are under 4 years
- Very rarely reported in Adults
- Cases has been described in the fetus, premature infants & the Newborn
Wilm’s Tumor (Nephroblastoma)...cont.

- This tumor arises from the primitive embryonic cells and produces a mixed histological picture of epithelial structure, mesenchymal tissues, including striated muscle fibers, possible all congenital.
AETIOLOGY

- Unknown but it is thought to arise from abnormal proliferation of the metanephric blastema.
- About 1% of cases are familial and 15% of patients have been associated with congenital abnormality such as aniridia (absent iris), mental retardation, hemihypertrophy of the body and Genito-Urinary anomalies.
PATHOGENESIS

- Nephroblastoma is an embryonic Tumour caused by disturbances during development.
- It is well encapsulated until it is very advanced & has a smooth or lobulated surface.
- In 5-10% of cases Tumour is bilateral. Histology is favourable when there is absence of anaplasia-focal or diffuse
- And unfavourable when there is the presence of anaplasia.
- Wilms Tumour spreads directly to the perinephric tissue
- Haematogenously to the lungs (commonest site), liver, brain & bone.
- Lymphatic spread occurs to para-aortic nodes (not to same extent as haematogenous spreading).
Because of its mixed origin, a variety of cells are observed on histological examination. These include:

- Epithelial cells (tubular or glomerular origin)
- Embryonic glomerulo-tubular structures with an immature spindle cell stroma (most common feature).
- Connective tissues
- Cartilage
- Bone, Fat
- Muscle fibres (usually smooth but could be striated)
- Mitotic figures are usually frequently
CLINICAL FEATURES

- Abdominal swelling (60%) that does not cross the midline.
- Abdominal pain
- Vomiting
- Fever (50%)
- Haematuria (12%)
- Hypochromic anaemia
- Malaise
- Anorexia
- Weight loss
- Hypertension
INVESTIGATION

- IVU (most important) - Calyces and pelvis are distorted.
- USG/CT (To diagnose Tumour extension into renal Vein & Inferior vena cava, liver & other abdominal metastasis).
- Chest X-ray with Tomography to rule out lung metastasis.
- Percutaneous needle biopsy – diagnosis in extensive disease
- FBC, RFT, LFT, Urinalysis.
DIFFERENTIAL DIAGNOSIS

- Hydronephrosis
- Renal Cyst
- Abdominal Lymphoma
- Neuroblastoma
- Polycystic Kidney Disease
- Rhabdomyosarcoma
- Renal Cell Carcinoma
MANAGEMENT

- Depends on staging

- Surgery is the method of Choice

- All patients should be treated even if there is multiple metastasis because Tumour is susceptible to several methods of therapy.
STAGING

- Is made from clinical findings, X-ray of chest, findings on USG, CT, surgery findings and histology.
- **Stage I**
  Tumour is confined to kidney and is completely resectable.
- **Stage II**
  Tumour has extended beyond the kidney but is still completely resectable without leaving residual Tumour in abdomen.
- **Stage III**
  There is residual Tumour in the abdomen after resection of renal Tumour (because of local infiltration into vital structures)
- **Stage IV**
  There is spread to distant organs such as liver, lung, bone & brain.
- **Stage V**
  Contralateral kidney is also involved by the tumour which may be primary or secondary.
- Most patients under 2 years usually have stage I or II.
The treatment options are:

- Surgery
- Chemotherapy
- Radiotherapy

**STAGE I & II**

- Nephrectomy (unilateral cases)
- Chemotherapy - Vincristine & Actinomycin D

**STAGE II (Unfavourable histology) & STAGE III**

- Nephrectomy (unilateral cases)
- Radiotherapy
- Chemotherapy - Vincristine, Adriamycin & Actinomycin D for 15 months.
TREATMENT Contd.

STAGE IV
- Nephrectomy (unilateral cases)
- Radiotherapy
- Chemotherapy - Vincristine, Adriamycin & Actinomycin D
- Addition of Cyclophosphamide may improve response in those with diffuse anaplastic tumour.

STAGE V
- Traditionally, Nephrectomy for larger tumour & Partial Nephrectomy for smaller tumour.
- Currently, staging laparotomy is done first.
- Then Combined Chemotherapy for 6 weeks - 6 months
- Then 2nd/3rd look laparotomy with intervening additional Chemotherapy or Radiotherapy.
- After which there will be down staging with Partial Nephrectomy and excisional biopsy can be performed.
COMPLICATIONS ASSOCIATED WITH TREATMENT

- Haemorrhage
- UTI
- Severe Thrombocytopenia
- Alopecia
- Cardiomyopathy
- Neuropathy
- Haemorrhagic Cystitis
- Vertebral hypoplasia & Scoliosis
**PROGNOSIS**

- Prognosis is good with an 80-90% chance of survival. Factors affecting survival include rate;
- Stage of Tumour at operation.
- Duration between appearance of swelling and Treatment.
- Age of patient (Patients under 2 years have good prognosis because they usually have Stage I & II.
- Size of Tumour (If greater than 375g the prognosis is worse)
- Histology pattern. Well differentiated Tumours have a survival rate of over 90%. In bilateral Wilms Tumour survival at 5 years is 75% and at 10 years is 70%.
Pediatric Pearls

Neuroblastoma:
- irritable child, tender
- skin: blueberry muffin
- eyes: raccoon eyes
- some degree of wasting
- urinary metabolites
- calcs on film

Wilms’ Tumor:
- asymptomatic
- marcoglossia
- aniridia
- hemihypertrophy
- “claw” on CT/IVP
- hypertension
- hematuria