

NEPHROBLASTOMA

⇒ highly malignant Primary embryonal tumor:
derived from nephrotic blastemal cell that replicate
the histology of developing kidney & show divergent pattern
of differentiation.

1st kidney tumor in childhood.

PATHOMECHANISMS:

located on chromosome 11p13

⇒ Mutation in WT1 And WT2 (tumor suppressor genes)

Congenital Malformation Associated with an ↑ Risk.

THREE CONGENITAL SYNDROMES:

- 1) WAGR (Wilms tumor, Aniridia, genital Anomalies, mental Retardation)
- 2) Denys-Drash syndrome (DDS)
- 3) Beckwith-Wiedemann syndrome (BWS)

⇒ ↑ Risk of nephroblastoma.

(C) BWS is on chromosome 11 distal to the WT1 locus.

↳ This Region contain several gene including
IGF-2 (Insulin-like growth factor)



This lead to overexpression of the IGF-2 protein
Responsible for both organ enlargement &
tumorigenesis.

MOLECULAR ABNORMALITIES IN NONSYNDROMIC NEPHROBLASTOMAS

- 1) Gain of function mutation of the paterin gene.
- 2) Recurrent mutation occur in gene encoding protein involved in micro RNA processing.
↳ These mutation lead to decreased level of many mature micro RNAs particularly those involved in mature micro RNA's path "mesenchymal to epithelial transformation"

↓
Absence of mesenchymal to epithelial transformation may lead to persistent blastemal "Rests" in kidney

↓ prognosis
nephroblastoma:

- 3) TP53 mutation
- 4) Nephroblastoma Also found in Association with other Malignancies (eg. Osteosarcoma, hepatocellular carcinoma)

MORPHOLOGY

GROSS:

→ Usually Appears as a large, single, Round, well-circumscribed mass.

β Catenin
enodes rich
in β catenin

Cut section: soft bulging, homogeneous, tan to gray.

MICROSCOPY:

three major components:

⇒ 3 types of cells:

- Undifferentiated blastemal component:

↳ small, round to oval blue cells.

scanty cytoplasm.

- Immature Stromal component

- Undifferentiated fibroblast like spindle cells or myxoid tissue

- Immature epithelial component:

classically tumours show a triphasic cell then cell type

- Anaplasia: associated TP53

pieces of cells with large hyperchromatic pleomorphic nuclei

C.F:

⇒ Hematuria, pain in the Abdomen.

Spread

⇒ Local, Lymphatic, Hematogenous.