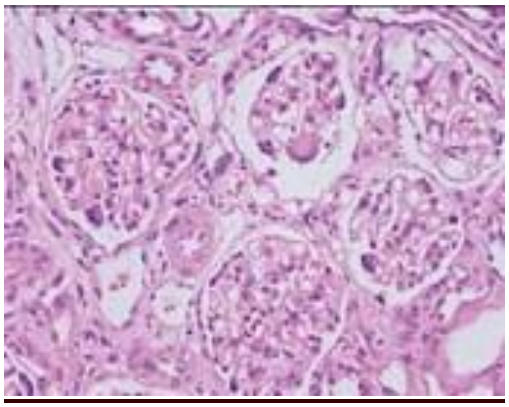
Nephropath teaching point 8:

Podocyte multinucleation



Previous nephropath teaching point question pertained to a seven year old girl presenting with failure to thrive, subnephrotic proteinuria and whose renal biopsy revealed prominent multinucleation of visceral epithelial cells (podocytes). Majority of readers (54.55%) have correctly identified Cystinosis as the associated condition.

Cystinosis is a rare autosomal recessive lysosomal transport disorder with an estimated incidence of 1 in 100,000 to 200,000 live births. Basic defect is deficiency of cystinosin, a lysosomal membrane protein encoded by a gene, *CTNS*, mapped to chromosome 17p13. Due to impaired transport of cystine, crystal formation occurs in the reticuloendothelial system, cornea, thyroid, and renal tubules, often leading to visual impairment, hypothyroidism, and Fanconi's syndrome. Cystinosis is classified into three forms:

(1) Infantile nephropathic cystinosis (INC) characterized by rapid progression to ESRD;

(2) Juvenile or late-onset cystinosis with slow progression without Fanconi's syndrome;

(3) Adult non-nephropathic cystinosis characterized by predominantly ocular involvement.

Cystine crystals, though present in renal biopsies of children with INC, are usually not

demonstrable in formalin-fixed and paraffin-embedded tissue due to the solubility of cystine crystals in aqueous solutions.(biopsy needs to be fixed in 100% ethanol for demonstration)

A unique histological finding that helps in diagnosis, is presence of multinucleated podocytes, which may also be observed in tubular epithelial and interstitial cells [Bonsib & Horvarth, Spear et. al., Feldhoff , Swetschin & Hagge, Chandra, Stokes & Kaskel and Sharma et. al] . This feature is considered to be relatively specific due to the rarity of this phenomenon in other renal diseases. Other conditions where multinucleation may be seen (though not as striking as in Cystinosis) include necrotizing glomerular diseases especially antiglomerular basement membrane disease (multinucleated giant cells of macrophage origin), after treatment with basic fibroblast or platelet-derived growth factor and in biopsies with collapsing glomerulopathy.

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