Chapter 7

RENAL TUBULAR DEFECTS

FANCONI SYNDROME

This is due to generalized defect of renal tubular function in proximal tubules. In consequence glucose, amino acid, uric acid, phosphate, sodium, potassium, bicarbonate and protein all have enhanced clearance and appear in increased quantities in urine.

Etiology and Pathogenesis:

Renal tubular damage may be produced by heavy metals such as lead, cadmium and uranium.

Syndrome may occur in Wilson disease, hereditary fructose intolerance, galactosemia, glycogenosis, tyrosinaemia and following use of outdated and deteriorated tetracyclins.

Fanconi syndrome is divided into two types:

1. More severe is associated with cystine storage in many tissues. It is inherited as autosomal recessive gene, presents in infancy and early childhood and progresses to produce glomerular damage and renal insufficiency. It is called cystinosis or Lignac Fanconi syndrome.
2. Second type usually presents in adult life. Autosomal recessive inheritance is described in some families. It is not associated with cystinosis and progresses to renal insufficiency much slowly.

Swan neck deformity of renal tubules are seen.

Clinical Features:

Disease presents in first few years of life, affecting males and females equally. Onset is with anorexia, vomiting, inability to thrive, polydipsia and polyuria. There are episodes of intense vomiting and fever leading to dehydration.

Examination reveals growth retardation and dehydration. There are deep rapid respirations associated with acidosis. Muscle hypotonia is present. Severe hypokalemia causes generalized muscular weakness and paralytic ileus.

Rickets is obvious with frontal bossing, craniotabes, swelling of metaphyses at wrists, knees, ankles and costochondral junctions. Bowing of tibia, fibula, femur may occur.

Cystine crystals may be identified by slit lamp examination of cornea. They may lead to photophobia.

Progressive advancing glomerular damage due to cystinosis leads to renal insufficiency. Then symptoms of chronic renal insufficiency supplant those due to tubular dysfunction. Hypertension, bleeding diathesis and neurological complications may occur. Anorexia, growth retardation, polydipsia and polyuria remain prominent symptoms.

Diagnosis:

Cystine storage may be detected by slit lamp examination of cornea or examination of peripheral leucocytes, bone marrow or renal biopsy specimen.

Routine urine testing shows presence of glycosuria and proteinuria. Proteinuria is tubular comprising of post albumin, alpha 2 and beta globulins.

Amino acid chromatography reveals generalized increase in amino acid excretion. Cystine, alanine and valine are especially prominent. Blood levels of amino acids are normal or slightly increased.

Hypokalaemia, hyponatraemia and hypochloraemia are present due to abnormal increased urinary loss. This contributes to dehydration.

Potassium loss is due to lack of proximal reabsorption and increased tubular secretion in effort to reabsorb more sodium from tubular fluid.

Diminution of capacity to concentrate urine is present and is due to combined effect of reduction of sodium transport by loop of Henle and of hypokalaemia.

Metabolic acidosis is due to lack of proximal tubular bicarbonate reabsorption. Distal tubular secretion of H ions is unimpaired.

Occasionally alkalosis may occur due to renal salt wastage.

Rickets is demonstrable radiologically. Serum calcium levels are normal but inorganic phosphorus levels are low and alkaline phosphatase very high. Boney lesions are due to decreased tubular phosphate reabsorption and poor hydroxylation of 25-hydroxy cholecalciferol by kidney.

Uric acid clearance is increased. Hypercalciuria is found only when sodium excretion is also excessive. Progressive deterioration in glomerular filtration rate and renal blood flow are found.

Intravenous urogram shows poor dye concentration.

Percutaneous renal biopsy reveals cystine crystals.

Treatment:

Tubular dysfunction can not be corrected but secondary effects can be improved. Replacement of water and electrolytes is required. 5-10 meq per kg per

day are required of sodium and potassium. Addition of sodium bi-carbonate and potassium chloride to intravenous infusion may be necessary to control acidosis.

Thiazide diuretics which increase salt depletion and increase proximal tubular bicarbonate reabsorption are used to correct acidosis.

Vitamin D in doses of 25000-50000 iu per day are given. Addition of oral phosphate supplement improves rachitic changes with smaller dose of vitamin D.

Penicillamine and diet low in cystine are given.

LOWE SYNDROME
(Oculo Cerebro Renal Syndrome)

Lowe and his coworkers in 1952 described 3 boys with syndrome of mental retardation, organic aciduria, cataract and glaucoma. It is X linked recessive disease of males transmitted by female carriers who are normal or have early onset of cataract. Abnormality of Kreb cycle and particularly of ornithine arginine metabolism is postulated.

Clinical Features:

Boys present from age 3 months onward with typical head with large ears, prominent forehead, flattened nasal bridge and prominent scalp veins in pale skin. Cataract as rule is shown in early cases by slit lamp examination.

Inconstant features are obesity, deafness, cryptorchidism and eczema.

Intermittent pyrexia and growth retardation is usual. Inability to thrive, osteoporosis and rickets occur.

Mental deficiency is severe with hypotonia, lax joints, hypermobility of joints and absent or greatly diminished tendon reflexes.

Eyes are often rolled wildly in pseudonystagmus. Finger pressure on eyeballs produce visual hallucinations.

EEG may show fast 24 cycles per second general activity.

Buphthalmos and congenital glaucoma may be present.

Proteinuria occurs with complicated tubular dysfunction.

Distal renal tubular acidosis is always present.

There is hyperphosphaturia with hypophosphataemia, normocalcaemia and elevated levels of alkaline phosphatase.

Defective tubular ammonium production and defective tubular bicarbonate absorption occurs.

Hyperaminoaciduria especially lysinuria and tyrosinuria is seen.

During febrile episodes hypernatraemia and dehydration may occur.

Renal biopsy reveals tubular damage and dilatation with relatively normal glomeruli.

Treatment:

Good nutrition and hygiene.

Surgery for cataract and glaucoma. Sodium bicarbonate for metabolic acidosis. Calciferol for rickets.

During infancy there are recurrent infections and renal insufficiency.

RENAL GLYCOSURIA

Normally, filtered glucose is almost completely reabsorbed in proximal tubule. But at high blood glucose levels, usually in excess of 180 mg/dl, glucose begins to appear in increasing quantities in urine. Renal threshold for glucose is exceeded.

When renal threshold is reduced glycosuria occurs at lower blood sugar levels than normal ie renal glycosuria.

Small amount of glucose, upto 5 mg/dl is found in normal urine. Its absence is used as indication of presence of glucose consuming bacteria in urine.

There are two types:

1. Threshold for glucose and maximal rate of tubular reabsorption are uniformly diminished throughout nephron. Such situation is found in various forms of Fanconi syndrome whether idiopathic, related to cystine storage or secondary to Wilson disease or heavy metal toxicity. It may also occur as isolated tubular defect and is inherited in dominant fashion.
2. Renal glycosuria due to heterogeneity between different nephrons or because of abnormal enzyme system with reduced affinity for glucose. Glucosuria appears at low levels of blood glucose from minority of affected nephrons. This type produces no clinical disturbance, is of uncertain inheritance and unassociated with other evidence of renal tubular dysfunction.

Importance of this condition lies in distinguishing it from diabetes mellitus by measurement of blood glucose or performance of glucose tolerance test in conjunction with observation of urinary glucose excretion.

To ensure that urinary reducing substance is indeed glucose and not fructose, galactose or homogentisic acid glucose oxidase method is specific but chromatography and osazone synthesis may also help.

Intravenous glucose tolerance test curve is normal but oral glucose tolerance test may show flat curve reminiscent of malabsorption and indication that perhaps as in Hartnup disease and cystinuria transport defect is shared by jejunum.

No therapy is needed. Urinary loss of glucose is less than 30 gms per day per 1.73 square meter and therefore insignificant in terms of nutritional requirements. ❑