RENAL INSUFFICIENCY IN WILSON’S DISEASE - A CASE REPORT

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Abstract:
Wilsons disease also known as hepatolenticular degeneration is one of the commonly inherited metabolic disorder which has been frequently reported in our community. The mutation affects the transport protein which is required for transport of copper into bile and its incorporation into ceruloplasmin. Main sites of involvement are liver and brain, producing liver disease and neuropsychiatric symptoms. They may have renal manifestations like haematuria, proteinuria, acute kidney injury or chronic renal insufficiency. Here we had a 20 years old male who presented with the complaints of cough with expectoration along with swelling of legs and decreased urine output. On examination patient had pallor, bilateral pitting pedal oedema, kayser Fleischer rings. Renal parameters were elevated with hyperkalaemia, Along with proteinuria. Ultrasound abdomen showed chronic liver disease with ascites, bilateral chronic kidney disease. Serum copper and ceruloplasmin levels were within normal range. 24 hours urinary copper excretion is elevated along with serum non ceruloplasmin copper. The patient was diagnosed to have chronic liver disease with portal hypertension, presenting with features of renal insufficiency due to Wilsons disease along with pulmonary tuberculosis. This case is presented because our patient had no past history of Hepatic or Neurological manifestation of Wilsons disease presenting with renal insufficiency. Renal insufficiency as initial symptom of presentation in Wilsons disease is a relatively rare presentation.

Keyword : hepatolenticular degeneration, renal insufficiency

CASE REPORT:
20 yrs. old male, presented with the complaints of cough with expectoration, along with blood stained sputum, fever on and off for past one month. Hematemesis for past one week, 2 to 3 episodes per day, last episode – 50 to 100 ml. H/O swelling of legs with decreased urine output and loss of appetite is present. No H/O passing red coloured urine. No H/O jaundice, melena or other bleeding manifestation. No H/O abdominal pain, distension, itching or passing pale coloured stools. Patient is a known case
of pulmonary tuberculosis diagnosed 3 years back and defaulted after 2 months of ATT. No H/O jaundice, tattooing or blood transfusion in the past. H/O Alcohol intake 180 ml/day for past 1 year & smoking for past 2 years. In General examination patient had pallor, bilateral pitting pedal oedema & kayser – Fleischer rings. Patient did not have clubbing, cyanosis or any signs of liver cell failure. Vitals: Pulse – 82/minute, regular. Blood pressure – 100/70 mmHg in right upper limb in supine posture. Abdomen: Liver enlarged 4 cms below right costal margin in midclavicular line, firm tender, liver span is 16 cms. Respiratory system: Coarse crepitation’s in left hemi thorax. Cardiovascular system, Nervous system – normal.

PICTURE SHOWING KF RING

INVESTIGATIONS:
Complete blood count: ESR – 136 mm/hour, Hb – 4.1 g/dl, PCV – 13%, TC – 6900 / cu mm, Platelet – 2.8 lakh / cu mm, RBC count - 1.65 million / cu mm. Liver function test: Total bilirubin – 0.7 mg/dl, SGOT – 49 U/L, SGPT – 76 U/L, ALP – 110 U/L, Total protein – 7.6 g/dl, Albumin – 3.8 g/dl.
Renal function test: Urea – 85 mg/dl, Creatinine – 7.9 mg/dl, Sodium – 137 meq/L, Potassium – very high. Urine analysis: Protein – ++, Sugar – nil, with occasional sediments and 24 Hours urine: protein - 290 mg, creatinine - 52 mg.

USG abdomen: Liver was 15.5 cms with increased echoes, Spleen was 12.5 cms, Kidney size was 8.9 × 5.7 cms – right, 9.7 × 5.1 cms – left along with features of Increased echoes & loss of Cortical-medullary differentiation. Pelvicalyceal system – normal, Free fluid was present. Impression: Chronic liver disease with ascites and bilateral chronic kidney disease. Portal Doppler revealed portal hypertension, while Upper GI scope showed distal esophagitis with inflamed fundus & pale GI mucosa. Chest X-ray showed left destroyed lung. HbsAg, Anti – HCV were negative, PT – 24 seconds, INR – 1.8, Sputum AFB was Positive, Sputum C/S – Klebsiella pneumoniae. Ophthalmic evaluation showed bilateral kayser – Fleischer rings.

Provisional diagnosis of chronic liver disease with chronic kidney disease with pulmonary tuberculosis with features suggestive of Wilson’s disease present.

Serum copper – 127.6 µg/dl (Normal: 70-150 µg/dl). Serum ceruloplasmin – 23.3 mg/dl (Normal: 20-35 mg/dl). 24 hours urinary copper excretion – 139.26 µg/day (Normal: 15-40 µg/day). Non ceruloplasmin copper = serum copper (µg/dl) – 3.15 × serum ceruloplasmin (mg/dl) = 127.6 - 3.5 × 23.3 = 54.21 µg/dl (Normal: <15 µg/dl, Wilson’s disease >20 µg/dl) Patient was found to have chronic kidney disease and chronic liver disease due to Wilson’s disease with pulmonary tuberculosis. Patient was treated with dialysis, IV diuretics, modified dose of ATT and started on zinc treatment.
DISCUSSION:
Wilson’s disease was first described in 1912 by Dr. Samuel Alexander Kinnier Wilson – A Neurologist.

GENETICS:
Wilson’s disease gene – mapped to chromosome 13 – expressed primarily in liver, kidney and placenta. The gene codes for p-Type (cation transport enzyme) ATPase that transports copper into bile and incorporates it into ceruloplasmin. Inherited as an autosomal recessive pattern, most have no family history of the condition.

SYMPTOMS & SIGNS:
Main sites of copper accumulation are liver and brain, consequently liver disease and neuropsychiatric symptoms are main features that lead to diagnosis. Liver problem comes to medical attention earlier than the neurological symptoms. Hepatic manifestations: acute hepatitis like picture, chronic liver disease, hepatosplenomegaly, ascites, fulminant hepatic failure which may be accompanied by acute intravascular haemolysis and renal failure. They characteristically have disproportionately low aminotransferase levels. May present with cholelitiasis, increased bleeding tendency, hepatic encephalopathy or portal hypertension. Neuropsychiatric symptoms – initial symptoms subtle, change in behaviour, micrographia, hyphonia. Movement disorder – dystonia, incoordination, tremor. Pseudobulbar features – dysarthria, drooling, dysphagia, peripheral neuropathy, and dysautonomia or seizures. Loss of emotion control, depression, hyperactivity or loss of sexual inhibition can occur. Ophthalmic manifestations – KF ring due to copper deposition in descemet’s membrane, fluid streaming favours accumulation near the limbus. Present in 30-50% - hepatic forms, 99% - neurologic forms, disappears with chelation. Sunflower cataract – due to copper deposition in lens, does not interfere with vision, disappears with chelation. Musculoskeletal – arthritis, osteoporosis, osteochondritis dissecans, vit D resistant rickets, rhabdomyolysis. Haematological – combs negative haemolytic anaemia. Endocrine – hypoparathyroidism, infertility or repeated spontaneous abortion, testicular problems. CVS – cardiomyopathy, cardiac arrhythmia. GIT – pancreatitis. Renal – microscopic haematuria, nephrolithiasis, ARF in acute haemolysis or rhabdomyolysis, nephrotic syndrome due to penicillamine therapy, chronic kidney disease. The thickening of basement membrane interferes with the absorption of amino acids, glucose and protein.

DIAGNOSIS:
LFT – abnormal usually, mild to moderate elevation of serum aminotransferase, ALT lower than AST. Serum ceruloplasmin – normal 20-35mg/dl, typically decreased below 20mg/dl in Wilson’s disease due to failure to incorporate copper and the secretion of Apoprotein is devoid of enzymatic activity which is rapidly degraded. Serum copper – normal – 70-150 µg/dl, total serum copper is reduced because ceruloplasmin contains most of serum copper, nonceruloplasmin copper is elevated > 20 µg/dl. 24 hrs. urine copper - basal excretion is elevated at least 2 to 3 times normal in vast majority of patients. > 100 µg / day is diagnostic of Wilson’s disease. Liver biopsy - ideal test is assessed microscopically for the degree of steatosis and cirrhosis, and histochemistry and quantification of copper are used to measure the severity. A level of 250 g of copper per gram of dried liver tissue confirms Wilson’s disease.
TREATMENT:
Dietary - diet low in copper-containing foods is recommended, with the avoidance of mushrooms, nuts, chocolate, dried fruit, liver, and shellfish. Penicillamine was previously the primary anti-copper treatment but now plays a minor role because of its toxicity and because it often worsens existing neurologic disease if used as initial therapy. Patients with hepatitis or cirrhosis, but without evidence of hepatic decompensation or neurologic/psychiatric symptoms, zinc is the therapy of choice. Produces a negative copper balance by blocking intestinal absorption of copper, and it induces hepatic metallothionein synthesis, which sequesters additional toxic copper. All presymptomatic patients should be treated prophylactically. Elemental zinc 50mg three times daily, each dose separated from food and beverages other than water by at least 1 h, and separated from trientine or penicillamine doses by at least 1 h. Trientine and penicillamine dosage for both drugs is 500 mg twice daily, each dose at least 1/2 h before or 2 h after meals.Evaluating patients presenting with hepatic decompensation is to establish disease severity -using the Nazer prognostic index which includes serum bilirubin, serum AST and prolongation of prothrombin time. Low scores are treated with medical therapy while high scores are recommended for liver transplantation. Initial neurologic therapy, tetrathiomolybdate is emerging as the drug of choice because of its rapid control of free copper, preservation of neurologic function, and low toxicity. Anticopper therapy must be lifelong. With treatment, liver function usually recovers after about a year, although residual liver damage is usually present. Neurologic and psychiatric symptoms usually improve after 6 to 24 months of treatment. When first using trientine or penicillamine, it is necessary to monitor for drug toxicity, anticopper effects of trientine and penicillamine can be monitored by following 24-h "free" serum copper. Zinc mainly affects stool copper, 24-h urine copper can be used to reflect body loading.

CONCLUSION:
The manifestation of renal impairment in hepatolenticular degeneration is varied. Therefore hepatolenticular degeneration should be excluded from patients with oedema, haematuria, proteinuria and other abnormalities that cannot be explained by primary renal disease. Also patients with hepatolenticular degeneration should have urinalysis, renal function and ultrasound done to found out renal involvement.

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