AN INTERESTING CASE OF NEUROLOGIC WILSONS DISEASE
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Abstract: Wilson disease is a rare autosomal recessive copper storage disease resulting from an inability of the liver to excrete copper. The buildup of copper leads to damage in the liver, brain, and eyes. Here we present the case report of a young female presented with neurological manifestations and characteristic radiological findings and was diagnosed to be wilson’s disease.

Keyword: WILSONS, NEUROPSYCHIATRIC, COPPER, MRI BRAIN, KF RING.

INTRODUCTION
In 1912 Samuel Alexander Kinnier-Wilson, an American neurologist described a neurologic disorder associated with progressive lenticular degeneration of the brain and cirrhosis of the liver that came later to be known as Wilson’s disease, or hepatolenticular degeneration. Wilson’s disease is an autosomal-recessive disorder of copper metabolism due to absence or dysfunction of a copper-transporting, P type ATPase which is essential for the transport of copper into bile. Prevalence of approximately 1 case in 30,000 live births in most populations. The primary consequence in WD is liver disease, appearing in late childhood or early adolescence as acute hepatitis, liver failure, or progressive chronic liver disease in the form of chronic active hepatitis or cirrhosis of the liver. The neurologic presentation of Wilson disease are less common and tends to occur in the second and third decades or later.

CASE REPORT
18 yr old female patient was admitted in emergency department with complaints of involuntary movements and stiffness of limbs and face for 2 months. Complaints started initially in the right upper limb later on progressed to involve the face and other limbs. Associated with severe pain and inability to use limbs. Later she developed slurring of speech and inability to walk. No history of bowel and bladder incontinence, loss of consciousness, frothing from mouth or tongue bite. Patient gives history of occasional gum bleeding for the past 3 months. She is third child born out of nonconsangineous marriage. Family history nil significant. She attained menarche at the age of 14 yrs. She complaints of irregular menstrual cycles for the past 1 year. Physical examination pallor present, vitals were stable, abdominal examination revealed splenomegaly. Neurological examination revealed dysarthria, rigidity in all four limbs, power was 4+ in all 4 limbs, DTR was just present in all limbs and plantar reflex was flexor bilaterally.

Dystonic posturing of right upper limb was present. No cerebellar signs. No signs of meningeal irritation. Skull and spine normal. Routine investigations were done which showed hemoglobin 10.7g/dl. Platelet count was 56000cells. Renal and liver function tests were normal. Thyroid function was also normal. ECG s/o normal sinus rhythm within normal limits. CT BRAIN was normal. Neurologist opinion was obtained.

Figure 1a) Figure 1b)
Physiologic aberration is excessive absorption of copper from the deposition of copper in the liver, brain, and other tissues. The major ocular evaluation revealed Kayser Fleischer ring in both eyes of the patient. USG Abdomen revealed contracted liver and moderate splenomegaly. OGD Scopy was done Grade 1 oesophageal varices. Serum ceruloplasmin -12g/dl (.2-.6g/dl) was reduced. Serum copper –64microgram/dl (80-155microgram/dl) was reduced. Dieselization of central tegmental tracts with hyperintensity of Pons with hypointensity of central tegmental tracts with hyperintensity of

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PATHOGENESIS
The estimated total body copper content is 50-100 mg, with an average daily intake of 1-2 mg/d. Copper is an important component of several metabolic enzymes. Intestinal copper absorption and transport into hepatocytes is intact in Wilson disease. After copper reaches the hepatocyte, it is incorporated into copper-containing enzymes, including ceruloplasmin. Excess copper may be rendered nontoxic by forming complexes with apometallothionein to produce copper-metallothionein, or it may be excreted into bile. In Wilson disease, the processes of incorporation of copper into ceruloplasmin and excretion of excess copper into bile are impaired. The transport of copper by the copper-transporting P-type ATPase is defective in Wilson disease secondary to one of several mutations in the ATP7B gene. The excess copper acts as a promoter of free radical formation and causes oxidation of lipids and proteins. In the earliest stages of hepatocellular injury, ultrastructural abnormalities involving the endoplasmic reticulum, mitochondria, peroxisomes, and nuclei have been identified. Initially, the excess copper is stored in the liver and causes damage to the hepatocytes. Eventually, as liver copper levels increase, it is released into the circulation and deposited in other organs.

GENETICS
Wilson disease is an autosomal recessive disorder of hepatoocyte copper trafficking due to dysfunction of P type ATPase, encoded by ATP -7B gene located on chromosome 13q14. This gene consists of 21 exons.

PATHOLOGY LIVER
Initial stages show diffuse cytoplasmic copper accumulation detected by immune histochemical stains. Later it progresses to an intermediate stage characterized by perportal inflammation, mononuclear cell infiltrates suggesting hepatitis. Followed almost invariably by cirrhosis.

Brain There is evidence of putaminal softening, ventricular dilatation and atrophy, white matter cavity and central pontine myelolysis like changes. Other features like spongiform degeneration, astrocytosis, neuronal loss and characteristic large opaliski cells exhibiting fine granular cytoplasm and abnormal nuclei.

CLINICAL FEATURES
Wilson disease has diverse manifestations. A high index of suspicion is required in diagnosis and treatment. Most of the patients present with hepatic manifestations which include acute hepatitis, persistently elevated liver enzymes, chronic hepatitis, cirrhosis and fulminant hepatic failure. Neuropsychiatric manifestations include dystonia, tremor, dysarthria, parkinsonism, ataxia, pseudo bulbarpalsy, chorea, seizures, cognitive impairment, bipolar affective disorder, depression, neuroses, personality changes, psychosis, mental retardation. Hematological like hyperplenism, bleeding gums hematemesis, pallor. Ocular features like kayser fleischer ring which is usually bilateral but unilateral cases are described and sunflower cataract. Other manifestations include renal tubular acidosis, menstrual irregularities, recurrent abortion, hyperpigmentation.

DIAGNOSIS
Diagnosis is made from history, physical examination and investigations. Slit lamp examination of eyes reveal Kayser Fleischer ring which is an important feature in diagnosis. Laboratory tests include low serum total copper, low serum ceruloplasmin and elevated 24-hr urinary copper. Other tests like liver function tests, renal function tests, haematological profile, abdominal ultrasound, endoscopic examination are also indicated. MRI BRAIN shows anatomical and pathological correlates of clinical manifestations. It is used for diagnosis and prognosis. The presence of central pontine myelolysis, mid-brain tectal plate signal changes, and giant panda sign differentiates Wilson disease from other extrapyramidal disorders. MR SPECTROSCOPY shows ongoing biochemical changes.

MANAGEMENT
Walsh introduced pencillamine as de –coppering therapy in 1955. A number of drugs like zinc, trientine, and ammonium tetrahydromolybdate were found to have beneficial effect and used in treatment. Liver transplantation is the most definitive treatment for Wilson disease. Symptomatic treatment for hepatic dysfunction, portal hypertension, osseous changes, extrapyramidal and psychiatric manifestations may become necessary. Surgical interventions like thalamotomy indicated for resistant tremor in WD.

PROGNOSIS
Wilson disease is a potentially treatable disorder now. Most of the patients can lead a normal life with the available treatment. But still the outcome of this disease is variable.
BIBLIOGRAPHY