

## CASE REPORT:

# WILSON'S DISEASE

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In March 2002, a young man of 19 from a small village of Dera Ismail Khan District was brought to the Medical OPD. He had involuntary movements of right side of the body, and slurred speech. On the first clinical examination he was considered as a possible patient of rheumatic chorea, epilepsy or a space-occupying lesion of the brain. He was admitted in the medical unit for further evaluation. Proper history revealed that he was normal few years back but slowly and gradually people around him noted that he had involuntary movements and slurring of speech in a course of few months. His condition deteriorated, the involuntary movements increased in frequency as well as duration, moreover his slurring of speech also increased. He was taken to various doctors, spiritual healers and *Hakeems*, most of them labeled him epileptic and treated as such. Spiritual healers as usual blamed "ghosts" for their notorious act on his body. As his condition did not improve he was taken to a teaching hospital where he was diagnosed and treated as epileptic. With passage of time he developed generalized weakness, blurring of vision and difficulty in swallowing and chewing.

His past history revealed an attack of jaundice two years back and family history revealed death of a sibling with jaundice and similar symptoms few years back.

He had normal sleep and bowel habits but looked apathetic and depressed. He used to be a smoker but left it five months back.

Physical examination revealed a slight yellow tinge of his sclera. Systemic examination was generally un-remarkable except for neurological signs of slurring of speech, involuntary movements especially of right side of the body and reduced power 4/5 on Medical Research Council (MRC) scale in the lower limbs.

Varied neurological features, history of jaundice, family history and young age prompted us to the diagnosis of Wilson's Disease (WD). Careful examination of eyes revealed Kay-Fleischer ring over the corneal margin (it is a ring of brownish green pigments around the corneal margin due to deposition of copper). Ophthalmologist confirmed it by slit lamp examination. Laboratory investigations showed low serum ceruloplasmin and copper while high 24 hours urinary copper excretion. Other investigations were unremarkable except slightly raised Alanine aminotransferase and slightly enlarged liver on abdominal ultrasonography. He was started on D-Penicillamin and carefully monitored. All his symp-

toms improved dramatically except his speech which remained slurred for few months. In order to avoid unwanted side effects of penicillamin his blood complete and routine urine examination was performed on each visit. He regularly visits our clinic and is symptom free after a year.

Wilson's Disease (WD) or Hepato-lenticular degeneration is an autosomal recessive disorder with variable clinical presentation. It may present between the ages 6-60 years. Disturbance of copper metabolism may result in accumulation of excess copper in the liver, basal ganglia (lenticular degeneration), the kidneys, cornea (Kayscher-Fleischer rings) & other tissues.<sup>1</sup> The gene responsible is located on chromosome 13.<sup>2</sup> Molecular & genetic analysis is complex, as more than 200 unique mutations have been identified & most individuals are compound hetrozygotes.<sup>3</sup> Elucidation of molecular genetic basis of WD has permitted new insights into the mechanism of cellular copper homeostasis.<sup>4</sup>

Wilson's disease can be effectively treated so it is extremely important for physicians to learn to recognize & diagnose the disease.<sup>5</sup>

Patients suffering from Wilson's disease can be divided into two main sub-groups: Neurological & non-neurological WD.<sup>6</sup> The clinical symptoms are due to copper deposition in various tissues including liver, Brain, Kidneys, Cornea & others.<sup>7</sup>

WD should be considered as a possible diagnosis in any child, adolescent or young adult with liver damage without other explanation when haemolysis is present. It may also present in adolescent or young adults with neurological signs confined to the motor system. The diagnosis of WD is frequently overlooked; non-specific symptoms and multi system involvement may mimic other disease states such as neurological and psychiatric disorders.<sup>1,8</sup> The age of liver dysfunction patients is significantly younger than that of CNS manifestation patients.<sup>9</sup> Presentation in Childhood may include chronic hepatitis, cirrhosis or acute liver failure. In young adults neuro-psychiatric symptoms predominate & include hysteria, tremors, personality changes & cognitive impairment secondary to copper deposition in CNS.<sup>4</sup>

Diagnosis of WD depends on a combination of clinical and laboratory findings. Twenty four hours urinary copper excretion seems to be the most sensitive test for diagnosis of Wilson's disease particu-

larly when liver biopsy can't be performed due to coagulation abnormalities.<sup>10</sup> Slit lamp examination of the eye may reveal Kayser-Fleischer ring.<sup>11</sup>

All close relations of an identified patient must be screened as well.

Side effects of therapy are detected by estimation of urinary total protein, Full blood count, Clotting factors & LFTs.<sup>12</sup>

The key strategy of treatment is to reduce the amount of copper in the liver and other tissues by administering copper chelating agents and a low copper diet.<sup>7</sup>

D-penicillamin is considered to be the first choice as a copper chelating agent. Patients require 15-25 mg/Kg daily in the early stages of treatment. D-penicillamine administered 1 hour before the morning and 1.5 hour before the evening meals has better results as compare to 2 hour after meals or 30 minutes before meals in terms of urinary copper excretion.<sup>13</sup> It is a relatively safe and effective long term treatment in patients with Wilson's disease.<sup>14</sup> Some undesirable or serious side effects such as systemic lupus erythomatosus and nephrotic syndrome do occur in 20-25% of all the patients. In such cases Triethylene tetra-amine (trientine) appears to be as effective as penicillamine. It is given in doses of 40-50mg /kg daily in the same manner as for D-penicillamine.

Tetrathiomolybdate may also be used for treatment of W.D.<sup>2</sup>

Zinc salt administration has also emerged as an interesting supportive therapy. A dose of 5-7.5mg/kg daily is given before meals. Zinc administration in vitro increases metallo-thionine concentration which may prevent oxidative toxicity.<sup>15</sup>

Life long treatment with chelating agents (D-penicillamine or trientine) or zinc sulphate is usually sufficient to stabilize the patient and to achieve clinical remission in most. Compliance with chelating therapy (penicillamin or trientine) or administration of metal antagonist tetrathiomolybdate or zinc is monitored by determination of serum free copper which should be maintained at or near 1.6 mmol/liter (10mgm/100ml).

The copper contents of the diet should be less than 1mg/day in the early stages of the treatment. Liver transplantation is performed in many countries for patients with either fulminant or chronic progressive type of WD.<sup>7</sup>

Patient with most advanced liver disease benefit from orthotopic liver transplantation.<sup>16</sup>

Major challenges ahead include closing the remaining therapeutic hiatuses, cloning and expressing the gene to understand its function and improving clinical diagnosis, so that therapy can be instituted as quickly as possible.

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