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Case Report

Neurological presentation of Wilson's disease without overt hepatic involvement

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ABSTRACT

Wilson disease (hepatolenticular degeneration) is a rare autosomal recessive disease. Here, we report a child affected by Wilson disease with only neurological manifestations without hepatic involvement.

Keywords: Kayser Fleischer ring, S. Ceruloplasmin, Panda sign

INTRODUCTION

Wilson disease results in systemic overload of copper affecting brain, liver, kidney and eyes.[1] Reported prevalence of this disease is 1 in 30,000 people and carrier frequency is approximately 1 in 90.[2] Symptoms usually begin between 5-35 years. The defective gene ATP7B is located on chromosome 13q14.3 which encodes copper transporting ATPase.[3]

CASE REPORT

A 15 years old male child muslim by religion born out of consanguineous marriage presented with repetitive rhythmic involuntary movements of right forefinger starting 3 months back which gradually progressed to involve right hand, right forearm and right lower limb. These movements were aggravated by stress, emotions and voluntary movements and disappear during sleep. Child was on some medication since last 3 months but symptoms persisted. Since last one-month child developed difficulty in articulation and pain in both knee joints. Child also developed aggressive behavior and drooling of saliva while talking and sleeping since last 20 days. There was no history of fever, abdominal distension, pallor, convulsions, jaundice, swelling of feet, hematemesis or rectal bleed. At 10 years of age child developed fever and pain abdomen in the right hypochondrium associated with icterus. Child was given some medications in a private hospital but cause of jaundice was not evaluated. Child recovered fully in between. Developmental history was normal. No history of similar illness in the siblings.

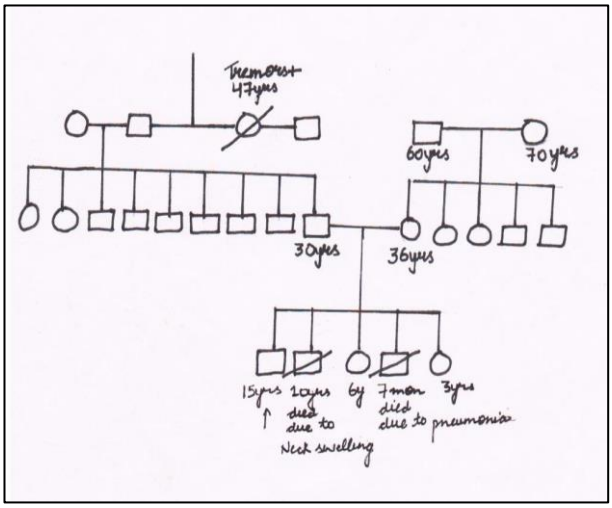

Figure 1: Pedigree chart.

However, there was history of similar complaints in paternal aunt, who expired undiagnosed at the age of 47 years. No history suggestive of liver dysfunction in any family member could be elicited.

On examination

Patient was calm, conscious, cooperative, well oriented to time, place and person with weight-40.2 kgs (expected 53 kgs), height- 176 cms (expected 165cm) and HC- 52 cm (expected 51 cm). Vital parameters were normal. SMR staging was 4. On abdominal examination- there was no distension or visible veins. Liver was palpable 1 cm below the right costal margin, non-tender with smooth surface and round margins. Liver span was 10.8 cm. Spleen was palpable 1.5 cm below the left costal margin.

No stigmata of chronic liver disease like ascites, edema, palmar erythema, dupytren's contracture, icterus, gynecomastia, spider nevi were detected.

Neurological examination

Higher mental functions, cranial nerves were normal. Tone, power and deep tendon reflexes were normal. Plantars were flexors. Coarse tremors in the form of regular, rhythmic movements of hand and fingers of right side which were aggravated with emotions/stress and disappear during sleep but aggravated by voluntary movements.

Bilateral Kayser Fleischer Ring (Figure 2) visible with naked eye was further confirmed on slit lamp examination by ophthalmologist. Rest of the systemic examination was normal.

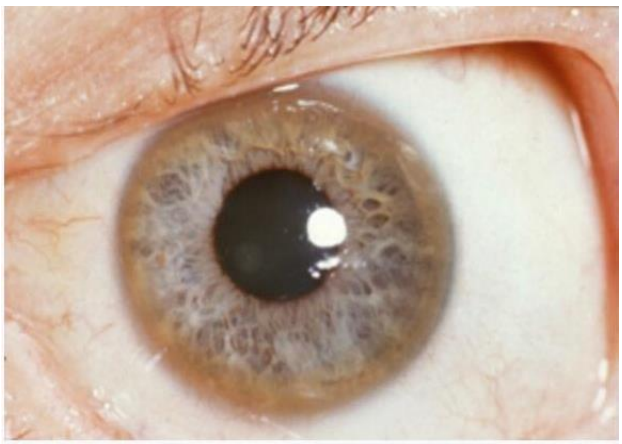

Figure 2: Kayser Fleischer Ring.

Investigations

Hb- 12.7 gm/dl, TLC- 6000/cumm, neutrophils-67%, lymphocytes-28%, Platelets-1.8 lac/cumm, PCV-36.3 %, PBF- normocytic normochromic with few microcytes.

Serum bilirubin: total/direct -0.342/0.097 mg/dl, AST-31.7IU, ALT-31.8 IU, ALP- 1297.2 IU, S. Protein-6.6 gm/dl, S. Albumin-3.86 gm/dl, S. Globulin-2.7 gm/dl, AST/ALT>1, ALP/total bilirubin<4. Urine routine examination was normal. S. Ceruloplasmin-9(20-60 mg/dl), 24 hrs. urinary Cu excretion≥500ug/day (<40ug/day).

USG abdomen

Revealed mild splenomegaly with early hepatic parenchymal changes. MRI Brain: Suggestive of bilateral symmetrical hyper intensities in bilateral putamen, ventral aspect of thalamus, posterior limb of internal capsule, midbrain (with relative sparing of red nucleus and substantia nigra), dorsal and ventral pons (Figure 3) panda sign.[4]

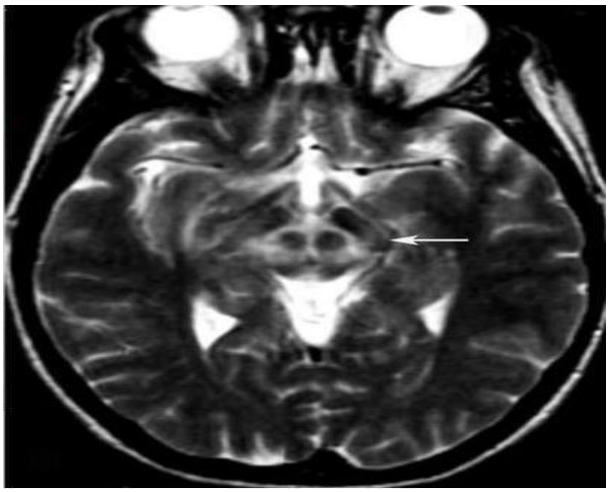

Figure 3: MRI T2 -weighted image.

Patient has been started on D-pencillamine 250 mg bid before meals along with Zinc 25 mg TDS (empty stomach) and pyridoxine 40 mg/day. Advised to avoid foods rich in copper like nuts, chocolates, non-veg diet, not to store water in copper vessels, shellfish, beans (<1 ppm/day intake of copper). Advised family screening.

DISCUSSION

Wilson disease is a rare autosomal recessive inborn error of copper metabolism caused by mutation in copper transporting gene ATP7B which was first described by Dr. Samuel Alexander Kinnier Wilson in 19125. Copper first accumulates in liver then nervous system, cornea, kidneys, eyes and other organ systems. Main clinical presentation of Wilson disease - Hepatic involvement (42%) including acute liver failure with Coombs negative hemolytic anemia, cirrhosis, acute/ chronic hepatitis. Hepatic copper accumulation is the hallmark of Wilson disease. Hepatic copper concentration more than 250 mcg/g of dry weight on liver biopsy is confirmatory diagnostic test.[6]

Neurological involvement (35%) predominantly extrapyramidal like dystonia, tremors, dysarthria, ataxia.

KF ring is seen in 44-52% of patient with Wilson disease. KF rings are seen in 95% pts. with neurological symptoms.[7] Majority of the patients present in second decade with primary hepatic presentation. Hepatic involvement is seen 10 years before neurological involvement. After 20 years of age, neurological involvement is pre dominant.8. Neurological involvement can be seen as early as 6 years of age.[9]

Untreated patients die because of hepatic and neurological complications. Prognosis for the patients receiving pencillamine is excellent. Trientine is less toxic. Drug of choice in neuropsychiatric symptoms is ammonium tetrathiomolybdate which is not easily available. LEIPZIG scoring system:[10]

Score>4=definitive diagnosis of Wilson disease.

1) KF ring- 2 points 2) Neurological involvement- 2 points 3) ↓ S. ceruloplasmin- 2 4) ↑ Urinary copper excretion-2.

Liver transplant is the ultimate resort for the patients presenting with fulminant liver failure.[11]

CONCLUSION

Index case in our study has neurological involvement without any overt hepatic involvement. So, a high index of suspicion is required in any adolescent presenting with abnormal body movements and neuropsychiatric symptoms. Early detection is critical as early treatment can prevent the progression of disease. Our patient presented with neurological manifestations at 15 years of age. Similar observations were made in other Indian studies possibly due to higher average copper intake due to practice of cooking food and storing water in copper utensils.

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