Chronic Acquired Hepatocerebral Degeneration: A Case Report

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ABSTRACT

Introduction: Chronic acquired hepatocerebral degeneration is a rare disorder typically accompanied by cognitive disturbances and parkinsonian features secondary to liver disease. It is the deposition of manganese in the basal ganglia leading to T1 hyperintensity on MRI of these patients and the resulting clinical features. Familial association is found in some cases.

Case report: Here, we report the case of a 32 year old post partum female who presented with tremors and history of liver disease. MRI of the brain showed symmetric hyperintensities in globus pallidi, substantiae nigrae, and superior cerebral peduncles in T_1-weighted images. Although liver transplantation is the best modality of treatment at present, the patient showed improved on treatment with Levodopa+carbidopa.

Conclusion: It is important to recognize this disease entity for symptomatic relief of the patient. However further research is required for better management.

Keywords: Chronic Acquired Hepatocerebral Degeneration

INTRODUCTION

Familial hepatocerebral (or hepatolenticular) degeneration, now known to be related to excessive copper accumulation in liver and brain, was described in 1912 by Wilson.[1] Two years later, van Woerkom described a non-familial form of hepatocerebral degeneration with progressive tremor, rigidity, somnolence and emotional instability in the setting of acquired liver disease.[2] Subsequently several authors reported such cases who lacked family history, had normal ceruloplasmin and had no evidence of excessive copper accumulation. By reporting this case, we are emphasizing on this widely known, but often missed, condition.

CASE REPORT

A 32-year-old lady was brought in our emergency department in the state of altered sensorium six days after she delivered a preterm baby vaginally. Two days ago, she had melena. When her sensorium improved two days later, the patient developed tremors, slowness of movements, difficulty in speaking and difficulty in walking. On examination of the patient when she was alert, vitals were normal. She had mild icterus, pedal edema and splenomegaly. She had slowed mentation. Detailed higher function tests could not be done. Oculomotor examination showed that she had increased saccadic latency, slow saccades and normal pursuit movements. Her voice was tremulous. Motor examination showed that she had normal muscle bulk, cogwheel rigidity of limbs and normal muscle power. She had coarse large amplitude tremors of about 4 Hz frequency involving both upper and lower extremities symmetrically. Tremors were present at rest and involved distal as well as proximal parts of the extremities. Tremors worsened with sustained posture and during action, and disappeared during sleep. In addition, there were orofacial, head and trunk tremors. The patient had hyperreflexia with extensor plantar responses. Sensory examination was normal. Finger to nose and heel to shin tests were impaired due to coarse tremors. She walked with upright posture. Her tandem walk was impaired.

Blood investigations showed hemoglobin 10.3 g/dL, leukocyte count 5600/µL, platelet count 49,000/µL, bilirubin 1.3 mg/dL, albumin 3.2 gm/dL, ALT 16 IU/L, AST 112 IU/L, ammonia 130 µmol/L, INR 1.3, and ceruloplasmin 35.5 mg/dL.Blood sugar, serum creatinine, TSH and electrolytes were normal. HIV, HBsAg, anti-HCV and ANA were non-reactive. Urinalysis was normal and 24-hour urinary copper was 14.8 µg. Slit lamp examination of the eye did not show Kaiser-Fleisher ring. Chest x-ray was normal. Ultrasound abdomen showed chronic liver parenchymal changes, evidence of portal hypertension and splenomegaly. MRI of the brain showed symmetric hyperintensities in globus pallidi, substantiae nigrae, and superior cerebral peduncles in T_1-weighted images (figure 1).

When the patient was brought in altered sensorium, she was initially treated with intravenous fluids, Pantoprazole 40 mg/day, Rifaximin 100 mg/day and Lactulose enema. Later when she had troublesome tremors, clonazepam 0.5 mg/day and Propranolol 80 mg/day were started. Within few days, tremor nearly disappeared from the extremities. But she continued to have intermittent orofacial tremors. Tetrabenazine 75 mg/day (gradually escalated) was started. However, it had to be discontinued because the patient developed marked bradykinesia. After adding levodopa/carbidopa 100//25 mg (gradually escalated to thrice daily), her movements improved. She went home and later discontinued the medications. A local physician placed her on nitrazepam and metronidazole. When patient followed up at three months, she had faint orofacial tremor but no visible extremity tremor. She did not have bradykinesia and rigidity. Review of the patient's previous records showed that she had undergone liver biopsy (suggestive of cirrhosis) and Coomb's test (normal). Detailed evaluation for cause of cirrhosis could not be done due to her poor financial condition. There was no family history of jaundice or similar neurological

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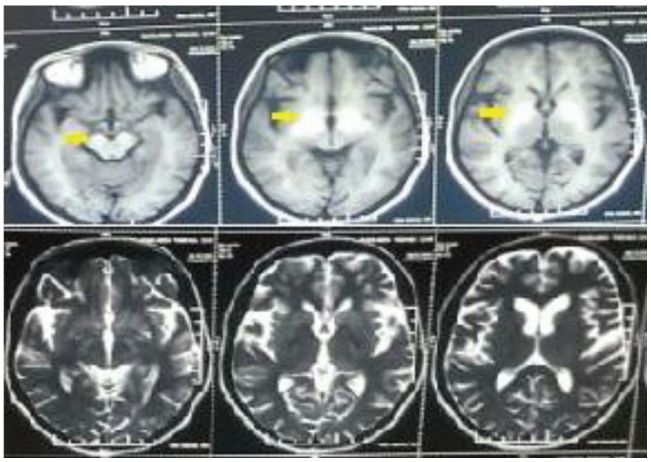

Figure-1: MRI of the brain in our patient of CAHD showing T_1 hyperintensities in the globus pallidi and the cerebral peduncles; T_2-weighted images are normal

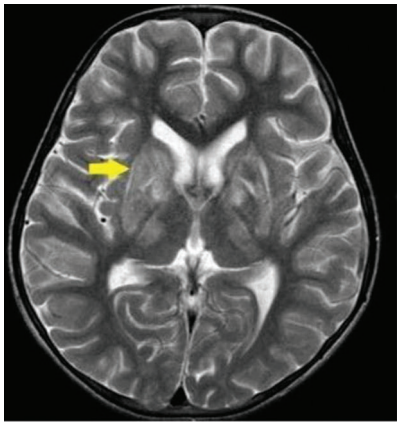

Figure-2: MRI of the brain in a patient of Wilson's disease showing T2 hyperintensities in the basal ganglia

disorder. There was no history of consanguinity. She had been taking propranolol 60 mg/day, clonazepam 1 mg/day, tetrabenazine 50 mg/day and trihexyphenidyl 6 mg/day for about two years, but had discontinued treatment in the later stages of pregnancy.

DISCUSSION

The clinical and pathological features of chronic acquired hepatocerebral degeneration (CAHD) were lucidly described by Victor and colleagues in 1965. Patients may present with neuropsychiatric symptoms (encephalopathy, apathy, lethargy, somnolence, hyperactivity, aggression) or movement disorder (ataxia, tremor, parkinsonism, chorea, myoclonus, dystonia) or more commonly, both.[3] Additionally, patient may have pyramidal signs, myelopathy, neuropathy or myeloneuropathy.[4] Pathologically, there is patchy neuronal loss and spongy degeneration in various areas of the cortex and characteristic vacuolation of the basal ganglia. There is also cerebellar atrophy with vacuolation of the dentate nucleus. Microscopic features include polymicrocavitation in the neural tissue and proliferation of Alzheimer type II astroglial cells.[2] This neurodegeneration may be seen in several hepatic disorders (alcoholic liver disease, chronic viral hepatitis, hemochromatosis, sclerosing cholangitis, primary biliary cirrhosis). It may also be seen in patients with portosystemic shunts in non-cirrhotic liver disease due to schistosomiasis and congenital cystic fibrosis, and with portal vein thrombosis or surgical shunting. Thus, portosystemic shunting leading to accumulation of several toxins (ammonia,γ-aminobutyric acid, aromatic amino acids, manganese) is central to the pathogenesis of CAHD.[5,6]

Several types of movement disorders are seen in patients of CAHD in isolation or combination. Patients commonly have postural and action tremor involving the upper extremities more than the lower extremities. Tremor is predominantly distal, large amplitude and has frequency of 4-7 Hz. Tremor can progress proximally and also involve head and trunk. There can also be fine lip, orofacial and tongue tremor. Spontaneous resolution of tremor may occur, but with hepatic encephalopathy there may be reappearance or exacerbation of tremor. Patients may also have rest tremor as a component of parkinsonism, other features being bradykinesia and rigidity. Chorea is another common movement disorder. It may resemble tardive dyskinesia. There is prominent orofacial and lingual chorea with protrusion-retraction movements of tongue. Chorea may be exacerbated by voluntary movement. Dystonia is uncommon in patients of CAHD as compared to patients of Wilson's disease. Ataxia is a prominent feature of alcoholic cerebellar degeneration, but may be seen in non-alcoholic CAHD. Asterixis (negative myoclonus) usually exists with acute exacerbations of hepatic encephalopathy. Action myoclonus may persist even without obvious encephalopathy. Gait is impaired if legs are involved.[5]

MRI of the brain in patients of CAHD shows characteristic hyperintensities in globus pallidi in T_1-weighted images. There can also be involvement of caudate and putamen. This is believed to be due to accumulation of manganese. Other findings include subcortical white matter hyperintensities and cerebral and cerebellar atrophy.[6] These are in sharp contrast to the changes induced by copper accumulation in Wilson's disease, which are prominent in T_2-weighted images (figure 2). Another important neurological disorder of manganese accumulation is manganese transporter deficiency due to recessive mutation in SLC30A10 gene. Patients have onset of symptoms in the first decade of life. Typically, they have dystonia with characteristic cock-walk gait. There can be dysarthria, parkinsonism, pyramidal signs, motor neuropathy and neuropsychiatric symptoms. Patients also develop chronic liver disease and polycythemia.[7] There can be neurological involvement in patients with occupational manganese exposure.[8]

There is no specific treatment of CAHD. Beneficial effects of lactulose, branched chain amino acids, and trientine were reported by some authors. Symptomatic therapy for tremor, chorea and parkinsonism may benefit some patients. However, response is not predictable. Liver transplantation appears to be the most promising treatment.[9] However, reappearance or persistence of abnormal movements due to persistent portosystemic shunts is known.[6]

Our patient had cirrhosis of liver (Child Pugh class B and MELD score 10) due to unknown etiology. She had combination of movement disorders (tremor and parkinsonism) with marked fluctuations. It seemed that tremors responded to medications. However, we believe that she had spontaneous improvement following exacerbations related to intermittent decompensation.

CONCLUSION

Even though treatment is not satisfactory, it is important to recognize CAHD. It has been seen that patients may present with a movement disorder without obvious hepatic encephalopathy and other features of hepatic disease.[10] Future research and controlled trials are required to guide in treatment.

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