COMMENTARY

Neuropsychiatric manifestations of Wilson disease in Sudan

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Elhafyan HJ, Osman AHM, Younis YO. Neuropsychiatric manifestations of Wilson disease in Sudan. J Clin Psychiatry Neurosci 2021;4(4):10-11.

Delineating the neuropsychiatric pattern and features of Wilson disease is essential step to better recognition and management of these presentations. To our knowledge this is the first large study of neuropsychiatric manifestations of Wilson disease in Sudan.
A comprehensive case finding survey was conducted over a six month period, in the Capital of Sudan, covering all secondary and tertiary services that cater for patients with Wilson disease. Patients' assessment was carried out using batteries of functional tests, including, ICD10 research criteria for major psychiatric categories, Mini Mental State Examination, ADHD scale, school records, parental reports. All neurological findings were conducted and verified by two neurologists. Neuropsychiatric symptoms and disorders are highly prevalent in Wilson disease patients regardless of age, or stage of illness. Even though, patients in our sample had had an average of 6 years follow up duration, non-had shown evidence of liver failure. This shows an early indication of possibly benign trajectory course of the illness in Sudan.
Key Words: *Neuropsychiatric; Parkinsonism; Dystonia; Hepatic encephalopathy*

DESCRIPTION

Wilson's disease is an autosomal recessive illness that arises due to a defect in the gene ATP7B (on chromosome 13q (long arm)), leading to an impairment in cellular copper transport (packaged in ceruloplasmin into bile), resulting in an excessive accumulation of copper in the liver, brain, cornea, bones and other tissues [1,2]. Over time, this leads to progressive liver damage, eventually culminating in cirrhosis of the liver and, potentially, acute hepatitis. Deposits of the metal in the brain lead to a wide range of neuropsychiatric symptoms and disorders [3].

Although the mechanism of copper excretion is defective from birth, most patients present with symptoms between the ages of 5 and 35. A minority do not show symptoms until later in life [4].

The lifetime prevalence of WD is estimated to be 1:30,000 in many countries, although prevalence as high as 1:7000 have been reported [5].

Neuropsychiatric syndromes

Neurological or psychiatric symptoms can emerge at any time during the course of the illness; however, the salient pattern of these conditions occurs as a result of subcortical deposition of copper in the basal ganglia, with putamen degeneration or cortical involvement of the frontal lobe [6]. In the former, this can result in extrapyramidal symptoms, such as tremors, rigidity, Parkinsonism, chorea, athetosis, ataxia, dysarthria, dysphagia, dystonia, drooling, dysdiadochokinesis, micrographia and coordination problems. Other neurological manifestations include hyperreflexia, tics and unusual stereotyped movement [7]. Frontal lobe involvement leads to frontal lobe syndrome, with personality and behavioural abnormalities. Here, patients can present with impulsivity, sexual disinhibition, labile mood [8], promiscuity, irritability or apathy, indecisiveness, lack of planning and executive dysfunction. Other psychiatric symptoms and disorders may emerge as a consequence of hepatic encephalopathy, and other organ disorders such as kidney, haemolytic anaemia, endocrine failure, or osteopathy and osteoporosis leading to fractures [9]. By the time patients with WD present with neuropsychiatric symptoms, almost 50% will have developed liver cirrhosis, both of which are preventable with early detection and treatment with chelating agents [10]. Neuroimaging advances have shed light on the specific pathology associated with WD. The typical neuroimaging finding of WD is the "face of giant panda" sign, with hyper-intensities in the basal ganglia, tectal plate and the central pons; involvement of the thalamus and brainstem are also characteristic of WD [3].

The majority of WD patients present with liver symptoms, however, 30% of patients will present for the first time with psychiatric manifestations. Almost all sufferers will display psychiatric symptoms at some point during the course of the illness [5], and psychiatric presentations often (60%) co-occur with neurological involvement. Little is known of the factors influencing the phenotypic expression of WD (hepatic vs. neurological or psychiatric presentation), although perhaps age of presentation may play a role [10].

The typical psychiatric domains that get affected during the course of WD include affective manifestations, behavioural and personality disturbances, psychosis and cognitive impairments.

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Received date: *July 07, 2021;* ***Accepted date:*** *July 21, 2021;* ***Published date:*** *July 28, 2021*

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