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A Rare Case of First Attack Psychosis and Wilson's Disease

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ABSTRACT:

A rare case of first attack psychosis and Wilson's disease

Wilson disease (WD) is an infrequent genetic disorder of copper metabolism (chromosome 13), with decreased transport of copper by hepatic lysosomes due to mutation in the Wilson disease protein (ATP7B) gene. Hence, accumulating copper is primarily affecting the liver, brain, cornea, and kidneys, after then leading to their symptomatic damages. During early ages, the patients are mostly presymptomatic. The worldwide prevalence was reported to be 1 in 30.000. Psychiatric symptoms are common with Wilson's disease. Pychosis can be an initial manifestation and often leads to an inaccurate diagnosis. As is seen, clinical syndrome may be very complex. Therefore, detecting mental health disorders of secondary origin is very important for the mental health professionals. In conclusion, one must be aware of the possibility of an organic cause in patients who are admitted with psychiatric symptoms, for the first time. On the other hand, medical causes of psychiatric symptoms should always be considered. Here, we report on a case of psychotic disorder due to Wilson's disease, presenting with psychotic symptoms and bizarre behaviour.

Keywords: mental health disorders, psychosis, copper, atypical antipsychotic, wilson disease

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INTRODUCTION

Wilson's disease (WD) (also called hepatolenticular degeneration) is an infrequent autosomal recessive disorder of copper metabolism (chromosome 13) with decreased transport of copper by hepatic lysosomes due to mutation in the Wilson' disease protein (ATP7B) gene. Accumulating copper is primarily affecting the liver, brain, cornea, and kidneys, after then leading to their symptomatic damages (1). But, during early ages, the patients are mostly presymptomatic. The worldwide prevalence was reported to be 1 in 30,000 (2). According to literature findings, psychiatric symptoms associated with WD have been divided into four areas, including the personality changes, affective and psychotic disorders, and cognitive impairment (3,4). The most common psychiatric features were abnormal behavior and personality changes, although depression and impairment of cognitive function were also rated frequently. Compared to other psychiatric symptoms, psychosis is less commonly described in patients with WD (5).

Therapeutic outcome of WD significantly depends upon its early recognition. Because, WD is one of the few curable disorders provided; it is diagnosed and treated early. Diagnosis of WD is often made clinically by the presence of Kayser-Fleischer (KF) rings, adjacent to cornea, low levels of serum ceruloplasmin (alpha-2 globulin, a serum glycoprotein), elevated concentrations of copper in the cerebrospinal fluid, and hyper intensities in the basal ganglia and thalamus of the brain (1,2). KF ring is present in 99% of neuropsychiatric patients (6). Here, we report a 42 years old woman presenting with bizarre behaviors and psychotic manifestations who was treated for Wilson's disease, at the age of 33.

CASE PRESENTATION

A 42 years divorced woman, housewife, living with three children was referred to our psychiatry clinic at the Dicle University School of Medicine, by the family physcian and gastroenterologist. Over the past few weeks her family have noticed increasingly bizarre behaviors.

Our case presented with two months history of psychotic symptoms and behavioral changes, associated with significant dysfunction of daily activities. The patient had completed elementary school and had been working as a baby-sitter until she became ill. The patient agreed unwillingly to psychiatric examination, associated with poor insight. On a mental status examination, the patient seems to be dirty and disheveled. Her affect was anxious and labile. She exhibitd minimum eye contacts. However, she stated that her mood is "okay." Her thought processes were tangential and loose associations were noted. Her thought content is positive for delusion of reference and persecution with auditory hallucinations. She had impaired abstract thinking and could not explain the meaning of a given idiom. The patient was found to be conscious and oriented to time, place, person, and situation. Over the next few days, her psychotic symptoms became more extensive and systematized. Hence, she became socially isolated and dysfunctional as a result of these symptoms. The patient said that her ex-husband and several other people were conspiring against her and disturbed her. The auditory hallucinations consisted of different voices including the her ex-husband, commenting on the patient's behavior and giving her commands. She denied any suicidal and homicidal ideations.

She had no known drug allergies as well as she had no history of alcohol, tobacco, or illicit drug use with any psychiatric disturbances. Family history of WD or other neurological and psychiatric disorders was negative. She had past history of hypercholesterolemia, and hypothyroidism diagnosis in seven years ago, which remitted with appropriate treatment. Detailed neurological examination as well as the electroencephalography (EEG) has been found unremarkable. Magnetic resonance imaging (MRI) of the brain showed T2 hyperintensities in bilateral thalamus, lenticular nuclei, and brainstem as well as cortical atrophy and white matter changes. Ophthalmological examination revealed presence of KF ring. Laboratory studies showed decreased serum ceruloplasmin (5 mg/dl; normal range 15–45 mg/dl) and elevated urinary copper (265.06 μg/day; normal range 15–60 μg/day). The rest of the hematological and biochemical investigations were all within normal levels, including the complete blood count, renal function test, thyroid function test, random blood sugar, serum magnesium, etc. Also, screening for human immunodeficiency virus, hepatitis B, hepatitis C viruses and VDRL were all negative. During admission, abdominal ultrasound revealed hyperechoic hepatic parenchyme with no masses or abscesses. Apart from this, complete physical examination of her body showed practically normal findings (afebrile, eupnoic, normotensive etc.).

At the age of 33, she was admitted to the gastroenterology department, complaining with weakness and persistent pruritus. At that time, she was diagnosed with WD, after laboratory and other investigations. During that period, oral penicillamine 500 mg/day, in divided doses was started, by the gastroenterologist. After then, the dose of oral penicillamine was gradually reduced with which symptoms resolved. She had been off penicillamine for 2 months and had continued to take zinc acetate 150 mg/day for WD.

Currently, she was referred to our department of psychiatry, after then started on an atypical antipsychotic, quetipine fumarate, extended release (XR). Initially, the patient tolerated 100 mg/day of quetiapine XR. Over 3 weeks, the dose was titrated up from quetiapine XR 100 mg/day to 800 mg/day, with intermittent adherence, additionally lorazepam 2.5 mg/day. Subsequently, her psychiatric symptoms improved, and she became less irritable, more calmer and manageable. Hence, she was discharged home. The patient was diagnosed with "psychotic disorder due to WD, with delusions" per Diagnostic and Statistical Manual of Psychiatric Disorders, 5th Edition (DSM-5) (10).

She was followed-up regularly for 12 months. She was on atypical antipsychotic treatment for 6 months, at the time this case was reported and did not experience any adverse events. Her family described her as being as completely busy with them, as she had been before her illness. Currently, she has continued to take only zinc acetate 150 mg/day at bedtime, as maintenance treatment for WD. The patient showed no active symptoms either from neuropsychiatric or any other domain of WD, for this period.

Written informed consent was obtained from the patient for publication of this case report.

DISCUSSION

Our patient had no history of psychiatric disorders until the age of 42. She presented with psychotic symptoms, such as paranoid delusions (reference and persecution) with auditory hallucinations. At diagnosis, the most common psychiatric symptoms have been reported to be personality change, inappropriate behavior, irritability, anxiety, depression, emotional lability, impulsiveness, as well as self-injurious behavior (3,7). Psychosis and cognitive impairment are less common forms of WD presentation (1,8). Overall, the prevalence of psychosis in patients with WD varies from 0% to 11.3% (9). For our case, psychotic symptoms including the paranoid delusions (reference and persecution) and auditory hallucinations, strong premorbid psychosocial functioning, and lack of prodromal symptoms of chronic primary psychotic disorder, therefore a diagnosis of psychotic disorder due to WD, with delusions was confirmed (10). In our case, all of psychiatric symptoms were not related with any altered cognitions, hallucinations in any modality, thought disorder, depressive symptoms, head injury or substance abuse.

The mechanism of psychiatric symptoms in WD is not clear. It was thought that basal ganglia abnormalities led to various psychiatric symptoms through dopamine dysregulation (12). Alternatively, too much copper stimulates production of the neurotransmitters, such as epinephrine, norepinephrine and dopamine (14). Because of the toxic effects of excess copper on catecholamine synthesizing enzyme systems (15); there is softening and atrophy of basal ganglia nuclei, resulting in neuropsychiatric symptoms, eventually cell death (1,6).

Abnormal behavioral and psychiatric symptoms are quite common, also some of them may precede neurologic or hepatic symptoms (3,7). In our case, on the basis of clinical symptoms and laboratory findings, a diagnosis of WD was made, at the age of 33. The most patients who diagnosed to WD, develop symptoms between the ages of 5 and 35, as in our case. It rarely remains masked until after the age of 40 (1). The average duration between onset of psychiatric symptoms and diagnosis of WD was 864.3 days (12). But, in another study found that, the mean delay in correct diagnosis was 8 years (range 6 months to 20 years) (13). Similar cases were described in literature (11,14).

For our patient, remission of psychiatric symptoms was achieved after 6 months of treatment. This slow recovery may have been due to the slow reduction of copper levels in the brain. In literature, there are no certain data regarding the duration of treatment with psychotropic drugs in WD. Indeed, psychiatric symptoms can occur in both untreated and treated patients with WD (14). The drug treatment of Wilson's disease is based on the use of copper chelators to promote copper excretion from the body, or zinc to reduce copper absorption, or both. Furthermore, penicillamine reverses both neurological as well as behavioral symptoms of WD. It has been shown that, early detection and treatment of WD, by penicillamine therapy could improve the psychosis without the need of treating with antipsychotic medications (1,15). The diagnosis of WD is not difficult if the physicians including the psychiatrists thinks of it and include it in differential diagnosis. As a result, underlying medical history should be investigated in of all patients the psychiatric disorders including the psychosis. Interdisciplinary approach and collaboration of all physicians are quite important in order to treat rare disorders such as WD.

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