Case Report

Mismanagement of Wilson's disease as psychotic disorder

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Abstract

Wilson's disease (WD) or hepatolenticular degeneration is an inherited neurodegenerative disorder of copper metabolism (autosomal recessive, chromosome13). Psychiatric disorders in WD include dementia, characterized by mental slowness, poor concentration, and memory impairment. Symptoms may progress rapidly, especially in younger patients, but are more often gradual in development with periods of remission and exacerbation. Delusional disorder and schizophrenia-like psychosis are rare forms of psychiatric presentation. In this report, the patient with WD presented by psychosis symptoms and treated mistaken as schizophrenia for almost ten years. Although he has treated with antipsychotics, he had periods of remissions and relapses and never was symptoms free. Since psychosis can be the manifestation of medical diseases such as WD, overall view of these patients is necessary and medical diseases should be considered as a differential diagnosis.

Key Words: Psychotic disorder, schizophrenia, Wilson's disease

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INTRODUCTION

Wilson's disease (WD) or hepatolenticular degeneration is an inherited neurodegenerative disorder of copper metabolism (autosomal recessive, chromosome13).[1] Ocular and hepatic abnormalities are the most prominent non-neurologic manifestations of WD. The most common ocular findings is Kayser–Fleischer rings which are present in virtually all patients with neurologic.[2]

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Psychiatric manifestation is strongly associated with WD and may precede neurological signs and symptoms. It is estimated that more than 50% of patients exhibit mental disorders and a large proportion of patients start with psychiatric treatment.[1,3] It has been shown that male gender is more likely to present with neurological manifestations.[4] The most common psychiatric manifestations of WD are behavioral and emotional disorders, personality disorders, cognitive impairment and depression.[5] Symptoms may progress rapidly, especially in younger patients, but are more often gradual in development with periods of remission and exacerbation.[2] Delusional disorder and schizophrenia-like psychosis are rare forms of psychiatric presentation and only a few cases have been reported before.[4,5]

CASE REPORT

A 33-year-old single and unemployed male patient

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with irritability and life of a recluse since 10 years ago was socially active until the onset of the Wilson's disease (WD). The patient is the second child of a five children family and the parents are fourth degree relatives. He had the history of four times febrile seizures in his childhood. He had a developmental retardation in comparison with the others of his age and because of some behavioral problems and a decrease in his educational function he was expelled from school at the age of eighteen. The patient's sister was diagnosed with bipolar disorder type I and was under treatment with depakin. No other disorders including WD were reported in his family.

The first signs and symptoms (elementary visual pseudohallucination, commanding auditory hallucination, delusion of grandiosity, delusion of reference, inappropriate affect and abstract thinking, excessive anger, irritability, physical quarrel, inappropriate laugh, early insomnia, disinhibited behaviors such as masturbation in front of the others) appeared at the age of 23.

After visiting by a psychiatrist, diagnosis of schizophrenia was made for him based on his symptoms. Therefore, he has started to take antipsychotic medications including haloperidol 0.5 mg/day, chlordiazepoxide 25 mg/day, thioridazine 110 mg/day, and piracetam 800 mg daily was prescribed for him but without resulting in any significant changes in his symptoms and he had several periods of partial remissions and relapses. Because of no significant improvement in his disease course other therapies like mood stabilizer (carbamazepine, lithium), TCA (amitryptiline), benzodiazepines (chlordiazepoxide, clonazpam), piracetam, and trihexyphenidyl was used for him for almost ten years. The patient's response to new medication was desirable and most of the symptoms were relieved after adding them to his therapy. At the age of 33-year old, the patient was brought to emergency room (ER) due to sever aggression, stereotypic movements (circulatory movements of fingers), dystonia in his neck and right shoulder, irritability, and inappropriate laughing. He was admitted to the psychiatry ward and auditory hallucination, idea of reference, poverty of content of thought, decreased attention, no orientation of time, impaired recent memory, impaired judgment and poor insight were detected during his interview. In Wechsler test for adults (WAIS-III) mild mental retardation (verbal IQ = 60, full scale = 69) was detected. He was also complaining of sever itching and icteric sclera was detected in his physical examination. Therefore, liver function test (LFT) was performed, and these results were reported: Total bilirubin = 10.2 mg/dl, Direct bilirubin = 7.8 mg/dl, Aspartate aminoteransferase = 37 IU/L, Alanine aminoteransferase = 48 IU/L, Alkaline phosphatase = 301 IU/L. In other laboratory data, microcytosis anisocytosis in his complete blood count, negative HCV and negative HIV were reported. Substance test result was negative. Patient's EEG was reported normal. His psychotic symptoms were managed by using antipsychotics and consultation with an Internist was made regarding his other problem. Finally, the abnormalities in his laboratory tests was considered as the side effect of some of his anti-psychotic medications like Clozapine which were discontinued at the time of diagnosis and patient was discharged from the hospital after ten days of therapy.

After three months, he came to the ER again, with the prominent signs of cholecystitis. He was still icteric and the laboratory test results were: Total bilirubin = 5.8 mg/dl, Direct bilirubin = 3.7 mg/dl, Aspartate aminoteransferase = 112 IU/L, Alanine aminoteransferase = 192 IU/L, Alkaline phosphatase = 344 IU/L. Patient was admitted to the surgery ward and cholecystectomy was performed and another consultation with an internal medicine specialist was made. After laboratory and neuroimaging examinations he was diagnosed with WD. The patient was diagnosed with DSM-IV Axis I psychotic disorder due to WD, with delusions. The ceruloplasmin blood concentration was 9 mg/dl (reference range 30–58 mg/dl) and copper blood concentration was 48 μg/dl (reference range 70–140 μg/dl), with urine copper excretion 2945 μg/day (2000 ml; reference range 15–60 μg/day), repeated in the control examination. No other biochemical abnormalities were found. The ophthalmologist diagnosed bilateral Kayser–Fleisher rings. He was given penicillamine 500 mg/day.

After six months of follow up, a significant improvement with his psychotic symptoms was observed. The remission of psychosis with complete relief of systemic delusion resulted in the re-establishment of chelating therapy accompanied by normalization of biochemical assays and gradual improvement of neurological state. Informed consent for the publication of the case was obtained from the patient.

DISCUSSION

As mentioned in this report, co-occurrence of schizophrenic-like symptoms with WD is uncommon and there are just a few reports of the WD cases with psychiatric presentation. In a report, three patients have been described with Wilson's disease. There were two men and one woman (age range: 20–26 yr.). The early presentations were psychiatric symptoms and epileptic seizures. The psychiatric features were usually misinterpreted as schizophrenia-like disease

and the diagnosis was delayed, but their magnetic resonance imaging (MRI) showed asymmetric cerebral white matter lesions in the frontal lobe which revealed the diagnosis.[6] There is also a report of an 18-year-old male first presented a clinical picture of acute psychosis with two recurrences at ages 22 and 23. The diagnosis made at that time was paranoid schizophrenia. Twelve years after his first psychiatric hospitalization, it was discovered that he was suffering from WD.[7] Another case was a 26-year-old woman with clinical picture of acute psychosis, as the first and main manifestation of WD, is presented. She developed abnormal involuntary choreoathetoid limb movements, few days after initiation of neuroleptic therapy. At the first movement neurological symptoms were misinterpreted as side effect of haloperidol, but consulted neurologist suggested additional diagnostic procedure which confirmed WD.[8] The study which was conducted by Wichowicz and *et al*., demonstrates the importance of considering WD diagnosis in psychotic patients because of uncommon psychiatric manifestations of WD.[5]

In this case report, the patient with Wilson's disease presented by psychosis symptoms and were treated mistaken as a schizophrenic patient. During the time, he had periods of remissions and relapses and never was symptom free. It has been shown that early detection and treatment of WD by Penicillamine therapy could improve the psychosis without the need of treating with neuroleptic medications.[9]

Along with other reports, the present case demonstrates the importance of considering WD diagnosis in psychotic patients because psychiatric manifestations in WD are known to be uncommon. Therefore, patients with psychiatric manifestations with clues such as history of jaundice, family history of neuropsychiatric manifestations and sensitivity to neuroleptics should be evaluated for WD to avoid delay in diagnosis and associated morbidity. Here we re-emphasize the importance of behavioral manifestations in Wilson disease in terms of diagnosis and management difficulties.

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