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Psychiatric Onset in Wilson's Disease: A Case Report

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Abstract **Case Report**

Wilson's disease is a rare autosomal recessive disorder resulting from a loss of function of adenosine triphosphatase secondary to a mutation. This leads to a decrease or absence of copper transport in the bile and its accumulation in organs, particularly the brain. It can manifest initially as hepatic, neurological, or psychiatric disorders in at least 90% of patients. Cases appearing beyond the age of 50 are rare. In some patients, central nervous system involvement can be predominant, presenting as behavioral disorders, depression, or psychosis indistinguishable from schizophrenia or manic-depressive psychosis. Diagnostic criteria include low ceruloplasmin, Kayser-Fleischer ring, low serum copper, and high urinary copper. Genetic testing can be done through familial linkage analysis or direct genotypic diagnosis. We present an original clinical case where the onset of Wilson's disease presents as a late-onset psychotic episode. Although rare, Wilson's disease is crucial in psychiatry, as psychiatric manifestations may precede somatic symptoms, aiding in early diagnosis. Early diagnosis is vital, as the disease is fatal without specific treatment.

Keywords: Psychosis, Wilson's disease, case report, mental disorders, copper levels, treatment.

INTRODUCTION

Wilson's disease is a hereditary condition where a defect in copper biliary excretion leads to its excessive accumulation in the body [1]. This accumulation primarily manifests as hepatic and neuropsychiatric abnormalities. Despite its rarity, understanding its manifestations is essential, as a suspected diagnosis can be quickly confirmed through simple investigations. In this clinical case, we report on a patient with psychiatric symptoms as the inaugural manifestation of Wilson's disease.

PATIENT AND OBSERVATION

Mr. A, a 54-year-old resident of the El Haouz region, married with two children, the fourth of five siblings, employed in a carpentry workshop, presented to psychiatric emergencies with behavioral disturbances evolving over several months. Consanguinity in Mr. A's parents is reported. There are no known personal or family psychiatric history. The family reports a progressive change in the patient's attitude. Approximately seven months ago, Mr. A began isolating himself, remaining mute for most of the day, withdrawing from family life. This behavior change was initially subtle.

Over the past three weeks, behavioral disturbances worsened, with Mr. A exhibiting bizarre behaviors, unexplained agitation, a reversal of the circadian rhythm, and a refusal of food. His statements became incomprehensible to those around him. He spent part of his days prostrated inside his home.

Upon admission, examination revealed a frozen presentation, a state of anxious perplexity. During the interview, contact was difficult, responses were brief, but the patient was vigilant, with preserved spatial orientation but disturbed temporal orientation. Memory disorders were noted, with lacunar and retrograde amnesia. The mood was sad, with evident psychomotor slowing and suicidal thoughts. Spontaneous statements were incoherent (neologisms) without a clear delusional organization. The patient was urgently admitted to the psychiatric service, with a provisional diagnosis of probable psychotic disorder.

Physical examination noted mild jaundice and slight abdominal distension. A complete organic assessment was prescribed, and psychotropic treatment initiated (sertraline 50 mg/day and risperidone 3 mg/day).

Clinical evolution revealed a highly fluctuating picture in the first days of hospitalization, unimproved

by chemotherapy. Two days after admission, the symptomatology was complicated by the onset of medium-abundance upper digestive bleeding with hematemesis, requiring transfer to somatic emergencies.

Clinical examination found a jaundiced patient with hepatomegaly and neurological disorders such as limb tremors.

Para-clinical exploration revealed hemolytic anemia, esophageal varices, and hypertensive gastropathy on upper digestive endoscopy. Liver biopsy and histopathological analysis revealed established hepatic cirrhosis with abnormally high copper levels in hepatocytes.

Subsequent cupremia and cupruria assays were above physiological values (cupremia at 85 µmol/L and cupruria at 11 µmol/L). The ceruloplasmin level was 10 mg/dL. Ophthalmologic examination using the slit lamp revealed the Kayser-Fleischer ring. The diagnosis of Wilson's disease was established.

Curative treatment with D-penicillamine was proposed. Three months later, there was regression of neurological symptoms, especially tremors. However, complications of cirrhosis, such as ascites and digestive bleeding, persisted in this patient. The short-term psychiatric evolution was unfavorable, with minimal clinical improvement at three months. The patient, from a remote rural area, did not attend follow-up appointments.

DISCUSSION

In some individuals, Wilson's disease can manifest as isolated behavioral disturbances, dementia syndrome, schizophrenic syndrome, or manic-depressive syndrome [2, 3]. The prevalence of psychiatric disorders in Wilson's disease patients varies widely (major depressive disorder, 4-47%; bipolar disorder, 18-39%; psychosis, 1-11%) [4]. In Mr. A, the initial manifestations of Wilson's disease are psychiatric, representing only 10% of cases according to the literature [5, 6]. Psychiatric symptoms can occur before, during, or after the diagnosis and treatment of Wilson's disease. Thirty to forty percent of patients have psychiatric manifestations at the time of diagnosis, and 20% have consulted a psychiatrist before the diagnosis was established [7]. Psychiatric disorders can be inaugural or accompany neurological manifestations [8, 9]. They are more severe when neurological symptoms are advanced [10, 11]. Central nervous system involvement initially isolated in our patient led to psychiatric hospitalization, considering multiple differential diagnoses:

- Late-onset psychosis: Given the patient's age (54 years), insidious evolution of symptoms, behavioral oddities, and nocturnal agitation. No clear delusional organization or dissociative elements were observed.
- Depressive state: Considered due to sadness, withdrawal, mutism, sleep and appetite disturbances, and suicidal thoughts.
- Delirium: Considered due to temporal-spatial disorientation and memory impairments.

Additionally, Wilson's disease usually manifests between 10 and 20 years of age, rarely as late as in Mr. A. The disease is rare, almost exceptional after 40 years. Bellary and Vian Thiel [12] reported two late-onset clinical cases in 1993, one with hepatic onset (42-year-old woman) and the other with neurological onset (56-year-old patient). The author emphasized the rarity of late-onset forms [13]. Mr. A's clinical history draws attention to a rare disease that can manifest late, beyond 50 years, with a relatively straightforward diagnosis. In patients with psychiatric illness, the presence of ceruloplasmin deficiency suggests Wilson's disease, confirmed by detecting the Kayser-Fleischer ring with slit lamp examination.

CONCLUSION

Current treatments for Wilson's disease have significantly improved the prognosis of a disease with a pejorative natural history, especially when applied early [14]. This underscores the importance of an early diagnosis and family screening for subclinical forms. Despite its rarity, Wilson's disease is crucial in psychiatry, as its psychopathology and psychiatric manifestations may precede somatic symptoms, aiding in early diagnosis. Furthermore, these manifestations may regress with copper-chelating treatment [15], but the later the diagnosis, the lower the chances of regression [11].

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