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Wilson's Disease: About A Family Case

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1. Abstract

Wilson's disease is an autosomal recessive disease causing progressive copper overload. It is an initially hepatic affection which can evolve towards a multi-systemic attack with an accumulation of copper in the brain, the eye, the kidney, the heart. The diagnosis is carried out on a bundle of clinical, biological and radiological findings. Treatments associate a diet low in copper, copper chelators or zinc salts. Liver transplantation is the treatment for fulminant liver forms. This rare genetic disease has a good prognosis if treatment is started early and continued for life. It is therefore important to know the clinical manifestations of the disease and the diagnostic tests to evoke it quickly in order to ensure regular clinical and biological monitoring of patients. In this context, we report a familial case of Wilson's disease with its neurological, psychiatric, hepatic and ophthalmological manifestations.

2. Introduction

Wilson's disease is a rare inherited autosomal recessive disorder caused by a defective biliary elimination of copper which results in its toxic build-up in organs, particularly the brain, liver, eye and kidney [1]. Its clinical presentation is variable and its prognosis is dominated by hepatic and neurological damage. Early treatment allows reversibility of the deficits; untreated Wilson's disease is fatal [2]. Although this condition is rare, it is important to know its manifestations. Indeed, the diagnosis, once evoked, can be quickly confirmed by simple investigations. In this regard, we present a familial case of Wilson's disease initially discovered in a 16-year-old adolescent revealed by psychiatric manifestations associated with a disturbance of liver function tests, of which family screening has found chronic liver disease with an abnormal cupric assessment in the 2 siblings.

3. Patient and Observation

Three siblings from a first-degree consanguineous marriage were affected by Wilson's disease in its four clinical forms: psychiatric, neurological, ophthalmological and hepatic. The first, sixteen-year-old, with no particular pathological antecedents, was admitted to the gastroentero-hepatology department of the Arrazi hospital of the Mohammed VI University Hospital of Marrakech for etiological assessment of a disturbance of liver function tests with moderate cytolysis (<3N) and cholestasis (<3N), with negative hepatitic and autoimmune serologies, associated with neuropsychological disorders such as dysarthria, permanent laughing without cause, school difficulties with frontal headaches. The diagnosis was made after an ophthalmologic examination finding a bilateral Keyser Fleisher ring with a low level of ceruloplasmin (<0.2g / l) and a high cupruria at 137 (normal <20ug / day). Radiologically, cerebral magnetic resonance imaging was performed finding a bilateral and symmetrical signal abnormality of the striatums with involvement of the tegmentum, associated with diffuse cortico-subcortical atrophy and expansion of Virchow Robin spaces (Figure 1). The other manifestations of Wilson's disease were sought, in particular renal and cardiovascular impairment, which were absent. The search for clinical, biological, endoscopic and morphological signs of cirrhosis was carried out systematically in our patient, with the absence of any clinical sign pointing to a PH syndrome or signs of impaired liver function. Biologically, PT was low at 61.6%. A screening EGD was performed not showing esophageal or gastric varices. The abdominal ultrasound noted the presence of an aspect compatible with chronic hepatopathy without

any sign of PH. Liver elasticity on fibro-scan was estimated at 20 kPA. The patient was put on D-Penicillamine (Trolovol) at a progressive dose, with good clinical and biological tolerance and a favorable outcome. Genetic counseling was offered for the rest of the siblings following which they were also diagnosed with Wilson's disease. The second child, 13-year-old, and the 3rd, 9-year-old, without particular pathological antecedents, were clinically asymptomatic, no Keyser Fleisher's ring was found upon ophtalmological examination, liver function tests were in the normal range; though they presented levels of ceruloplasmin, cupruria and cupremia in favor of Wilson's disease, and an aspect compatible with chronic liver disease on ultrasound with no evidence of portal hypertension.

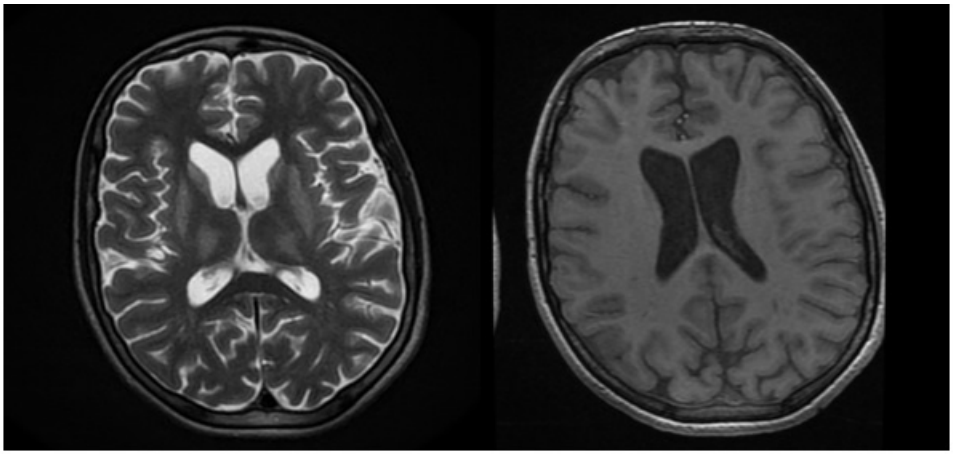

Figure 1: cerebral magnetic resonance imaging: Bilateral and symmetrical signal abnormality of the striatums with involvement of the tegmentum, associated with diffuse cortico-subcortical atrophy and expansion of Virchow Robin spaces.

4. Discussion

Wilson's disease is an autosomal recessive disease expressing before 40 years of age, its prevalence is 1 in 30,000. It is characterized by reduced biliary excretion of copper due to mutations in ATP7B, leading to pathological accumulation of copper in the liver, brain and other tissues [3-5]. Long before the gene responsible for it was identified, it had been shown that two major disturbances in copper metabolism were at its origin, the decrease in biliary excretion on the one hand and the decrease in ceruloplasmin uptake on the other hand [6-9]. The mechanisms of copper toxicity are still very poorly understood. Symptoms usually appear between adolescence and early adulthood, but can occur at any age. It requires lifelong treatment to prevent, reduce or stabilize symptoms [3, 4]. The clinical presentation of Wilson's disease is varied and supports the fact that it is a disease that primarily affects the liver and the brain. However, several organs, including the heart, kidneys, and intestines, may be involved with a wide range of signs and symptoms. The expression of Wilson's disease in children is predominantly hepatic [10]. Symptomatic and non-symptomatic liver damage is constant in Wilson's disease. The way in which hepatic damage is revealed is variable depending on the stage of development, and may affect the life prognosis. They range from steatosis and a slight elevation of liver enzymes to cirrhosis and acute liver failure with hemolysis and hepatic necrosis. Portal hypertension can also reveal Wilson's disease by the first discovery of splenomegaly, oesophageal varices on the occasion of digestive hemorrhage, or abnormal blood count due to hypersplenism [11].

Neuropsychiatric manifestations are, in order of frequency (35%), the second circumstance of discovery of Wilson's disease [12]. Neurological involvement is a supporting argument for the diagnosis of Wilson's disease in a child with liver disease for which the aetiology has not been found. It is characterized by personality change, mood disorders (depression, mania, bipolar disorder), gait and balance disorders, involuntary movements, dystonia, parkinsonism, dementia are the main psychiatric manifestations often associated with neurological symptoms [13]. In the predominant neurological forms, imaging shows a T2 hyper signal in the striatum. Lesions extend to the basal ganglia, thalamus, brainstem, and white matter. These lesions are reversible if treatment is early. The Kayser-Fleischer ring is almost constant in patients with neuropsychic manifestations while it may be lacking in hepatic forms. It is formed by infiltration of copper particles present in the aqueous humor through the endothelium to the descemet membrane. Treatment leads to disappearance of the ring in 80% to 90% of cases, its reappearance despite treatment signals non-compliance with treatment. Renal involvement manifests by renal tubular acidosis and decreased clearance of the creatinine. The diagnosis of Wilson's disease is made by disturbances in copper metabolism with hypoceruloplasminemia, hypocupremia and 24-hour hypercupruria. These disturbances are non-specific. They are lacking in 56% of cases with liver symptoms. A study has shown that hypoceruloplasminemia is found in 95% of symptomatic patients, 24-hour hypercupruria is found in 80 to 100% of cases [14].

This biological triad characteristic of Wilson's disease makes it possible to make the diagnosis and start treatment as was the case in our patient. However, when the results of the assays are doubtful, we will resort to the measurement of copper on a fragment of liver biopsy which was not done in our patient given the degree of hepatocellular insufficiency. The treatment of Wilson's disease is based on medical therapy associated with a low copper diet. It is recommended to avoid foods rich in copper [15]. Most patients are treated with copper chelators to remove it from albumin [16]. D-penicillamine was the

first copper chelator on the market. It binds to extracellular copper and excretes it via the kidneys into the urine. Due to interference with the action of pyridoxine, it should be administered in combination with 25 to 50 mg of vitamin B6. D-penicillamine has a proven and significant efficacy in improving disease course [17]. Within 1 to 2 years, patients become normal [18]. By this time, the transaminases should also be normalized [16]. In some cases, (14%), an initial deterioration of neurological symptoms is observed, but the pathophysiology remains unclear [19]. In the event of side effects, treatment should be switched to trientine or zinc. Zinc is less dangerous when it comes to adverse events [20]. Only abdominal discomfort was recorded, which in severe cases leads to its discontinuation [21]. The recommended dose for adults is 3 × 50 mg per day and for children and adolescents 3 × 25 mg per day [22]. It is only in rare cases that zinc is combined with chelators, both at reduced doses. The efficacy of bis-choline-tetrathiomolybdate (TTM) is currently being evaluated in clinical trials. In fulminant liver failure, liver transplantation is the first choice of treatment. The success rate of the operation in Wilson's disease is quite high compared to other causes of acute liver failure [23]. Still a 10-20% mortality rate in the first year after transplantation is too high to recommend this procedure to the general Wilson's disease population [24, 25]. The prognosis depends on the severity of the disease at the time of diagnosis and the quality of management.

5. Conclusion

Wilson's disease is a rare genetic disorder that is most often revealed by liver or neurological damage. Improved prognosis requires early diagnosis through family screening.

References

1. Brewer GJ. Diagnosis of Wilson's disease: an experience over three decades. Gut. 2002; 50: 136.
2. Brewer GJ. Recognition, diagnosis, and management of Wilson's disease. Proc:Soc Exp Biol Med. 2000; 223: 39–46.
3. EASL Clinical Practice Guidelines: Wilson's disease. J Hepatol. 2012; 56: 671-685.
4. Roberts EA, Schilsky ML. Diagnosis and treatment of Wilson disease: an update. Hepatology 2008; 47: 2089-2111.
5. Czlonkowska A, Litwin T, Dusek P, Ferenci P, Lutsenko S, Medici V, Rybakowski JK et al. Wilson disease. Nat Rev Dis Primers 2018; 4: 21.
6. Beinhardt S, Leiss W, Stattermayer AF, Graziadei I, Zoller H, Stauber R, Maieron A, et al. Long- term outcomes of patients with Wilson disease in a large Austrian cohort. Clin Gastroenterol Hepatol 2014; 12: 683-689.
7. Bruha R, Marecek Z, Pospisilova L, Nevsimalova S, Vitek L, Martasek P et al. Long- term follow-up of Wilson disease: natural history, treatment, mutations analysis and phenotypic correlation. Liver Int. 2011; 31: 83-91.
8. Dziezyc K, Karlinski M, Litwin T, Czlonkowska A. Compliant treatment with anti-copper agents prevents clinically overt Wilson's disease in pre-symptomatic patients. Eur J Neurol. 2014; 21: 332- 337.
9. Czlonkowska A, Tarnacka B, Litwin T, Gajda J, Rodo M. Wilson's disease-cause of mortality in 164 patients during 1992-2003 observation period. J Neurol. 2005; 252: 698-703.
10. Labrune P, Cedex C. Maladie de Wilson. Med Ther/Pédiatrie. 1999; 2: 461-5.
11. Ledoux, Corbusier M. Hereditary elastolysis. Dermatologica. 1985; 171: 407-18.
12. Valmary J, Ricordel I, Maziere B. Les formes hépatiques de la maladie de Wilson. Ann Gastroenterol Hepatol.1998; 24: 197-203.
13. Keun-Hwa Jung, Tae-Beom Ahn, Beom S Jeon. Wilson Disease with an Initial Manifestation of Polyneuropathy. Arch Neurol. 2005; 62: 1628-31.
14. Kuo YM, Gistschier J, Pack S. Developmental expression of mouse mottled and toxic milk genes suggests distinct functions for the Menkes and Wilson disease copper transporters. Hum Mol Genet 1997; 6: 1043-9.
15. West H. 8 aliments riches en cuivre - fondés sur des preuves. Healthline-Nutrition. 2018. Derniere consultation le 1er avril. 2020.
16. Ferenci P, Czlonkowska A, Stremmel W et al. EASL Clinical Practice Guidelines: Wilson's disease. J Hepatol. 2012; 56: 671-85.
17. Stremmel W, Meyerrose KW, Niederau C. Maladie de Wilson: tableau clinique, traitement et survie. Ann Intern Med. 1991; 115: 720-6.
18. Hedera P. Prise en charge clinique de la maladie de Wilson. Ann Transl Med 2019; 7: S66. 10.21037/atm.2019.03.18.
19. Merle U, Schaefer M, Ferenci P. Présentation clinique, diagnostic et résultat à long terme de la maladie de Wilson: une étude de cohorte. Gut 2007; 56: 115-20. 10.1136/gut.2005.087262.
20. Brewer GJ, Dick RD, Johnson VD. Traitement de la maladie de Wilson avec le zinc: XV études de suivi à long terme. J Lab Clin Med. 1998; 132: 264-78. 10.1016/S0022-2143(98)90039-7.
21. Camarata MA, Ala A, Schilsky ML. Thérapie d'entretien du zinc pours la maladie de Wilson: Comparaison entre l'acétate de zinc et les préparations alternatives au zinc. Hepatol Commun. 2019; 3: 1151-8. 10.1002/hep4.1384.
22. Ranucci G, Di Dato F, Spagnuolo MI. La monothérapie au zinc est efficace chez les patients atteints de la maladie de Wilson atteints d'une maladie cardiaque légère diagnostiquée dans l'enfance : une étude rétrospective. Orphanet J Rare Dis. 2014; 9: 41. 10.1186/1750-1172-9-41.
23. Weiss KH, Schäfer M, Gotthardt DN, et al. Résultat et développement de symptômes après une transplantation hépatique orthotopique pour la maladie de Wilson.Clin Transplant 2013;27:914-22. 10.1111/ctr.12259.
24. Ferenci P, Steindl-Munda P, Vogel W. Valeur diagnostique de la détermination quantitative du cuivre hépatique chez les patients atteints de la maladie de Wilson. Clin Gastroenterol Hepatol. 2005; 3: 811-8. 10.1016/S1542-3565(05)00181-3.
25. Cope-Yokoyama S, Finegold MJ, Sturniolo GC. Maladie de Wilson: corrélations histopathologiques avec le traitement lors de biopsies hépatiques de suivi. World J Gastroenterol 2010; 16: 1487-94. 10.3748/wjg.v16.i12.1487.