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CAS CLINIQUE

Mode d'entrée psychiatrique dans la maladie de Wilson : à propos d'un cas à début tardif

The onset of psychiatric disorders and Wilson's disease

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MOTS CLÉS
Maladie de Wilson ;
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Anneau de Kayser-Fleischer ;
Cuprémie, cupriurie ;
Céruloplasmine ;
Traitement à vie

Résumé Décrite en 1912, la maladie de Wilson est une pathologie rare, autosomique récessive, résultant d'une perte de fonction d'une adénosine triphosphatase (ATP7B ou WDNP) secondairement à une mutation, insertion ou délétion du gène ATP7B situé sur le chromosome 13q14.3—q21.1. Cela entraîne une diminution ou une absence du transport du cuivre dans la bile et son accumulation dans les organes, en particulier le cerveau. Elle débute sous la forme d'une maladie hépatique, neurologique ou psychiatrique chez au moins 90 % des patients. Les formes se révélant au-delà de 50 ans sont rares. Chez certains patients, l'atteinte du système nerveux central peut être prédominante. La maladie de Wilson peut alors se traduire par des troubles du comportement, une dépression ou par une psychose impossible à distinguer d'une schizophrénie ou d'une psychose maniacodépressive. L'association d'une céruloplasmine basse, d'un anneau de Kayser-Fleischer, d'une cuprémie basse et d'une cuprurie élevée permettent de poser le diagnostic. En cas d'hémolyse, la cuprémie peut être élevée. L'IRM peut retrouver des anomalies de signal des noyaux gris centraux, de la substance blanche et du tronc. L'étude génétique est actuellement réalisée de deux façons. En cas d'antécédent familial par l'analyse de liaison (dans le cadre du dépistage familial) et par recherche directe de mutation, c'est-à-dire par diagnostic génotypique direct (différentes mutations peuvent être constatées au sein d'une même famille, ainsi qu'une diversité d'expression phénotypique d'organe parmi les membres d'une fratrie porteur de la même mutation). Nous présentons un cas clinique original où l'entrée dans la maladie de Wilson prend la forme d'un tableau de psychose tardive de l'adulte. Bien que rare, la maladie de Wilson est importante à aborder en psychiatrie car

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les manifestations psychiatriques peuvent précéder les troubles somatiques et aider à poser le diagnostic. Nous soulignons l'importance du diagnostic précoce d'une pathologie dont l'issue est fatale en absence d'un traitement spécifique.

KEYWORDS
Wilson's disease;
Polymorphous psychotic disorder;
Autosomal recessive;
Kayser-Fleischer's ring;
Ceruloplasmin;
Treatment for life

Summary Wilson's disease is an infrequent, autosomic recessive pathology, resulting from a loss of function of an adenosine triphosphatase (ATP7B or WDNP), secondarily to a change (more than 60 are described currently), insertion or deletion of the ATP7B gene located on the chromosome 13q14.3—q21.1, which involves a reduction or an absence of the transport of copper in the bile and its accumulation in the body, notably the brain. Wilson's disease is transmitted by an autosomic recessive gene located on the long arm of chromosome 13. The prevalence of the heterozygote is evaluated at 1/90 and the homozygote at 1/30,000. Consanguinity, frequent in the socially geographically isolated populations, increases the prevalence of the disease. The toxic quantities of copper, which accumulate in the liver since early childhood and perhaps before, remain concentrated in the body for years. Hence, cytological and histological modifications can be detected in the biopsies, before the appearance of clinical or biological symptoms of hepatic damage. The accumulation of copper in the liver is due to a defect in the biliary excretion of metal and is accompanied invariably by a deficit in ceruloplasmin; protein synthesized from a transferred ATP7B gene, which causes retention of the copper ions in the liver. The detectable cellular anomalies are of two types: hepatic lesions resulting in acute hepatic insufficiency, acute hepatitis and finally advanced cirrhosis and lesions of the central nervous system responsible for the neurological and psychiatric disorders. In approximately 40—50% of the patients, the first manifestation of Wilson's disease affects the central nervous system. Although copper diffuses in the liver towards the blood and then towards other tissues, it has disastrous consequences only in the brain. It can therefore cause either a progressive neurological disease, or psychiatric disorders.

Wilson's disease begins in the form of a hepatic, neurological, or psychiatric disease in at least 90% of the patients. In some rare cases, the first manifestations of the disease can be psychiatric which, according to the literature, accounts for only 10% of the cases. The disease can be revealed by isolated behavioral problems, an irrational syndrome, a schizophrenic syndrome, or a manic-depressive syndrome. Damage to the central nervous system can be more severe, thus, several differential diagnoses have been discussed:

- a psychotic disorder of late appearance;
- a depressive state;
- a mental confusion disorder.

The clinical syndrome is complex. Indeed, it is the polymorphism, which dominates in the description of the psychiatric demonstrations of the disease. This can lead to prejudicial diagnostic wandering, particularly since heavy sedative treatment may be required to suppress behavioral problems.

Clinically, Wilson's disease generally appears between the age of 10 and 20. It rarely remains masked until after the age of 40. The first manifestations are hepatic (40% of the cases), neurological (35%) or psychiatric (10%). The inaugural disorder can finally take on a haematological, renal, or mixed form in approximately 15% of the cases. We have detailed the principal clinical elements. In approximately 40—50% of the patients, the first manifestation of the disease affects the central nervous system, where it can cause either a progressive neurological disease, or psychiatric disorders.

The ophthalmologic disorder is dominated by Kayser-Fleischer's ring, representing a green or bronze colored ring on the periphery of the cornea. It occupies the higher pole of the cornea, then the lower pole, and extends to the whole circumference. It is generally only visible under examination with a slit lamp. It disappears on average within 3—5 years following copper chelating therapy. Kayser-Fleischer's ring has been described other than in Wilson's disease, in exceptional cases of prolonged cholestasis. On haematological level, the hyperhaemolysis is due to the toxicity of the ionic copper, released massively in the plasma by hepatocellular necrosis. The other manifestations can be found in the following organs: renal, osteoarticular, cardiac, endocrine, cutaneous, and in the teguments.

Until 1952, the diagnosis was evoked only on clinical symptomatology. It can henceforth be marked unambiguous, even in the absence of any symptom, by the description of a ceruloplasmin plasma concentration of less than 200 ml/l, and of a Kayser-Fleischer's ring. Hepatic copper on sample is constantly increased during the disease (from 3 to 25 μmol/g of dry weight). On the