Research, Society and Development, v. 11, n. 3, e13111326095, 2022
(CC BY 4.0) | ISSN 2525-3409 | DOI: http://dx.doi.org/10.33448/rsd-v11i3.26095

Wilson's disease associated with psychotic episode - case report

Doença de Wilson associado a surto psicótico - relato de caso

Enfermedad de Wilson asociada con episodio psicótico - reporte de caso

Received: 01/24/2022 | Reviewed: 01/28/2022 | Accept: 02/10/2022 | Published: 02/15/2022

Raianny Cunha Duarte
ORCID: https://orcid.org/0000-0001-6218-6793
University of Uberaba, Brazil
E-mail: raiduartemed@gmail.com
Clara Porto de Souza
ORCID: https://orcid.org/0000-0003-2766-6841
University of Uberaba, Brazil
E-mail: claraportos@outlook.com
Andressa Paes Medeiros de Freitas
ORCID: https://orcid.org/0000-0002-7817-2262
University of Uberaba, Brazil
E-mail: andressa.pm.freitas@gmail.com
Letícia de Almeida Dutra
ORCID: https://orcid.org/0000-0002-8192-8745
University of Uberaba, Brazil
E-mail: le_almeidadutra@hotmail.com
Douglas Reis Abdalla
ORCID: https://orcid.org/0000-0002-6971-1201
Faculty of Human Talents, Brazil
E-mail: drabdalla@facthus.edu.br
Geisa Perez Medina Gomide
ORCID: https://orcid.org/0000-0002-6657-5515
University of Uberaba, Brazil
E-mail: geisa.gomide@uniube.br
Fernanda Oliveira Magalhães
ORCID: https://orcid.org/0000-0002-0581-4279
University of Uberaba, Brazil
E-mail: fernanda.magalhaes@uniube.br

Abstract
Wilson's Disease is a rare genetic disorder characterized by a failure in copper metabolism, which promotes copper deposition in both the liver and the brain, which can lead to serious complications if not diagnosed early and treated properly. The present case report exposes a psychotic episode in a patient previously diagnosed with Wilson's Disease and undergoing treatment, who exhibited failures in the follow-up of therapy associated with the excessive use of alcoholic beverages and especially of marijuana cigarettes since adolescence. Therefore, a bibliographical research on the themes was carried out and the discussion permeated about the possible correlations of these factors for the case described. It was concluded that the patient likely had an underdiagnosed psychiatric underlying illness that was exacerbated by accumulation of copper and drug use, causing the psychotic break to occur and thus later allowing for its diagnosis.
Keywords: Copper-transporting ATPases; Copper; Psychotic disorders; Marijuana abuse; Alcohol-induced disorders.

Resumo
A Doença de Wilson é uma doença genética rara caracterizada por uma falha no metabolismo do cobre, que promove a deposição de cobre tanto no fígado quanto no cérebro, podendo levar a complicações graves se não diagnosticada precocemente e tratada adequadamente. O presente relato de caso expõe um episódio psicótico em um paciente previamente diagnosticado com Doença de Wilson e em tratamento, que apresentou falhas no seguimento terapêutico associado ao uso excessivo de bebidas alcoólicas e principalmente de cigarros de maconha desde a adolescência. Para tanto, foi realizada uma pesquisa bibliográfica sobre os temas e permeou a discussão sobre as possíveis correlações desses fatores para o caso descrito. Concluiu-se que o paciente provavelmente tinha uma doença de base psiquiátrica subdiagnosticada que foi exacerbada pelo acúmulo de cobre e uso de drogas, causando o surto psicótico e, assim, permitindo seu diagnóstico posterior.
Palavras-chave: ATPases transportadoras de cobre; Cobre; Transtornos psicóticos; Abuso de maconha; Distúrbios Induzidos pelo álcool.

Resumen
La enfermedad de Wilson es un trastorno genético raro caracterizado por una falla en el metabolismo del cobre, que promueve la deposición de cobre tanto en el hígado como en el cerebro, lo que puede provocar complicaciones graves si no se diagnostica a tiempo y se trata adecuadamente. El presente reporte de caso expone un episodio psicótico en un paciente previamente diagnosticado con Enfermedad de Wilson y en tratamiento, quien presentó fallas en el seguimiento de la terapia asociado al uso excesivo de bebidas alcohólicas y en especial de cigarrillos de marihuana desde la adolescencia. Por lo tanto, se realizó una búsqueda bibliográfica sobre los temas y se permeó la discusión sobre las posibles correlaciones de estos factores para el caso descrito. Se concluyó que el paciente probablemente padecía una enfermedad psiquiátrica de base infradiagnosticada que se agudizó por la acumulación de cobre y el consumo de drogas, provocando el brote psicótico y permitiendo así su posterior diagnóstico.
Palabras clave: ATPasas transportadoras de cobre; Cobre; Desórdenes psicóticos; Abuso de marihuana; Trastornos inducidos por el alcohol.

1. Introduction

Wilson's Disease (WD) is an autosomal recessive disease that, in the face of 700 types of mutations (Human Gene Mutation) alters copper metabolism, compromising the structure of ceruloplasmin (glycoprotein synthesized in the liver that contains 6 copper atoms per molecule – carrier of copper in the blood) and causing erroneous deposition of it in several places of the organism, mainly in the liver, brain, cornea and kidneys (Brito et al, 2005).

The classic form of the disease was first described in 1912 by Kinnear Wilson as a progressive lenticular cell degeneration observed in the brain (in the basal ganglia) and related to liver problems. (Brito et al, 2005). Although its description was made in 1912, it was only in 1993 that the genetic character of DW was described, and after 10 years of research, its autosomal recessive characteristic was identified, not related to sex, but related to the ATP7B gene present on the chromosome. 13 coding for the protein of the same name (Pfeiffer, 2016).

Copper is a transitional element obtained through nutrition, part of it needs to be absorbed as it makes up several enzymes, but it is known that 50% of what is ingested is not absorbed by the proximal portions of the duodenum, and needs to be eliminated in the bile (manure and urobilin) (Guyton, 2006). However, in this disease, copper elimination is impaired because the liver "reaches its maximum storage capacity", thus copper "overflows" into the circulation without binding ceruloplasmin which causes it to be deposited in corneas, liver , kidneys and brain (Oliveira-Júnior, 2013).

The ATP7B gene present at locus 14 of the long arm of chromosome 13 at position 13q14-q21 contains 22 exons that have high mRNA expressivity in the liver (MS 2013 - SUS). The ATP7B protein is involved in copper homeostasis and has two functions within hepatocytes: (1) the incorporation of copper into apoceruloplasmin to form holoceruloplasmin which is excreted into the bloodstream, and (2) the physiological elimination of copper in bile and feces (Poujois et al., 2017).

According to Aurelia Poujois (2017), several mutations can happen in this gene and be responsible for DW. Apparently the product of this gene resides in the Golgi complex and is fundamental for the transport of copper across the membranes of intracellular organelles (intracellular transmembrane transport) (Czlonkowska et al., 1996; Czlonkowska et al., 2017). Thus, the absence or reduction of gene function/protein alteration reduces hepatic copper excretion and causes metal accumulation, the so-called DW (Oliveira-Júnior, 2013). In other words, according to Poujois and Cols (2017), the protein is essential for the excretion of copper through the biliary route, because, once it is deficient, the copper starts to accumulate in the liver, which promotes toxic effects due to oxidative damage, thus the liver begins to be injured when the hepatic copper storage capacity exceeds the limit.

Furthermore, with the progression of the disease, Ceruloplasmin, which is a liver-producing enzyme associated with copper transport, is affected by the defect in intracellular transmembrane transport, causing a decrease in the incorporation of copper into ceruloplasmin, which makes the protein molecule more unstable, which is why the circulating level of this glycoprotein in patients with WD is reduced (Oliveira-Júnior, 2013). Copper not bound to ceruplasmin has an increase in its

serum levels, causing the accumulation of copper, for example, in the brain, which justifies the neurological and psychiatric manifestations of the disease (Oliveira-Júnior, 2013).

The disease initially presents as hepatitis, cirrhosis or liver decompensation, and may appear in the middle or late adolescence, usually starting between 11 and 25 years of age (Poujois et al., 2017). On the other hand, neurological manifestations such as dystonia, tremor, incoordination, dysarthria, dysphagia, among others, usually start in the second decade of life; while psychiatric manifestations commonly occur about five years before the disease is diagnosed. Its symptoms consist of neurological, hepatic, psychiatric and ocular manifestations, such as the Kayser-Fleischer ring, and in recent decades, there have been radiological findings of brainstem alterations known as "panda faces" signs, which have shown significant value in the study of hepatolenticular degeneration. (Poujois et al., 2017).

As for the carriers of ATP7B gene mutations, it is estimated that around 1% have 1 mutated allele out of 90, that is, only this 1% is homozygous and thus presents the manifestations of the disease (Czlonkowska et al., 1996; Czlonkowska et al., 2017). In most populations, the frequency of Wilson's Disease is 1 in 30,000 to 40,000 (Conitec Protocol 2018). Studies from Germany and Japan during the 1970s showed that incidence is more common in regions with the presence of consanguinity, such as the Canary Islands (1:2600); it is also common among Chinese (58.7 per 1,000,000), Japanese, Jews, and Italians (Czlonkowska et al., 1996; Czlonkowska et al., 2017). In Brazil, the exact number of individuals with the disease is not known (Oliveira-Júnior, 2013). The recommended therapeutic approach is based on removing copper, and therefore will depend on the disease state. If there is liver decompensation, it is necessary to assess the severity of the disease, which can be done using the prognostic index by Nazer et al., (1986).

Drug treatment is based on the administration of chelators, zinc salts (Anderson et al., 1998) and their association (Oliveira-Júnior, 2013). The chelators are: penicillamine (Czlonkowska et al., 1996; Czlonkowska et al., 2017), dimercaprol, trientine (Walshe, 1982) and tetrathiomolybdate and act by removing intra and extracellular copper (Lance et al., 2009) . Zinc salts, on the other hand, reduce the intestinal absorption of copper (Sturniolo et al., 1999).

Usually the treatment starts with chelators, associated or not with zinc salts, to remove excess deposited copper. Of the chelators, trientine is the least toxic agent and is often used if the patient has hepatitis as a result of the disease. Zinc is also proven to be effective, but it should not be used concurrently with trientine, as one cancels the effect of the other. To treat neurological manifestations, tetrathiomolybdate and zinc are recommended. (Oliveira-Júnior, 2013).

Some authors recommend that, after removal of this excess copper by chelators, zinc salts could be used in monotherapy to prevent metal re-accumulation (Linn et al., 2009). However, this approach is not uniform, as there are reports in the literature of cases of neurological worsening and progressive hepatic decompensation refractory to treatment reinstitution caused by the interruption of chelators (Czlonkowska et al., 1996; Czlonkowska et al., 2017). Regardless of positive treatment outcomes, copper removal therapy should be chronic. (Oliveira-Júnior, 2013).

2. Methodology

In order for the present report/case study to be carried out in accordance with current bioethics standards, a research project was developed which was submitted to the Research Ethics Committee and approved by it (CAAE: 54042921.70000.5145). The work is a report/retrospective case study on the medical record of a patient that seeks to correlate the bibliography of the disease with the patient's condition, through reading articles about it and tabulating the patient's symptoms and found in the descriptions. of the disease.

The methodology of the report/case study was therefore divided into 3 phases: a) Bibliographic reading and establishment of the main signs and symptoms described. b) Evaluation of the patient's medical record and tabulation of signs and symptoms presented. c) Correlation between what was presented in the patient and what was described in the literature.

That is, after approval by the Ethics Committee, access to the patient's chart was allowed to survey the signs, symptoms and results of laboratory tests. While part of the authors was responsible for collecting data from the medical records, another group was directed to establish the main signs and symptoms that have been described in the literature, in order to avoid possible biases. After the two initial phases, correlations were built between what was seen in the patient and what was presented in the literature review, in order to establish a correspondence.

3. Results and Discussion

Case report:

The patient is currently 21 years old, seeks care at another service in February 2018, at age 19, for investigation of various papules on the penis. At this visit he was diagnosed with condyloma acuminata by HPV with a loss of 5 kg in 2 months. Furthermore, her laboratory tests had pancytopenia.

The patient was admitted to investigate the cause of pancytopenia and to treat the condyloma. During hospitalization, splenomegaly (spleen 12cm from the border) was observed and, on abdominal CT, an altered liver was found, thus diagnosing Chronic Liver Disease with no apparent cause. During the investigation of such etiology, low ceruloplasmin (6), low serum copper (42) and low calculated free copper (23.1) were identified, in addition to the presence of Kaiser-fleisher rings in both eyes of the patient, thus closing the diagnosis of Wilson's Disease after elimination (clinical history and laboratory tests) of other differential diagnoses for Liver Cirrhosis (Chronic Liver Disease), viral hepatitis, autoimmune hepatitis, primary biliary cholangitis, hemochromatosis, alcoholism and NASH (non-steatohepatitis recognized as one of the most frequent liver diseases today).

During hospitalization, the penile lesions were treated and the patient was also diagnosed, after an upper digestive endoscopy, with medium-caliber esophageal varices, having received primary prophylactic treatment with Propranolol. The patient was discharged for outpatient follow-up.

The dosage of urinary copper (24hrs) was performed on an outpatient basis: 135.9 - Urinary copper>2x ULN and due to its high levels, treatment with the copper chelator D-penicillamine was requested (started on 08/07/2018, but stopped in January/2019 due to unavailability), together with the replacement of Pyridoxine (exchanged in March/2019 for Zinc Sulfate due to unavailability).

He continued the medication for another two months, when in May/June 2019 he complained of fine tremors in the extremities and began to be monitored by the Clinical Neurology, which guided the prescription of Primidone with resolution of the symptom. In Dec/2019, he started using Nortriptyline 10 mg at night due to headache, prescribed by neurology.

In January 2020, the use of Penicillamine made available by the SUS returned. It continued use and was progressing well until the last consultation at the outpatient service, on 08/11/2020, when 3+ of proteinuria in type 1 urine was identified and 24-hour urine was requested and nephrology evaluation scheduled for 08/19/2020, but patient did not attend.

On September 2, the patient was referred from the Municipal Emergency Care Unit to the MPHU service due to a psychotic episode. The patient reported hyporexia, use of marijuana cigarettes and alcohol for 3 days, as well as suspension of all medications for 1 day, due to a fight with his girlfriend 5 days ago. On the day of the psychotic condition, he reports having taken the medication with alcoholic beverages.

L.N.L.F. he doesn't remember the outbreak, but according to his mother, he was aggressive and confused, with disjointed speech and a desire for self-extermination. On the same day, he undressed and wandered down the street, where he had short-term syncope episodes, with falls from his own height and bruises as a result. He was taken to the UPA by the Mobile Emergency Care Service (SAMU), where he was sedated with 2 ampoules of diazepam, 2 ampoules of aldol, 50mg of

amplictil and 2 ampoules of fenergan, and mechanically contained. So it remained without improvement for a day. When he recovered, he was transferred to tertiary service.

On the 1st day of hospitalization, the patient was EGF, self-oriented and allo-oriented, with jaundice 1+/4+, with no other changes. Laboratory routine was requested for the first attack, cranial CT, prescribed, and psychiatric evaluation.

He reported the use of propranolol 40 mg 2cps a day, penicillamine 250mg 2cps 2 x/day, primidone 100mg 1cp 12 in 12hrs and nortriptyline 40mg at night (he claimed to have suspended all these medications 5 days before the episode of psychotic episode on 08/31/ 2020). Laboratory routine was requested for the first attack, cranial CT, prescribed and psychiatric evaluation.

Given the case presented, this study aims to clarify whether or not there was a correlation between Wilson's Disease and the use of alcohol or cigarettes by the patient, so that it can be evidenced whether the patient's psychotic episode was caused by this condition.

Wilson's disease

To perform the diagnosis of DW we can base it on the presence of 2 of the following criteria: (1) Presence of the KF ring; (2) ceruloplasmin with a value below 20 mg/Dl, (3) presence of this pathology in the family history, (4) serum free copper greater than 25 µg/dL and 24-hour urinary copper above 100 µg/24h (Sócio et al , 2010).

In order to assess the evolution and severity of this disease, two predictive indices can be used: Nazer and Dhawan, which were detailed in the table below (Tables 1 and 3) (Sócio et al, 2010).

Table 1 shows the Nazer classification:

Table 1 – Nazer index.

Points	Bilirubin	AST	RNI
0	<5,8	<100	<1,3
1	5,9-8,8	100-150	1,3-1,6
2	8,9-11,7	151-200	1,6-1,9
3	11,8-17,5	201-300	1,9-2,4

Source: Nazer et al (1986).

The patient's laboratory tests were presented in the medical record and results were entered in the table 2 according to the data in which they were presented and then classified in the Nazer Score:

Table 2 – Patient record.

Date	Bilirubin T	AST/TGO	RNI	Nasser
19/06/18	1.605	30.8	1.7	1 point
27/08/2018	2.5	55.6	1.32	1 point
26/10/2018	1.51	28.8	1.3	1 point
11/01/2019	2.38	21.4	1.25	0 point
11/03/19	1.61	23.5	1.44	1 point
15/04/19	1.122	28.4	1.17	0 point
28/06/19	3.11	21.6	1.4	1 point
23/09/19	1.06	20	1.27	0 point
15/10/19	1.81	22	1.39	1 point
28/02/20	1.52	28	1.33	1 point
21/05/20	1.79	22	1.27	0 point
02/06/20	2.4	274	1.3	4 points
06/09/2020	0.9	32	1.24	0 point

Source: Authors (2022).

Table 3 – Dhawan classification.

Points	Bilirubin	AST	RNI	Leukocytes (109 /L)	Albumin
0	<5,8	:100	<1,29	0-6,7	>45
1	5,9-8,8	00-150	1,3-1,6	6,8-8,3	34-44
2	8,9-11,7	51-300	1,7-1,9	8,4-10,3	25-33
3	11,8-17,5	01-400	2,0-2,4	0,4-15,3	21-24
4	>17,5	>401	>2,5	>15,4	<20

Source: Dhawan et al., (2005).

The patient's laboratory tests were presented in the medical record and results were entered in the Table 4 according to the data in which they were presented and then classified in the Dhawan Score:

Table 4 – Patient record.

Date	Dhawn	TGO	Leukocytes	Bilirubin T	Albumin	RNI
11/01/2019	0	21.4	3070 1/60/1/0/27/11	2.383	4.82	1.25
21/05/2020	0	22	4000	1.79	4.9	1.3
03 e 06/09/2020	0	32	5190	0.8	3.4	1.23

Source: Authors (2022).

As previously mentioned, to diagnose WWD, we need to base some tests with reference values such as ceruloplasmin with a value below 20 mg/Dl and 24-hour urinary copper above 100 µg/24h. In the case of the patient, he presented on 05/22/2018 a ceruloplasmin of 6 and a 24-hour urinary copper of 135.9, raising the suspicion for the current diagnosis of WD. After three months of treatment (started on 07/08/2018), another dosage was performed again, so that ceruloplasmin continued 6 while copper was canceled due to insufficient sample. In January/2019, after five months of treatment, his urinary copper was reduced, by 103.8, however the ceruloplasmin had increased to 7. In November/2019 the results for urinary copper and ceruloplasmin were 100 and 7, respectively, this being your last dosage.

According to Poujois and Cols (2018), Wilson's Disease promotes copper deposition in the CNS and this can generate alterations in the structure of the CNS (midbrain, basal ganglia and cerebellum) and also in the patient's psyche.

The blood-brain barrier-forming astrocytes are the main cells capable of reducing the toxic effect of high amounts of copper (Scheiber et.al 2017). However, long-term exposure to high concentrations of copper results in non-selective necrosis of all elements of the brain parenchyma (Poujois et al., 2018). The most common lesions formed in WD are striated lesions, but they can be more diffuse in the pons, midbrain, thalamus, dentate nucleus and, less frequently, in the corpus callosum and cortex (Poujois et al., 2017). In addition, according to Poujois and Cols (2017), there is the formation of modified astrocytes in Wilson's disease, the so-called Opalski cells. At the biochemical level, copper toxicity leads to depletion of GSH and SOD1 from brain tissue (compromised antioxidant defense system (Scheiber et.al 2017).

Although Poujois et al. (2017), states that the copper content is not related to the severity of abnormalities found in patients with WD, when the CNS is affected, the patient may have several symptoms that are related to the dysfunctional Extrapyramidal System, or that is, it presents symptoms of involuntary movements such as tremor, dystonia, sardonic laughter (very common), dysphagia and dysarthria, parkinsonian tremors, chorea and even convulsions (Caitlin Mulligan); explained below:

a) Tremor: According to Czlonkowska et al (2017), the most characteristic neurological symptom seen in patients with Wilson's disease is tremor, and it can be of any type, including resting, postural - asterixes (usually with "knocking" features. wings") or kinetic. It can also be similar to essential tremor (ET), dystonic tremor, rubral tremor, and rarely, even at rest, tremor similar to parkinsonian tremor can occur. It is important to remember that pathophysiologically asterixes is not a tremor, but is actually a negative myoclonus, characteristic of severe encephalopathies (Anna Czlonkowska et al).

b) Dystonia: It can be in a specific segment, in several foci or even generalized and occurs in 11 to 65% of patients. According to Anna Czlonkowska et al dystonia includes sardonic laughter because spasms occur in the risorius muscle of the face (specific dystonia). Other focal dystonias can affect the neck, hands (writer's cramp), tongue, legs, and upper facial region (blepharospasm). More severe cases of Wilson's disease can even affect the patient's respiratory muscles, with high rates of death in these cases.

c) Ataxia: According to Czlonkowska et al (2017), ataxia is observed in the ataxic gait with a broad posture; gait with jerky steps that vary in length; in macrograph (due to action tremor); in intentional tremors (absent at rest); and in dysdiadochokinesia (interruption of alternating movements).

d) Chorea: chorea movements are found in 6 to 16% of patients with Wilson's Disease. (Czlonkowska et al., 1996; Czlonkowska et al., 2017)

e) Dysarthria: In some severe cases anarthria can be observed. It should be mentioned that dysarthria, dysphagia and the patient may be drooling. (Czlonkowska et al., 1996; Czlonkowska et al., 2017)

f) Dysphagia: In WD, dysphagia can be caused by slowness or lack of coordination, with additional involuntary movements of the tongue, lips, pharynx and jaws and also with reduced motility of the esophagus. (Czlonkowska et al., 1996; Czlonkowska et al., 2017)

g) Babar: Babar is a classic neurological symptom of the disease, especially in patients with orofacial dystonia. It can also be evaluated as dysphagia and dysarthria. Despite having its undefined/heterogeneous pathophysiology, it can occur as a result of excessive saliva production and difficulty in swallowing. There are also sensory alterations, neuromuscular dysfunction, anatomical abnormalities and orofacial dystonia. (Czlonkowska et al., 1996; Czlonkowska et al., 2017).

It turns out that different regions of the brain have different susceptibility to copper toxicity, and this is probably one of the causes of it becoming more prevalent in controlling regions of the psyche (Scheiber et.al 2017) causing symptoms such as personality change (added to aggression, disinhibition and obsession), depression, cognitive alterations and anxiety. (Caitlin Mulligan). According to Zimbrean et al., (2017), in 1940 the relationship between copper and schizophrenia was postulated and dw may present with a variety of psychiatric and cognitive symptoms dubbed the "great mask", which at times resemble the symptoms of schizophrenia. Also according to Zimbrean et al., (2017) these deficiencies can occur at different stages of the disease and with variable intensity in individual patients.

The psychotic break is common in depressive, schizophrenic patients or those suffering from some other psychiatric illness and may be accompanied by an episode of violence, amnesia, mania, depressive moments, an attempt at self-extermination, etc. During the patient's hospital stay and subsequent outpatient follow-up, it was possible to notice the presence of general and psychiatric symptoms described in the medical record and inserted in tables here.

Given two symptoms evidenced above, it was possible to tabulate the symptoms present in the patient and correlate them with the symptoms described in the literature, according to Table 5:

Table 5 – Patient symptomatology.

Date x Symptomatoly	16/6/20	14/7/20	11/8/20	2º day HU	3ºday HU	4º day HU	5º/9º day HU
Asthenia	absent	absent	present	present	present	present	Present
Mood change	present	present	present	present	present	present	Present
Memory lability	present	present	present	present			
Blurred vision	Absent						
Pulsatile headache	present	present	present	present	absent	present	Present
Night awakening	absent	present	present	present	absent	present	Present
Syncope	present		present				
Stock stop	present						
Fine hand tremor	absent	present	present	present	absent		Present

Source: Authors (2022).

Marihuana

Marijuana is the illicit drug with the highest consumption in most countries. In addition, recent epidemiological studies have shown that not only has the prevalence of the use of this drug throughout life increased, but also its consumption and dependence. Individuals seek this substance aiming at the changes in states of consciousness triggered by it acutely, such as: relaxation, time distortion, perceptual changes, but these effects can be general, neurological, cardiovascular and/or psychic (Oliveira Júnior 2013).

In psychic terms, marijuana generates acute changes such as: depersonalization, anxiety, confusion, hallucinations, loss of insight capacity and increased risk of psychotic symptoms (especially in patients with a family or personal history). In addition, the chronic use of marijuana can generate effects in systems such as acute use, with respect to psychics we highlight: rapid changes in mood, personality change, anxiety and depression, attempted self-extermination, panic attack (Oliveira Júnior 2013) . Regarding cognitive impairment, it is noteworthy that there is scientific evidence to suggest that the prolonged use of this drug illicit activity can cause damage related to the organization and integration of complex information and damage the processes of attention and memory, all this change can be noticed in a few years of consumption (Ribeiro et al, 2005).

It is noteworthy that this illicit drug is able to precipitate schizophrenia in individuals with predisposition and aggravate the condition of patients already diagnosed with the disease. Therefore, it is essential to explain to patients the risks of using this drug, especially in patients with this risk (Ribeiro et al, 2005).

4. Conclusion

As seen, the patient had several psychiatric symptoms such as hand tremor, mood swings and anxiety. Given its situation, we hypothesized that these symptoms could have been caused both by Wilson's Disease and by the abusive use of the drug, as seen in the previous table.

Therefore, as the neurological assessment did not show any significant visible change on CT that referred to WD, it is more likely that the patient already had an underdiagnosed underlying psychiatric illness, which was accentuated by the deposit of copper in the CNS and also by the use of drugs , since, as raised by Ribeiro (2005), an illegal drug such as marijuana is capable of precipitating schizophrenia in individuals with predisposition and also aggravating the situation of patients already diagnosed with such diseases.

For a better study of the case, it is suggested that there is more research on the disease, mainly focused on the psychiatric alterations that Wilson's Disease can cause. In addition, more data on the effects of alcohol and drug use by patients diagnosed with copper accumulation could have helped in the case study.

References

Anderson, L. A., Hakojarvi, S. L., & Boudreaux, S. K. (1998). Zinc Acetate Treatment in Wilson’s Disease. Annals of Pharmacotherapy, 32(1), 78–87. https://doi.org/10.1345/aph.17075

Brewer, G. J., Terry, C. A., Aisen, A. M., & Hill, G. M. (1987). Worsening of Neurologic Syndrome in Patients With Wilson’s Disease With Initial Penicillamine Therapy. Archives of Neurology, 44(5), 490–493. https://doi.org/10.1001/archneur.1987.00520170020016

Brito, J. C. de F., Coutinho, M. de A. P., Almeida, H. J. F. de, & Nóbrega, P. V. da. (2005). Doença de Wilson: diagnóstico clínico e sinais das “faces do panda” à ressonância magnética. Relato de caso. Arquivos de Neuro-Psiquiatria, 63(1), 176–179. https://doi.org/10.1590/s0004-282x2005000100034

Czlonkowska, A., Gajda, J., & Rodo, M. (1996). Effects of long-term treatment in Wilson’s disease with D-penicillamine and zinc sulphate. Journal of Neurology, 243(3), 269–273. https://doi.org/10.1007/BF00868525

Członkowska, A., Litwin, T., & Chabik, G. (2017). Wilson disease: neurologic features. Handbook of Clinical Neurology, 142, 101–119. https://doi.org/10.1016/B978-0-444-63625-6.00010-0

Dhawan, A., Taylor, R. M., Cheeseman, P., De Silva, P., Katsiyiannakis, L., & Mieli-Vergani, G. (2005). Wilson's disease in children: 37-year experience and revised King's score for liver transplantation. Liver transplantation : official publication of the American Association for the Study of Liver Diseases and the International Liver Transplantation Society, 11(4), 441–448.

Dubois, R. S., Rodgerson, D. O., & Hambidge, K. M. (1990). Treatment of Wilson’s disease with triethylene tetramine hydrochloride (Trientine). Journal of Pediatric Gastroenterology and Nutrition, 10(1), 77–81. https://doi.org/10.1097/00005176-199001000-00015

Faia, R., Lemos, L. M. de, Mourão-Júnior, C. A., & Andreazzi, A. E. (2016). Copper metabolism and Wilson’s disease: a review. Revista Médica de Minas Gerais, 26. https://doi.org/10.5935/2238-3182.20160133

Fernando, M., van Mourik, I., Wassmer, E., & Kelly, D. (2020). Wilson disease in children and adolescents. Archives of Disease in Childhood, 105(5), 499–505. https://doi.org/10.1136/archdischild-2018-315705

Guyton, A.C. (2006). Tratado de fisiologia médica. Elsevier Brasil.

Lance, L.L., Goldman, M.P., Armstrong, L.L., & Lacy, C.F. (2009). Drug Information Handbook, 18th.

Linn, F. H. H., Houwen, R. H. J., van Hattum, J., van der Kleij, S., & van Erpecum, K. J. (2009). Long-term exclusive zinc monotherapy in symptomatic Wilson disease: experience in 17 patients. Hepatology (Baltimore, Md.), 50(5), 1442–1452. https://doi.org/10.1002/hep.23182

Mulligan, C., & Bronstein, J. M. (2020). Wilson Disease: An Overview and Approach to Management. Neurologic Clinics, 38(2), 417–432. https://doi.org/10.1016/j.ncl.2020.01.005

Nazer, H., Ede, R. J., Mowat, A. P., & Williams, R. (1986). Wilson's disease: clinical presentation and use of prognostic index. Gut, 27(11), 1377–1381. https://doi.org/10.1136/gut.27.11.1377

Pfeiffer, R. F. (2016). Wilson Disease. CONTINUUM: Lifelong Learning in Neurology, 22(4), 1246–1261. https://doi.org/10.1212/con.0000000000000350

Poujois, A., & Woimant, F. (2018). Wilson's disease: A 2017 update. Clinics and Research in Hepatology and Gastroenterology, 42(6), 512–520. https://doi.org/10.1016/j.clinre.2018.03.007

Poujois, A., Mikol, J., & Woimant, F. (2017). Wilson disease: brain pathology. Handbook of Clinical Neurology, 142, 77–89. https://doi.org/10.1016/B978-0-444-63625-6.00008-2

Ribeiro, M., Marques, A. C. P. R., Laranjeira, R., Alves, H. N. P., Araújo, M. R. de, Baltieri, D. A., Bernardo, W. M., Lagp, C., Karniol, I. G., Kerr-Corrêa, F., Nicastri, S., Nobre, M. R. C., Oliveira, R. A. de, Romano, M., Seibel, S. D., & Silva, C. J. da. (2005). Abuso e dependência da maconha. Revista Da Associação Médica Brasileira, 51, 247–249. https://doi.org/10.1590/S0104-42302005000500008

Scheiber, I. F., Brůha, R., & Dušek, P. (2017). Pathogenesis of Wilson disease. Elsevier. https://pubmed.ncbi.nlm.nih.gov/28433109/

Silva, A. C. da, Colósimo, A. P., & Salvestro, D. (n.d.). Doença de Wilson (degeneração hepatolenticular): revisão bibliográfica e relato de caso. Rmmg.org, 20(Esp), 404–411. Retrieved December 27, 2021, from http://rmmg.org/artigo/detalhes/1175

Sócio, S. de A., Ferreira, A. R., Fagundes, E. D. T., Roquete, M. L. V., Pimenta, J. R., Campos, L. de F., & Penna, F. J. (2010). Doença de Wilson em crianças e adolescentes: diagnóstico e tratamento. Revista Paulista de Pediatria, 28, 134–140. https://doi.org/10.1590/S0103-05822010000200002

Sturniolo, G. C., Mestriner, C., Irato, P., Albergoni, V., Longo, G., & D'Incà, R. (1999). Zinc therapy increases duodenal concentrations of metallothionein and iron in Wilson's disease patients. The American Journal of Gastroenterology, 94(2), 334–338. https://doi.org/10.1111/j.1572-0241.1999.851_w.x

Oliveira-Júnior, H.P. (2013). Dependência química: maconha.Universidade Federal do Maranhão. UNASUS/UFMA. Disponível em: Ares.unasus.gov.br. https://ares.unasus.gov.br/acervo/handle/ARES/2048

Walshe, J. M. (1982). TREATMENT OF WILSON'S DISEASE WITH TRIENTINE (TRIETHYLENE TETRAMINE) DIHYDROCHLORIDE. The Lancet, 319(8273), 643–647. https://doi.org/10.1016/s0140-6736(82)92201-2

Zimbrean, P., & Seniów, J. (2017). Cognitive and psychiatric symptoms in Wilson disease. Handbook of) Clinical Neurology, 142, 121–140. https://doi.org/10.1016/B978-0-444-63625-6.00011-2