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Adult onset Hallervorden-Spatz disease with psychotic symptoms

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Hallervorden-Spatz disease is a rare neurological disorder characterized by pyramidal and extrapyramidal manifestations, dysarthria and dementia. Its onset is usually in childhood and most patients have a fatal outcome in few years. A high percentage of cases are hereditary with a recessive autosomal pattern.

In the majority of the patients reported, a mutation of the gene that encodes the pantothenate kinase (PANK2) located in the 20p13-p12.3 chromosome that causes iron storage in the basal ganglia of the brain has been found. Its diagnosis is based on clinical symptoms as well as specific MRI imaging findings.

The most common psychiatric features are cognitive impairment as well as depressive symptoms. There are few documented cases with psychotic disorders.

We present the case of a patient with late onset Hallervorden-Spatz disease and psychotic symptoms that preceded the development of neurological manifestations.

The pathophysiology and the treatment of psychotic symptomatology are presented and discussed.

Key words:

Psicosis, Hallervorden-Spatz, late onset, Basal ganglia.

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Enfermedad de Hallervorden-Spatz de comienzo tardío con sintomatología psicótica

La enfermedad de Hallervorden-Spatz es un raro síndrome neurológico caracterizado por signos piramidales y extrapiramidales, disartria y demencia. El inicio suele

ser en la infancia y la mayoría tienen un curso fatal en pocos años. Una gran proporción de casos es familiar con un patrón de herencia autonómico recesivo. En la mayoría se ha encontrado una mutación del gen que codifica la pantotenato kinasa (PANK2) situado en el cromosoma 20p13-p12.3 que conlleva a un acumulo de hierro en los ganglios basales cerebrales. El diagnóstico además de la clínica se realiza por imágenes típicas en RMN.

La afectación psiquiátrica suele ser un deterioro cognitivo, así como síntomas depresivos. Hay pocos casos documentados de trastornos psicóticos.

Presentamos un paciente con la enfermedad de Hallervorden-Spatz de comienzo tardío con episodios psicóticos que precedieron al desarrollo de la sintomatología neurológica.

Se presentan y se discuten la fisiopatología y el tratamiento de las manifestaciones psicóticas.

Palabras clave:

Psicosis, Hallervorden-Spatz, Comienzo tardío, Ganglios basales.

INTRODUCTION

Hallervorden-Spatz disease is a rare neurological disease characterized by progressive degeneration of the central nervous system (CNS) basal ganglia, *globus pallidus* and reticular part of the substantia nigra, produced by iron accumulation, with normal levels of this metal in blood and cerebrospinal fluid.¹

It was described in 1922 by Julius Hallervorden and Hugo Spatz. In most of the cases, a defect has been found in the pantothenate kinase 2 (PANK2) producing gene located in chromosome 20p13-p12.3.²

It is inherited as an autosomal recessive genetic trait, although 15% of the patients are sporadic. It occurs in all races and has a similar frequency in both genders. Typical

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onset is in childhood. The course is progressive and most have a fatal outcome in 2 to 10 years.

CT scan findings are non-specific. The MRI in the early stages is normal, with a characteristic alteration appearing later that permits its diagnosis.³

The psychiatric symptoms accompanying the disorder, as in other neurodegenerative type diseases, are generally nervousness, irritability, depressive symptoms, impulsiveness, behavior disorders and cognitive deficit.⁴ The presence of psychotic symptoms, however, has not been described in more than a few cases referenced in the literature.^{5, 6, 7} Therefore, this work is of interest.

We present the case of a male patient with adult onset Hallervorden-Spatz disease and with psychotic manifestations prior to the neurological ones.

CLINICAL CASE

A case of 30-year old male, without previous psychiatric, personal or family history, is presented. In the last year, he has been admitted three times urgently due to psychotic symptoms: visual and auditory hallucinations, delusional ideation with mystic-religious content and catastrophic experiences together with a state of psychomotor agitation.

During the outpatient follow-up in the Mental Health Unit, he reported thoughts such as: after seeing a lightning bolt, he felt as if everything had become clear and he understood that the world was going to be destroyed in two days, that he was the savior and he felt like Jesus Christ. God spoke to him and told him to go with his girlfriend. His speech was disorganized, splattered with delusional interpretations with some awareness and criticism, but fragilely. Occasional episodes of great psychomotor agitation appeared in relationship to ideas that went through his head that he, himself, described as "intuitions" accompanied by delusional interpretations of glances or gestures having jealous character. He described sensations such as having blocked thoughts, lack of concentration and low mood state.

He was under treatment with 6 mg of risperidone and 15 mg of aripiprazole with many side effects: motor clumsiness, frequent falls and somnolence that motivated progressive reduction of the drugs. Attention was drawn to difficulty for sedation in the psychomotor agitation episodes and low tolerance for the low maintenance doses.

Due to the motor problems observed, a brain MRI was performed. Bilaterally and symmetric hyperintense lesions in *globus palladium* in regards to the thalamus and caudate

were detected in the TM2. Laboratory tests and complementary studies were performed without significant findings.

The MRI was repeated several months later, obtaining symmetric images of both palladiums with central signal hyperintensities and peripheral hypointensities (eye of the tiger image) without alteration of the red nucleus or dentate nuclei of the cerebellum. Regarding the first study, apparent progression was observed that suggested greater neuronal degeneration and iron deposit. The X-ray image was typical of Hallervorden Spatz's disease.

Brain SPECT with IOFLUPANE I-123 showed conserved uptake in both striate nuclei and signs of presynaptic dopamine neuronal degeneration.

The genetic studies performed verified the presence of PANK2 gene mutation, associated to this neurodegenerative disease.

Diagnosis: Organic schizophrenia-like disorder. F06.2 (ICD-10, WHO). Hallervorden-Spatz's Disease.

From the pharmacological point of view, treatment was switched to low dose clozapine (100 mg) with good tolerability and control of the psychotic symptoms.

Neuropsychological study was performed with:

- The Trail Making A and B test, both being normal. The Stroop Test did not suggest organic involvement.
- The Rorschach test reflected isolated perseveration.
- Adult Weschler scale, Wais-III, offered the following scores: Total IQ: 90, Verbal IQ: 97, Manipulative IQ: 85. (*Mean intelligence*). *The difference between the verbal and manipulative part is important but not clearly significant.*
- The patient clearly demonstrated low performance on the Wisconsin Card Sorting Test in which he only completed 3 categories with irregular performance. The typical scores on the main dimensions orient towards a *"deterioration superior to the mean."*

CONCLUSIONS

The sudden onset psychotic symptoms, these being catastrophic experiences, delusional interpretations, incoherent thoughts with lax associations, visual and auditory hallucinations, suggest a psychotic episode. Attention is drawn to the impulsiveness of the patient, the problems to achieve sedation during periods of significant agitation and subsequent intolerance to low doses of atypical neuroleptics.

The neurological symptoms began afterwards. As the motor difficulties with significant clumsiness and frequent falls were observed, the neurological study was initiated to rule out the existence of an underlying organic base.

The evolution of the psychotic symptoms has been favorable, with disappearance of the positive symptoms and a very adequate criticism of them, although the patient continues to have a disproportionate emotional response to trivial events that reflect baseline impulsiveness.

As in one of the cases mentioned in the literature,⁵ there were hyperactivity attention problems in childhood and adolescence with difficulties to achieve adequate school performance.

In our case, as in others published,⁶ the neurological symptoms were not on the first level when the psychiatric symptoms began, as could be expected in this type of disorder. In regards to the cognitive study, the results of the test carried out detected alterations, so that it would be of interest to control the patient to observe the neurocognitive evolution.

In regards to the physiotherapy, it should be mentioned that the neuropsychiatric manifestations of the movement diseases having a neurodegenerative character such as those of Hallervorden, Huntington or Parkinson's, are linked to defects in the brain circuits, especially in the frontal-subcortical circuits. Specifically, if we consider the schizophrenia-like psychotic symptoms, the basal ganglia and cerebellum are involved in multiple neuronal loops and each loop is related with different aspects of behavior, cognition and motor function. The connections with frontal, prefrontal, inferior -temporal cortical zones and posterior parietal zones make it possible for the alterations in these networks on any level to produce specific symptoms similar to those produced in lesions of specific areas. Macro- and microcircuitry involvement in the brain is somewhat more likely in the disorder.^{8,9}

For many authors, the basal ganglia are very interesting in the pathogenesis of the psychotic symptoms for several reasons.¹⁰⁻¹³ The basal ganglia and cerebellum have reciprocal interconnections with the frontal lobes and the abnormalities in these areas, observed in some functional neuroimaging studies, could be due to diseases in the former more than to involvement of the frontal lobes per se.

Others conclude that the existence of patients with involvement of the basal ganglia who develop schizophrenic-like psychosis supposes the involvement of these structures in the production of psychotic symptoms.^{14,15} Thus, psychotic symptoms in Parkinson's disease are frequent, this being associated to greater comorbidity and worse prognoses,¹⁶ or in Chorea, where we find them in 3-12% of the patients.¹⁷

Regarding the pharmacological treatment of these symptoms, the use of conventional antipsychotics is not recommended. There are several works on the efficacy of clozapine in Parkinson's,^{18,19} as well as other atypical antipsychotics.²⁰ There are also studies with atypical antipsychotics in Huntington's disease.²¹

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