Dopamine agonist-induced Othello's syndrome (delusional jealousy)

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Dear Editor

The appearance of Delusional Jealousy (Othello's Syndrome) [OS] in patients diagnosed of Parkinson's Disease and treated with dopamine agonists is quite uncommon. However, its clinical intensity and repercussions may be of great importance. It is imperative for clinicians to know this syndrome in order to identify it early and approach it adequately. We present a care report of a female patient diagnosed of Parkinson's Disease who developed Othello's Syndrome.

Introduction

Parkinson's Disease (PD) is considered to be the second most frequent neurodegenerative disease. Levodopa (dopamine precursor) is the most effective drug. However, its use is somewhat limited due to problems with the appearance of side effects and lost of efficacy over time. Non-ergotic dopamine agonists (pramipexole, ropirinole and rotigotine) with more selective affinities (maximum for D3 receptors) are a useful alternative, both in monotherapy and associated with L-dopa.[1,2] In spite of their effectiveness, one of their possible side effects is the appearance of hallucinatory and delusional symptoms. Othello's Syndrome (Delusional Jealousy) is based on the absolute certainty of infidelity, it being characterized by morbid jealousy that may arise from multiple marital concerns.[3] The appearance of this condition may become potentially dangerous.[3]

Although few cases of Othello's Syndrome in the context of Parkinson's Disease have been documented,[4] one of the most important risk factors to develop psychotic symptoms in these patients is treatment with antiparkinsonian drugs (mainly dopamine agonists).[5-8]

This article aims to call attention to this syndrome as a potential side effect of antiparkinson treatment with dopamine agonists.

A case report

A 53-year old woman referred to the emergency service due to behavioral alterations within the family setting in the context of probable delusional jealousy.

She has no personal or family psychiatric history of interest. She is married and has two children who are already living independently. She completed secondary school. She works as an administrative worker in a large company, with adequate performance and has a high level of responsibility. She has practiced sports, and trained on a regular basis and participated in middle distance races.

She began to have non-specific motor problems in her left lower limb about four years ago. This was initially evaluated as a possible pyramidal muscle syndrome and it was treated on one occasion with botulinum toxin infiltration. However, the motor problem progressed, extending to the upper left limb. She had loss of postural reflexes and bradykinesia, greater in the left hemibody, but without associated tremor or clear muscular rigidity. She was referred to neurology for a specific consultation on abnormal movements and was diagnosed of early Parkinson's Disease. This diagnosis was obtained three years after the onset of the symptoms and one year before her current admission. Treated with Levodopa-Carbidopa (at a dose of 300-75), she initially obtained significant improvement. After, Pramipexole (up to a dose of 2.1 mg/day) was associated. After two months of taking this drug, she began to have personal conflicts. These occurred first with her in-laws and then the problems were focused on her husband. She began to notice strange attitudes in her husband, focusing on small details, and she made erroneous interpretations of supposed evidence and progressively developed delusional jealousy of infidelity. This entailed psychological malaise and frictions in the coexistence. She had emotional lability and disproportionate reactions to the smallest setbacks. Within this context, there was an argument in which there was a moment of heteroaggressiveness and threat of self-injury, which led to her referral to the Emergency service.

Although it has been assumed that the picture may be secondary to the medication, the intensity of the symptoms, full conviction and irrefutability in regards to the arguments, together with the significant behavioral repercussion and lack of disease awareness, her admission to an acute unit of Psychiatry was recommended.

The mental examination showed her to be conscious, alert, oriented on the three spheres, with a relatively calm and collaborating attitude, adequate visual contact, fluid and spontaneous speech in low tone and normal rhythm, coherent and organized speech, reiterative in regarding to the concern of possible infidelity of her husband. There were no formal thought disorders, there was no evidence of sensorial-perceptive alterations, increase of baseline anxiety,

with crying during the interview, she verbalized emotional malaise secondary to over-evaluated beliefs/delusional jealousy, mixed insomnia, with presence of vivid and anxiety-producing dreams, normal appetite, constitutional thinness. There were no signs of upper cognitive function deterioration. Null insight.

In agreement with the Neurology Department, it was proposed to withdraw Pramipexol and re-adjust the Levodopa-Carbidopa. A neuroimaging study was made with non-specific findings (scarce white matter hyperintensive lacunes on the magnetic resonance). Due to the persistence of the symptoms, it was decided to associate quetiapine (up to 200 mg/day). Mild improvement was observed, but her excessive concern persisted, although she was less reiterative and somewhat more accessible to criticism. This made it possible to discharge her for outpatient follow-up ten days after her hospital admission.

It took her about three months during the follow-up to make an adequate criticism of what had happened. It was then when she recognized the experience as disproportionate and absurd in some aspects. She returned to family life, which had been broken for some time. She felt sufficiently wanted and supported by her family setting.

Quetiapine was progressively withdrawn without the reappearance of psychiatric symptoms. The treatment of the Parkinson's Disease was maintained with Levodopa-Carbidopa. Response to this treatment was partial, with progression in the following months regarding the motor symptoms.

Discussion

Although few references have been found regarding the delusional jealousy disorder ("Othello's Syndrome" [OS])[9,10] and its appearance as an isolated symptoms in PD is uncommon, it is possible that its incidence is greater than thought up to now.

It has been demonstrated that the prescription of dopamine agonists in the treatment of PD favors the appearance of psychotic symptoms. Said symptoms occur two to three times more frequently in patients treated with non-ergotic dopamine agonists versus those treated with L-dopa[11-15] and tends to have greater intensity and be more florid.[16,17] There is no simple relation between antiparkinsonian treatment and the appearance of psychotic symptoms, since patients who take dopamine agonists for other reasons hardly have this complication.[18] The physiopathological hypotheses that explain these induced delusions suggest that they are due to an increase in dopamine in the mesolimbic pathway, causing thought disruption. It has also been verified that D3 agonists (such as pramipexole or ropirinole) induce a decrease in blood flow in the right frontal lobule.[5]

In most of the cases described, the appearance of OS occurred in patients with early onset of the Parkinsonian symptoms, subsequent to the establishment of treatment for PD, fundamentally with dopamine agonist drugs.[4]

It generally occurs in relatively young patients (50-55 years), without associated dementia and with moderate motor deterioration.[4,5,19]

In our case, the 53-year old female patient presented early development of Parkinsonian symptoms and was receiving treatment with a non-ergotic dopamine agonist (Pramipexole). Time from initiation of this treatment to the appearance of the delusional symptoms was 2 months.

We consider that this clinical condition must be taken into account since it is often underdiagnosed[4] and has an elevated negative repercussion on the patients as well as their nearby setting.[8,14,20]

Regarding the treatment, it stands out the most of the patients respond favorably to the reduction or withdrawal of the dopamine agonist drug.[14] In some cases, it may be necessary to associate an antipsychotic treatment. Clozapine is considered to be the first drug of choice by some authors,[21] although quetiapine may be a good alterative.[22-24] Other atypical antipsychotics such as risperidone and olanzapine[24] or ziprasidone[25-31] have been tested. In our case, it was necessary to use an antipsychotic (quetiapine), which was tolerated quite well. Improvement of her symptoms was progressive, although slow and gradual.

Recent studies indicate that Pimavanserin (ACP-103) -a highly selective inverse agonist drug of the 5-HT2A-receptors could be a good treatment for this syndrome in the future, with a clear improvement of the delusional symptoms together with limited motor repercussion.[27,32]

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