Clinical note

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Methylphenidate in depersonalization disorder: a case report

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The symptom of depersonalization is frequently associated with other mental disorders, physiological effects of substances or medical diseases. However, it is rare that, as in the case presented, the experiences of depersonalization form an isolated entity, a primary depersonalization disorder.

Among the many psychoactive drugs studied, none of them has been shown to be the treatment of choice. Among those with which the best results are obtained are opioid receptor antagonists (naloxone and naltrexone), the combination of selective serotonin reuptake inhibitors with lamotrigine and clorimipramine. Although with virtually no evidence, we are presenting a case that responded spectacularly to methylphenidate.

Keywords:
Depersonalization, stimulant, methylphenidate.

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El metilfenidato en el trastorno por despersonalización: a propósito de un caso

El síntoma de despersonalización aparece frecuentemente asociado a otros trastornos mentales, a efectos fisiológicos de substancias o a enfermedades médicas. Raramente, como es el caso presentado, las experiencias de despersonalización forman una entidad aislada, un trastorno de despersonalización primario.

Entre los múltiples psicofármacos estudiados, ninguno de ellos ha demostrado ser el tratamiento de elección. Entre los que obtienen mejores resultados destacan: los antagonistas de los receptores de los opioides (naloxona y naltrexona), la combinación de inhibidores selectivos de la recaptación de la serotonina con lamotrigina y la clorimipramina. Y, aunque con prácticamente nula evidencia, se presenta un caso que respondió de forma espectacular al metilfenidato.

Palabras clave:
Despersonalización, estimulantes, metilfenidato

INTRODUCTION

The depersonalization syndrome is defined as the experience of self-strangeness or sense of seeing oneself from a distance. The person feels like an outside observer of their own mental processes, own body or of a part. The patient generally describes it as a sensation of being dead, empty or like they are living in a dream or in a picture or of being an automaton. However, perhaps the most important is that the sense of reality remains intact (it is never experienced as something outside their own experience or imposed).[1]

Depersonalization generally accompanies several psychiatric conditions (anxiety or affective disorders, schizophrenia, dissociative disorders, personality disorders, substance abuse disorders, etc.). It may also appear as a symptom in different organic conditions (neurological diseases -temporal lobe epilepsy, migraine, brain tumors, etc., cardiovascular, endocrine and metabolic diseases), for which some authors have coined the term of "organic depersonalization."[2] In rare cases, it may be the principal symptom of the disorder, as occurs in the case herein presented, it being a primary depersonalization disorder.[3]

Depersonalization disorder is frequently accompanied by other symptoms: anxiety, depression, obsessive thoughts, rituals, somatic preoccupations, autoscopic experiences or subjective alterations in space and experience of time. It has an elevated comorbidity with mental disorders: anxiety disorder (social phobia, panic disorder, generalized anxiety disorder, obsessive-compulsive disorder), mood state disorder (major depression and dysthymia) and others (as for example

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bulimia, somatomorphic disorders, hypochondria or drugs). It also has comorbidity with personality disorders (avoidant disorder, borderline personality disorder and obsessive-compulsive disorder, in the majority of the cases).

It has been postulated that depersonalization may be mediated by neural and neurotransmitter pathways that intervene in the integration of the sensory process and the body schema, and in the mediation of the emotional experience and identification of the feelings. From the evolutionary point of view, depersonalization would be interpreted as a beneficial response to stress in which there would be deactivation of the limbic structures, which would make it possible to attenuate the emotional responses.[4]

In regards to prognoses, in general, it can be concluded from the largest series of cases reported in the bibliography that it tends to be chronic and persistent, that early-onset is associated with a more severe disorder, and that it is related with anxiety and depression more than with dissociation.[5]

CLINICAL CASE

The case of a 29-year old patient who was attended in the emergency service of our center due to a suicide attempt is presented.

There were backgrounds of affective disorders in her first-degree relatives. Her father had suffered a major depressive episode during a period in which he was unemployed, with subsequent complete recovery. Her mother had also suffered a depressive episode when her children were young, followed treatment and did not have any new relapses. One brother suffers bipolar disorder and is under treatment with lithium carbonate, and is currently asymptomatic. Her other brother is under psychological treatment due to probable adaptive disorder.

The patient is the youngest of 3 siblings of a family of musicians: mother, uncles and both brothers completed the musical career. She reports having had a normal childhood, without traumatic experiences.

Her academic performance was very good. She studied superior level of music simultaneously with the career of philosophy, musicology branch, with good results in both careers. After, she applied for and passed the examination of music professor, working, simultaneously, in the secondary teaching Institute and in a private music school. She also formed a part of a chamber music orchestra.

Regarding her sentimental relationships, she had two short lasting significant others. In regards to social and familial relationships, they were and continue to be good.

Standing out among her pathological backgrounds are that at 17 years of age, she had a picture consisting in anorexia nervosa. At that time, she maintained a highly restrictive diet, had symptoms of distortion of body image, amenorrhea and significant weight loss, reaching a body mass index of 15.9. Due to the admission of a female friend for the same problem, she became aware of the disorder and progressively recovered, without following any specialized treatment. At no time did she have symptoms of attention deficit disorder during her childhood.

From the character point of view, she could be described as having obsessive traits and high demanding personality.

Her psychiatric symptoms initiated 8 years earlier, when she began with an anxiety episode. The episode came on suddenly, while she was in the street, with significant vegetative symptoms, feelings of strangeness and sensation of imminent death. She went to the emergency service, to several private physicians and even visited a cardiologist. A few months went by before she was diagnosed of anxiety episode. During those months, there was daily repetition of the pictures of dizziness, palpitations, sweating, tachycardia, and sensation of death. Furthermore, the symptoms of depersonalization began exactly after that. At approximately 2 months of the first episode, she was diagnosed of anxiety disorder. In addition to drug treatment, she also underwent psychological treatment, undergoing cognitive behavioral therapy for one year. At that time, the complete anxiety episodes stopped and she has not had them again since then. However, generalized anxiety and feelings of continuous strangeness regarding reality have persisted and provoked intense discomfort and depressive feelings.

She made visits to many private psychiatrists during seven years. She received multiple antidepressants, several selective serotonin reuptake inhibitors (SSRI) and venlafaxine without clinical improvement. Furthermore, benzodiazepines and an antipsychotic, low doses of amisulpiride, were also added to the antidepressants, without any improvement.

She attempted suicide in March 2007 with an overdose of drugs with low rescuability, writing a farewell note, for which she was admitted to our hospital. On discharge from the hospital, her condition was oriented as generalized anxiety disorder and 150 mg per day of clomipramine and 0.50 mg per day of clonzaepam were prescribed.

During admission, the laboratory parameters and complete blood tests, formula, basic biochemistry, thyroid stimulating hormone, toxics in urine and serology (syphilis, hepatitis B, C and HIV) were normal or negative. The computed tomography showed a mild increase in the ventricular system bilaterally, affecting the lateral ventricles.

In the outpatient consultations after the discharge, she continued to have feelings of strangeness, feelings of losing her head, with the idea that she suffered schizophrenia, deterioration of cognitive functions and she continued to report observing herself from the outside and observing reality as a spectator of a picture. Furthermore, she had severe asthenia and loss of concentration, she could not concentrate or read or play the violin. All of this was accompanied by depressed mood, feelings of hopelessness and suicidal ideation. A psychotherapeutic plan was established with a problem-solving approach. Objective-setting techniques were performed, with low level of self-demand, by self-registries, reinforcing the situations in which she was capable of feeling pleasure. She was also taught several emotional self-control techniques. On the pharmacological level, the dose of clomipramine was decreased to 75 mg due to side effects. After, treatment with lithium carbonate was added, which was not effective in the improvement of the symptoms and also caused an increase in tremors that made it necessary to withdraw it as it interfered with her musical instrumentation. Immediately after, treatment was begun with lamotrigine (100 mg) which, in the beginning, reduced her feelings of depersonalization, the depressive symptoms persisting

At one month, her state of sadness deteriorated, with lack of concentration, difficulties to understand and feelings of hopelessness due to the chronicity of the picture, with elevated anxiety in all of her acts. She also reported severe hyposomnia and asthenia. Orthostatic hypotension that was attributed to the clomipramine and that improved with hygienic-postural measures appeared. A **selective norepinephrine reuptake inhibitor** (reboxetine) was added to the baseline treatment. The symptoms did not improve in spite of increasing the dose of reboxetine up to 8 mg per day in subsequent visits.

Finally, long-acting methylphenidate was added, with progressive dose increase up to 54 mg. With very good tolerability and at 2 months, improvement in her mood state was observed, with disappearance of the ideas of death and greater activity in her daily life, with increased sociability. At 4 months of the onset of the treatment, the depersonalization symptoms disappeared for the first time and the ideas of suffering a severe mental disease as well as the sensation of brain deterioration. She reported still having sporadical, but not daily, feelings of unreality "what is this?" and the fear of reappearance of the symptoms, which she was capable of controlling within a few minutes.

At present and although the patient is still on sick leave, in the last few months, she has been able to take her final exams for her upper level studies of musical instrumentation, with excellent result. She plans to return to her teaching work in the next course.

Discussion of the case

A case of primary depersonalization disorder, having a prolonged and incapacitating course, is presented due to its excellent response to methylphenidate, first in the affective accompanying symptoms and then in the key symptoms of depersonalization.

The review of the pharmacological treatment in depersonalization disorder indicates that among the drugs described as beneficial are the following: a) SSRI; b) tricyclic antidepressants (clomipramine); c) lamotrigine; d) opioid antagonists (naloxone and naltrexone) and e) stimulants (such as methylphenidate or pemoline). The SSRIs, and above all, fluoxetine were the most prescribed drugs for the disorder until Simeon et al. performed a clinical trial with 50 patients, 25 of whom were assigned treatment with fluoxetine and 25 with placebo, in which the fluoxetine was not superior to the placebo.[6] A study with clomipramine, with a limited number of cases (8 in all), found a significant improvement in 7, but three had to drop out due to adverse effects. [7] Lamotrigine in single drug therapy was not shown to be effective in a study performed with 9 patients.[8] On the contrary, the combination of lamotrigine plus SSRI was studied in a sample of 32 patients, 18 of whom improved since a reduction of $\geq$ 30% was found on the depersonalization scales during the follow-up.[9] The studies with opioid antagonists also showed encouraging results. Of the 14 patients who were administered intravenous naloxone up to a maximum dose of 10 mg, 7 improved and in 3, the depersonalization symptom completely disappeared.[10] Furthermore, of the 14 who received naltrexone (mean dose of 120 mg/day), a mean reduction of 30% was observed for the symptoms on the depersonalization scales used.[11] Shader, in 1994, had suggested, based on reports of isolated cases, that drugs that increased synaptic dopamine such as the amphetamines, methylphenidate, pemoline, bupropion, etc. seemed to be beneficial for depersonalization.[12] Except for this citation, no subsequent study has been found, nor any isolated cases using psychostimulants.

In conclusion, regarding the treatment, it can still be said that there is no definitive treatment, that the opioid receptor antagonists, the combination of SSRI plus lamotrigine and clonazepam (especially with SSRI and if there is comorbid anxiety) are the most recommended drugs.[13]

And finally, based on the results obtained in this case, methylphenidate may be a good anti-depersonalization drug.

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