

Suicide Attempt in a Patient with Sibutramine Associated Psychosis

Tentativa de Suicídio em Doente com Psicose Associada a Sibutramina



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Acta Med Port 2022 Mar;**35**(3):216-218 • <https://doi.org/10.20344/amp.14304>

ABSTRACT

Sibutramine is a serotonin-norepinephrine-dopamine reuptake inhibitor, initially developed as a potential antidepressant and later approved for the management of obesity. Sibutramine use is also associated with psychiatric symptoms, namely mania, panic attacks, and, less frequently, psychosis. We report the case of a 32-year-old man, admitted to our hospital due to a suicide attempt in the context of sibutramine-associated psychosis. The symptoms remitted completely after discontinuation of sibutramine and a brief period of anti-psychotic medication. The aim of this manuscript is to highlight the importance of the recognition of sibutramine-associated psychosis, to discuss the possible pathophysiology and the proper clinical and therapeutic management.

Keywords: Liaison Psychiatry; Psychotic Disorders; Sibutramine; Suicide

RESUMO

A sibutramina é um inibidor não seletivo da recaptção de serotonina-noradrenalina-dopamina, inicialmente desenvolvido como potencial antidepressivo e posteriormente aprovado para o tratamento da obesidade. O uso de sibutramina está também associado ao aparecimento de sintomas psiquiátricos como mania, ataques de pânico e, com menor frequência, psicose. Relatamos um caso de um homem de 32 anos, internado no nosso hospital devido a uma tentativa de suicídio no contexto de uma psicose associada à sibutramina. Os sintomas remitiram completamente após a descontinuação da sibutramina e um breve período de terapêutica antipsicótica. O objetivo deste artigo é destacar a importância do reconhecimento da psicose associada à sibutramina, discutir a sua possível fisiopatologia e o seu apropriado manejo clínico e terapêutico.

Palavras-chave: Perturbações Psicóticas; Psiquiatria de Ligação; Sibutramina; Suicídio

INTRODUCTION

Sibutramine, a serotonin-norepinephrine-dopamine reuptake inhibitor, was approved by the Food and Drug Administration (FDA) in November 1997 for weight loss and maintenance of weight loss in patients with a body mass index (BMI) greater than or equal to 30 (≥ 30) kg/m² or for patients with a BMI over 27 kg/m² with other cardiovascular risk factors, after being initially developed as a potential antidepressant.¹ Despite the marketing ban issued by the European Medicines Agency in 2010, due to cardiovascular safety concerns, its use remains common, although illegal, as an anti-obesity medication. Sibutramine can be bought in the black market, usually as a hidden ingredient of some illegal weight-loss products. Sibutramine use is also associated with psychiatric symptoms, namely mania, panic attacks, and, less frequently, psychosis,²⁻⁵ but the real incidence and frequency of these clinical features is difficult to determine because there is no reliable data on its consumption worldwide.

We report a case of suicide attempt in the context of sibutramine-associated psychosis, to highlight the importance of the recognition of this condition and to discuss the possible pathophysiology as well as the proper clinical and therapeutic management.

CASE REPORT

A 32-year-old single man from Brazil, working in Portugal as an elderly caregiver, with no personal history of previous psychiatric or neurological disorders, and with a family history of depressive disorder (namely his mother and a maternal aunt) was admitted to the emergency department due to a suicide attempt where the patient jumped from a 4th-floor window in December 2019. He was initially evaluated by orthopedic surgery, which documented several fractures. His mental status examination revealed perplexity, hyperprosexia (excessive fixity of attention on a stimulus object), anxious mood, behavior indicative of auditory hallucinations, kinesthetic hallucinations, suicide ideation and loss of self-boundaries (the loss of the awareness of the separation between the individual and the environment). Drug scan for amphetamines, cannabis, cocaine and opiates was negative. The patient was then admitted to the orthopedic surgery ward. Besides analgesic drugs, the patient was prescribed olanzapine 10 mg/day. One month following admission, after undergoing major surgical procedures, the patient was reassessed by liaison psychiatry and liaison psychology. The psychotic symptoms and suicide ideation had remitted. The patient disclosed that, since the age of 18, due to being overweight, he had been self-medicating with 15 mg sibutramine for 2-month length cycles. In the

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Recebido: 09 de junho de 2020 - **Aceite:** 24 de julho de 2020 - **First published:** 04 de maio de 2021 - **Online issue published:** 02 de março de 2022

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first of these cycles, at age 18, no associated psychiatric symptoms were reported. The second cycle, when the patient was 21, was associated with overvalued ideas of reference, suspiciousness, sadness, and a feeling of abandonment, and these symptoms were self-limited to the duration of the sibutramine cycle. Between the age of 22 and 32, the patient reported completing one to two cycles of 15 mg sibutramine per year, and all were associated with the same aforementioned symptoms. Eight months before admission, the patient reported a period of overwork, with an increased volume of night shifts and a subsequent inversion of his sleep-wake cycle. During that period, and in the three months before admission, he took a 15 mg sibutramine one-month cycle, followed by a 30 mg two-months cycle with the sibutramine pills that he had brought from Brazil. The patient reported the progressive appearance of overvalued ideas of guilt, reference, elementary auditory hallucinations, somatic anxiety, and mixed insomnia. These symptoms evolved to delusional reference and persecutory ideas, complex auditory hallucinations, accompanied by suicide ideation in early December 2019. Due to these symptoms, the patient abruptly stopped sibutramine a week before the hospital admission. However, the symptoms remained present, and the patient attributed his suicide attempt, a defenestration from his bedroom window to an impulsive, unplanned and desperate act to stop his suffering. Three months after admission, the patient was discharged without any psychotic symptoms, medicated with olanzapine 10 mg/day, and referred to both orthopedic surgery and psychiatric follow-up appointments.

DISCUSSION

There are few reported cases of sibutramine induced psychosis in the literature, and hence the importance of disclosing such clinical cases, in order to promote a better understanding of its clinical features. Clinically, the psychiatric symptoms of our patient are in line with the few reported cases of sibutramine associated psychosis: a case series of 16 patients with sibutramine associated psychosis revealed auditory hallucination in (63%), persecutory ideas (38%), delusions (25%), and suicidal ideation (13%).⁶

Initial reports regarding the receptor-binding properties of sibutramine and its metabolites underestimate the dopaminergic reuptake inhibition of sibutramine compared with the reuptake inhibition of serotonin and noradrenaline. However, more recently, some animal studies suggested a dose-related dopaminergic reuptake inhibition in both the striatal and hypothalamic regions.² This finding may explain, at least partially, not only the relationship between sibutramine and psychosis,⁷ according with the most accepted dopaminergic theory of psychosis, but also, the fact that our patient only developed psychotic symptoms and suicide ideation under a sibutramine 30 mg cycle and not with the previous 15 mg cycles. Furthermore, using the algorithm of Naranjo *et al*⁸ to estimate the probability of an adverse drug reaction, this case report would obtain a probable score of 7 points.

Regarding the delay between sibutramine intake and the onset of psychotic symptoms observed in our patient, some authors argue that it might be the result of a reverse tolerance phenomenon that is similar to the phenomenon described for cocaine and amphetamine abuse, or that sibutramine may act as a precipitating factor in psychosis-predisposed patients.⁹

In terms of the psychopharmacological approach, as in other case reports,² the symptoms remitted completely after sibutramine discontinuation and a brief period of antipsychotic medication.

Regarding limitations, we recognize that the absence of a collateral source of information, namely, a close relative, and the fact that the mental state examination had taken place in a liaison psychiatry setting may have limited the accuracy of some clinical elements. However, we tried to mitigate such facts by interviewing the patient in different moments in order to better characterize this case report.

CONCLUSION

Sibutramine may act as a risk factor for psychosis in predisposed patients. Suspension of sibutramine intake and treatment with a low dose antipsychotic, for a short period, appears to be effective in symptom remission. If, in a suspected case of sibutramine induced psychosis, the symptoms persist after those measures are taken, then the case must be reassessed, and another differential diagnosis should be considered. Further studies are required to elucidate the relationship between sibutramine and psychosis and the underlying pathophysiology.

AUTHORS CONTRIBUTION

PCP, CF: Substantial contribution for the draft of the manuscript. Clinical follow-up of the patient and case review.

ALS, JJ, LG: Substantial intellectual contribution. Case review and critical review of the paper.

PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association updated in 2013.

DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

PATIENT CONSENT

The authors received consent from the patient to publish the report and the information has been de-identified to protect anonymity.

COMPETING INTERESTS

The authors have declared that no competing interests exist.

FUNDING SOURCES

No subsidies or grants contributed to this work.

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Granulomas Sarcóides Sobre Cicatriz: Além da Sarcoidose

Sarcoid Granulomas Over Scars: Beyond Sarcoidosis



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Acta Med Port 2022 Mar;35(3):218-221 • <https://doi.org/10.20344/amp.13451>

RESUMO

Os granulomas sarcóides podem ser encontrados num vasto leque de doenças, pelo que diferenciar a sarcoidose de uma reação tipo sarcóide constituiu um desafio. Apresentamos o caso de uma jovem com lesões papulonodulares eritematovioláceas localizadas nos pavilhões auriculares sobre os locais de aplicação de *piercings*. A biópsia cutânea mostrou um infiltrado constituído por granulomas sarcóides ou focalmente tuberculóides, não excluindo a hipótese de sarcoidose. O estudo complementar, apesar de uma discreta elevação da enzima conversora da angiotensina, excluiu envolvimento ocular ou pulmonar por sarcoidose. Perante a localização das lesões foram realizados testes epicutâneos que revelaram uma reação fortemente positiva ao paládio e ao níquel, apoiando o diagnóstico de dermatite de contacto granulomatosa. Estão descritos escassos casos de dermatite de contacto granulomatosa ao paládio tendo o metal dos *piercings* como fonte de sensibilização. A formação de granulomas sarcóides pode representar quer uma reação tipo sarcóide, quer uma forma de sarcoidose cutânea, e os testes epicutâneos adquirem um papel fundamental no diagnóstico correto.

Palavras-chave: Cicatriz; Dermatite de Contacto; Granuloma; Paládio; Sarcoidose

ABSTRACT

Sarcoid granulomas can be found in a wide range of diseases and differentiating sarcoidosis from a sarcoid-like reaction may be a challenge. We present a woman with erythematoviolaceous papulonodular lesions located on the ears where piercings were placed. A skin biopsy showing an infiltrate of sarcoid and focal tuberculoïd granulomas did not exclude sarcoidosis. There was a slight increase in the level of angiotensin-converting enzyme. Systemic involvement due to sarcoidosis was excluded. Epicutaneous tests performed revealed a strong positive reaction to palladium and nickel, supporting the diagnosis of granulomatous contact dermatitis. There are only a few reports of granulomatous contact dermatitis to palladium with piercings as the source of sensitization. The formation of sarcoid granulomas can represent either a sarcoid-like reaction or a form of cutaneous sarcoidosis, and patch tests are essential in order to establish the diagnosis.

Keywords: Cicatrix; Contact Dermatitis; Granuloma; Palladium; Sarcoidosis

INTRODUÇÃO

Os granulomas sarcóides são constituídos por células epitelióides rodeadas por uma escassa coroa linfocitária e sem tendência à caseificação. Podem ser encontrados em lesões de sarcoidose, mas também num vasto leque de outras patologias tais como reações de corpo estranho, sífilis secundária, doença de Crohn, granuloma anular, linfomas e cicatrizes de herpes zoster. Constitui assim um desafio distinguir a sarcoidose de uma reação tipo sarcóide.^{1,2}

CASO CLÍNICO

Doente do sexo feminino, 23 anos, saudável e sem medicação habitual, recorreu à consulta de Dermatologia por lesões cutâneas assintomáticas dos pavilhões auriculares com cerca de 1 ano de evolução. Ao nível dos hélices e lóbulos das orelhas, observavam-se lesões papulonodulares, eritematovioláceas, firmes e de superfície lisa (Fig. 1), com distribuição irregularmente linear nos locais de

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Recebido: 17 de janeiro de 2020 - Aceito: 24 de julho de 2020 - First published: 06 de dezembro de 2021 - Online issue published: 02 de março de 2022

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