

## Book Chapter

# Mania as Debut of Cushing's Syndrome: A Case Report

Ricardo Álvarez Martínez<sup>1</sup>, Rosa María Tomé Rodríguez<sup>1</sup>, María Álvarez Ariza<sup>1,2</sup>, Carlos Spuch<sup>2,3\*</sup> and Jose M Olivares<sup>1,2,3</sup>

<sup>1</sup>Department of Psychiatry, Vigo Health Area, Hospital Álvaro Cunqueiro, Spain

<sup>2</sup>Translational Neuroscience Group, Galicia Sur Health Research Institute, Spain

<sup>3</sup>Centro de Investigación Biomédica en Red de Salud Mental (CIBERSAM), Spain

**\*Corresponding Author:** Carlos Spuch, Centro de Investigación Biomédica en Red de Salud Mental (CIBERSAM), Spain

Published **December 10, 2020**

This Book Chapter is a republication of an article published by Carlos Spuch, et al. at Case Reports in Psychiatry in March 2020. (Ricardo Álvarez Martínez, Rosa María Tomé Rodríguez, María Álvarez Ariza, Carlos Spuch, Jose M Olivares. Mania as Debut of Cushing's Syndrome. Case Reports in Psychiatry. Volume 2020, Article ID 9127632, 3 pages. <https://doi.org/10.1155/2020/9127632>)

**How to cite this book chapter:** Ricardo Álvarez Martínez, Rosa María Tomé Rodríguez, María Álvarez Ariza, Carlos Spuch, Jose M Olivares. Mania as Debut of Cushing's Syndrome. In: Miguel Borregón Rivilla, editor. Case Reports for Medical Practitioners. Hyderabad, India: Vide Leaf. 2020.

© The Author(s) 2020. This article is distributed under the terms of the Creative Commons Attribution 4.0 International License (<http://creativecommons.org/licenses/by/4.0/>), which

permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

**Acknowledgments:** The authors would like to thank the Galicia Sur Health Research Institute (Instituto de Investigación Sanitaria Galicia Sur) for their support. In addition, the authors are especially thankful for the aid provided by the Psychiatric Nursing and Psychiatry Services of the Álvaro Cunqueiro and Nicolás Peña hospitals.

**Conflicts of interest:** The authors report no financial or other relationship relevant to the subject of this article.

**Ethics approval and consent to participate:** All procedures were approved by Helsinki Declaration and with the approval of the Ethics Committee (Galician Network of Research Ethics Committees [Red Gallega de Comités de Ética de la Investigación]).

**Funding:** Funding/support: Carlos Spuch received support from Axencia Galega de Innovación (IN607C-2017/02) and Jose Manuel Olivares received support from ISCIII grant number PI16/00405, Ministerio de Sanidad grant number 2017/054 and from GAIN grant number (IN607B 2018/17).

## Abstract

This is a case of a patient affected by Cushing syndrome that was admitted at the hospital due to hormonal problems. He had presented psychiatric symptoms that were mistakenly considered not directly connected to the pathology causing the clinical condition, but a mere psychological reaction to it.

## Introduction

Cushing's syndrome is a hormonal disorder caused by excess glucocorticoids. In 70-80% of cases, this excess is due to an excess of ACTH, being the rest of them (10-20%) ACTH independent [1,2]. The usual symptoms in these patients include central obesity, abdominal stretch marks, moon-shaped face,

hirsutism, insulin resistance and facial plethora, although clinical presentation may be variable [3]. Early diagnosis is very complex due to its low incidence and the lack of specificity of its clinical manifestations, that can be seen in other pathologies, such as, metabolic syndrome [4]. The elevation of hormones also influences brain functioning and, therefore, this syndrome can be accompanied by several psychiatric manifestations, being the most common irritability, anxiety, depression and cognitive deterioration, and to a lesser extent mania or hypomania and psychosis [1]. In some cases, psychiatric symptoms may even precede for months or years the onset of the classical physical symptoms [5]. Psychiatric manifestations may completely remit after the correct treatment of the underlying cause.

## Case Presentation

A 37-year-old male who was admitted to the Acute Psychiatry Unit for a manic condition in which sleep disorders (insomnia of conciliation and maintenance), dysphoria, inadequate attitude and altered cognitions predominated. In the three months prior to admission, symptoms compatible with hypomania were described and treatment with Lithium (800 mg) and Olanzapine (10 mg) was initiated. For three years, the patient had also been in regular contact with the Department of Endocrinology, due to a mild hypertension and hypokalemia that received no treatment.

With progressive adjustments of the psychopharmacological treatment, a partial remission of the psychiatric symptomatology was achieved, olanzapine dose was maintained and risperidone (6 mg) and Rivotril (4 mg) were gradually introduced, reducing lithium treatment to 600 mg/day. High blood pressure levels persisted. An endocrinological study was then performed with specific tests for Cushing, and an elevated urinary cortisol (1719.94 micrograms/day) elevation of ACTH concentration (115 pg/ml) and altered dexamethasone suppression test (weak suppression of 20.66 ug/100 ml and strong suppression of 4.19 ug/ml) was detected, so the patient was transferred to the Endocrinology Department. NMR to check the pituitary did not show significant alterations, and the rest of hormonal tests did not show pathological data. including levels of metanephrine,

normetanephrine and 3 methoxytyramine with 257, 348 and 365  $\mu$ g/day respectively. He was, then, diagnosed of endogenous ACTH-dependent hypercortisolism of probable pituitary origin, and the psychiatric treatment was unchanged.

After being discharged, the patient gradually presented symptoms of anxiety and depression (apathy and clinophilia), partly modulated by his evident and progressive physical deterioration. The dose of risperidone was reduced to 3 mg in an attempt to achieve affective improvement without success. At the same time, follow-up was maintained the Endocrinology outpatient's clinic, a catheterization of lower petrosal sinuses was performed without abnormal results, suggesting an ectopic secretion of ACTH. A thoracoabdominal CT was then performed, showing a segmental bilateral pulmonary thromboembolism without clinical repercussion, and a 1.5 cm hypervascularity lesion that protruded in the posterior edge of the hepatic segment VI. This pointed to the differential diagnosis between haemangioma or possible hypervascularity tumour, not being able to make an anatomopathological diagnosis. After an urgent pneumology study, a diagnosis of venous thromboembolic disease was made; hepatic MRI was performed, suggesting the possibility of metastasis of a neuroendocrine tumour, because scintigraphy (administration of SPECT-CT with  $^{99m}\text{Tc}$ -Tektrotyd, dose: 20mCi) also showed a focal uptake at the height of the right adrenal gland, at the crossroads between liver tissue, vena cava and apex of the gland. In the following weeks the patient developed an important myopathy, a cushingoid phenotype with rounded face, and multiple falls and traumatism (particularly on his left knee). One month and a half after hospital discharge, he is admitted again to the hospital.

During the second admission, prostration, extreme weakness and severe protein malnutrition were the most relevant features. The patient was also suffering from pain in the left limb, so he was referred to a traumatologist who diagnosed a femoral head fracture. PET scans were performed which, except for hypermetabolism at left hip level, did not show any focal lesions suggesting tumoral pathology. The hypothesis of a neuroendocrine tumour was maintained and the hip fracture was

surgically intervened. The endocrinologist started treatment for associated comorbidities: Amlodipine for blood pressure correction, osteoporosis treatment, somatostatin analogues and protein and protein supplements due to protein shortage. Again, the patient is evaluated by the Psychiatry service to alleviate anxiety and sleep disorders, progressively decreasing the dose of neuroleptics (withdrawal of Risperidone) and introducing antidepressant treatment with Mirtazapine (15 mg/day).

During the evolution, a decrease in the concentration of ACTH (13.70 pg/ml) and in the concentration of cortisol (265.31  $\mu$ g/day) can be observed, and there is no modification of the mass found at the liver, whose study is pending completion. Follow-up by imaging tests (liver MRIs with and without contrast) to date supports that the liver lesion is a benign lesion in relation to focal nodular hyperplasia (lesion of 18mm). The pulmonary nodule continues to be studied with high-definition chest CT controls without having modified its characteristics.

## Discussion

The hypercortisolism in a rare disease, with affection of multiple systems, associated with a high morbidity and mortality if not treated in time. The prognosis of the disease is affected mainly by difficulties in diagnosis and treatment, which remain a challenge today. Another problem associated with hyperactivity of the hypothalamus-pituitary adrenal axis is the presentation of psychiatric diseases, such as mood disorders, usually depression. However, manic symptoms are not common at the onset of Cushing's syndrome

This clinical case reflects the importance of an adequate organic screening in the presence of psychopathological symptoms in a patient with an atypical picture and no previous remarkable antecedents, concomitant with high arterial pressure that had been present for years, and ionic alterations (hypokalaemia) of recent instauration that could indicate an organic origin symptom.

Psychiatric symptoms that appear in the context of a neuroendocrine disease often occur at an advanced stage of the disease. However, they can occur in very early stages and, as in the case we have presented, can even mean the debut of the disease. The signs and symptoms typical of Cushing's syndrome (central obesity, facial plethora, stress fractures, high blood pressure, glucose intolerance and myopathy) in our case have appeared after the debut of psychiatric symptoms [6]. It's worth to mention again that regular and complete physical examination is crucial when assessing patients with first-time or unexpected psychiatric symptoms.

In this case, psychiatric manifestations were signalling the onset of the disease and although initially no organic illness was suspected as the cause of the patient's symptomatology, the subsequent clinical evolution as well as the continuation of the study revealed an endocrinological origin. In Cushing's syndrome with psychiatric symptoms, psychopharmacological treatment is considered to be of support to alleviate the symptoms that may appear both as a consequence of the disease and as adaptive symptoms.

## References

1. Y Chen, Y Li, X Chen, Q Sun. Neuropsychiatric disorders and cognitive dysfunction in patients with Cushing's disease. *Chin. Med. J. (Engl)*. 2013; 126: 3156–3160.
2. Lacroix, RA Feelders, CA Stratakis, LK Nieman. Cushing's syndrome. *The Lancet*. Lancet Publishing Group. 2015; 386: 913–927.
3. HD García Botina, DR Lara Botina, F Mauricio Sánchez, A Román González. Presentación de tres casos y revisión en la literatura: Síndrome de Cushing. *Arch. Med*. 2017; 17: 415–424.
4. S Ummar, V Rajaraman, N Loganathan. Cushing's syndrome presenting as treatment-resistant bipolar affective disorder: A step in understanding endocrine etiology of mood disorders. *Indian J. Psychiatry*. 2015; 57: 200–202.
5. Sharma, N Sawant, N Shah. A Study on Psychiatric Disorders, Body Image Disturbances, and Self-Esteem in

- Patients of Cushing's Disease. *Indian J. Endocrinol. Metab.* 2018; 22: 445–450.
6. Lila, V Jagtap, P Menon, V Sarathi, T Bandgar, et al. Cushing's syndrome: Stepwise approach to diagnosis. *Indian J. Endocrinol. Metab.* 2011; 15: 317.