

A Case of Sibutramine-induced hyperprolactinemia

Carolina Garcia SOARES LEÃES, Júlia Fernanda Semmelmann PEREIRA-LIMA,
Miriam DA COSTA OLIVEIRA

Neuroendocrinology Center of Santa Casa de Porto Alegre, UFCSPA, Brazil

Correspondence to: Carolina Garcia Soares Leães, MD., PhD.
Neuroendocrinology Center of Santa Casa de Porto Alegre
Rua Faria Santos, 142, 90670-150 - Porto Alegre - RS, Brazil.
TEL: +55 51 3061-8814; FAX: +55 51 3029-9531; E-MAIL: dracarolina@cisa.med.br

Submitted: 2011-09-05 Accepted: 2011-09-25 Published online: 2011-11-12

Key words: hyperprolactinemia; weight gain; obesity; prolactin;
sibutramine; amenogalactorrhea

Neuroendocrinol Lett 2011;32(5):616-618 PMID: 22167128 NEL320511C05 ©2011 Neuroendocrinology Letters • www.nel.edu

Abstract

INTRODUCTION: Several drugs may cause hyperprolactinemia, especially antipsychotic drugs and prokinetic drugs. Serum prolactin concentrations increase within hours after acute administration of these drugs and return to normal within two to four days after cessation of chronic therapy. So far, sibutramine, a sympathomimetic drug used in the management of obesity, was not described to be associated with altered prolactin levels.

OBJECTIVE: The purpose of this study is to present a case of sibutramine-induced hyperprolactinemia.

CASE REPORT: A 38-year-old white female patient seeks medical attention complaining of weight gain (Body mass index: 35) associated with anxiety. She started sibutramine treatment and presented with amenogalactorrhea. Hyperprolactinemia was diagnosed (prolactin of 46 and 89.6 ng/mL) with normal thyroid, renal and hepatic function, and a negative pregnancy test. A sella MRI was performed and sibutramine was suspended. Prolactin levels returned to normal within 15 days of sibutramine cessation and remained normal within 90 days of follow-up, with resolution of the amenogalactorrhea syndrome.

CONCLUSION: sibutramine may be considered in differential diagnosis of drug-induced hyperprolactinemia.

INTRODUCTION

Hyperprolactinemia is the most common biochemical abnormality currently encountered in clinical neuroendocrinology. Once the diagnosis of pathological hyperprolactinemia has been established, the patient should be screened for the numerous causes of hormone hypersecretion, such as lactotroph adenomas and drug use (Molich 2008). A number of drugs may cause hyperprolactinemia, including antipsychotic drugs such as risperidone, phenothiazines, haloperidol, and butyrophenones, and the gastrointestinal motility

drugs metoclopramide and domperidone (Rivera *et al.* 1976; Davis *et al.* 2000; Bhuvaneshwar *et al.* 2009). Serum prolactin concentrations increase within hours after acute administration of these drugs and return to normal within two to four days after cessation of chronic therapy (Petit *et al.* 2003). So far, sibutramine, a sympathomimetic drug used in the management of obesity (Sabuncu *et al.* 2003; Godoy-Matos *et al.* 2005), has not been described as being associated with altered prolactin levels (Genazzani *et al.* 2008). The objective of this study is to present a case of sibutramine-induced hyperprolactinemia.

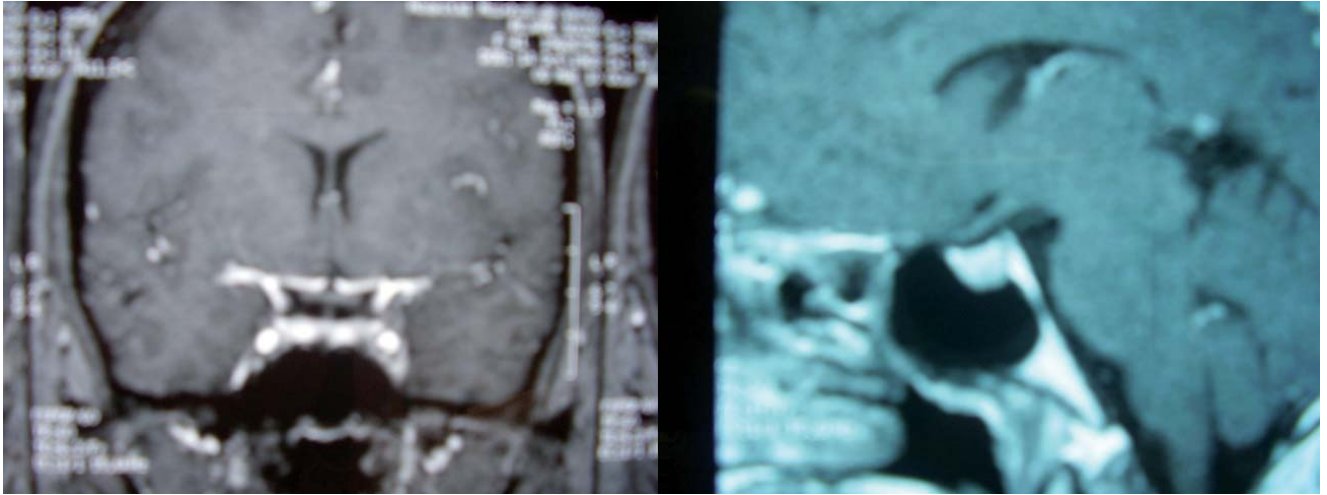


Fig. 1. MRI showing small faint area in the right paramedian region of the pituitary gland, measuring 0.4 cm in diameter (1a). On late post-gadolinium images (1b) the formation is seen to enhance homogeneously with the rest of the parenchyma. Pituitary stalk and other segments of the hypothalamic-pituitary axis are unaltered. This alteration may represent a pituitary microadenoma.

CASE REPORT

A 38-year-old white female seeks medical attention complaining of weight gain (body mass index: 35) associated with extreme anxiety. She started sibutramine treatment after six months of dietary intervention with exercises. She presented with amenorrhea-galactorrhea just after the start of sibutramine treatment. Hyperprolactinemia was diagnosed, with prolactin levels of 46 and 89.6 ng/mL (normal range for females: 3.1–27.3 ng/mL), together with normal thyroid, hepatic and renal function, and a negative pregnancy test. A sella magnetic resonance imaging (MRI) was performed and sibutramine was stopped. Prolactin levels returned to normal within 15 days of sibutramine cessation and remained normal for a 180-day follow-up period, with resolution of the amenorrhea-galactorrhea syndrome. MRI (Figure 1) showed a small area of hypointensity in the pituitary gland. Macroprolactin was not measured because at sample collection prolactin levels had already returned to normal.

DISCUSSION

This case well illustrates the association between sibutramine use, the increase in prolactin levels and the normalization of this hormone following drug cessation. The patient presented with typical clinical manifestations of hyperprolactinemia, including galactorrhea, decreased libido and amenorrhea (Bhuvaneshwar *et al.* 2009), shortly after the onset of sibutramine. To the authors's knowledge, no sibutramine-induced increase in prolactin has already been reported. Few data regarding the effect of sibutramine in prolactin secretion with conflicting results are available in literature. Previously, no change in prolactin levels in patients with polycystic

ovary syndrome (Florakis *et al.* 2008) and a significant decreased in prolactin levels in normal subjects (Genazzani *et al.* 2008) under sibutramine use were demonstrated.

Although MRI revealed a difference in intensity in the pituitary gland that could suggest the presence of a microadenoma, it is well known that about 10% of the population might show such a change on neuroimaging with no clinical repercussion, the so-called incidentalomas (Hall *et al.* 1994). Comprehensive endocrine evaluation is required to prevent misdiagnosis of microprolactinomas and, consequently, inappropriate treatment for the patient. It is also worth mentioning the need to always rule out the association of prolactin with medication use, even when such drugs are not classically described as being associated with hyperprolactinemia.

CONCLUSION

Sibutramine may be considered in the differential diagnosis of drug-induced hyperprolactinemia. Clinicians should be aware of the possibility of prolactin elevation and associated problems when using this medication, especially in patients with other factors that might stimulate prolactin release.

REFERENCES

- 1 Bhuvaneshwar CG, Baldessarini RJ, Harsh VL, Alpert JE (2009). Adverse endocrine and metabolic effects of psychotropic drugs. *CNS Drugs*. **23**: 1003–1021.
- 2 Davis SR, Taylor CC, Kinon BJ, Breier A (2000). The effects of olanzapine, risperidone and haloperidol on plasma prolactin levels in patients with schizophrenia. *Clinical Therapeutics*. **22**: 1085–1096.

- 3 Florakis D, Diamanti-Kandarakis E, Katsikis I, Nassis GP, Karkanaki A, Georgopoulos N, et al (2008). Effect of hypocaloric diet plus sibutramine treatment on hormonal and metabolic features in overweight and obese women with polycystic ovary syndrome: a randomized, 24-week study. *Internal J Obesity*. **32**: 692–699.
- 4 Genazzani AD, Lanzoni C, Ricchieri F, Campedelli A, Rattighieri E, Santagni S, et al (2008). Effect of short term sibutramine on gonadotropin spontaneous pulsatile release in normogonadotropinemic amenorrheic subjects. *J Chin Clin Med*. **3**: 361–369.
- 5 Godoy-Matos A, Carraro L, Vieira A, Oliveira J, Guedes OP, Mattos L, et al (2005). Treatment of obese adolescents with sibutramine: a randomized, double-blind, controlled study. *J Clin Endocrinol Metab*. **90**: 1460–1465.
- 6 Hall WA, Luciano MG, Doppman JL, Patronas NJ, Oldfield EH (1994). Pituitary magnetic resonance imaging in normal human volunteers: occult adenomas in the general population. *Ann Intern Med*. **120**: 817–820.
- 7 Molitch ME (2008). Drugs and prolactin. *Pituitary*. **11**: 209–218.
- 8 Petit A, Piednoir D, Germain ML, Trenque T (2003). Drug-induced hyperprolactinemia: a case-non-case study from the national pharmacovigilance database. *Therapie*. **58**: 159–163.
- 9 Rivera JL, Lal S, Ettigi P, Hontela S, Muller HF, Friesen HG (1976). Effect of acute and chronic neuroleptic therapy on serum prolactin levels in men and women of different age groups. *Clin Endocrinol*. **5**: 273–282.
- 10 Sabuncu T, Harma M, Harma M, Nazliqul Y, Kilic F (2003). Sibutramine has a positive effect on clinical and metabolic parameters in obese patients with polycystic ovary syndrome. *Fertil Steril*. **80**: 1199–1204.