

## Case Report

# Cushing's Syndrome in a Morbidly Obese Patient Undergoing Evaluation before Bariatric Surgery

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## Key Words

Cushing · Obesity · Bariatric surgery

## Abstract

**Objective:** Cushing's syndrome (CS) is extremely rare in morbidly obese patients. To date, no occurrences in obese patients with BMI above 60 kg/m<sup>2</sup> have been reported in the literature.

**Case Report:** This case report describes a patient who was admitted to the ward of the Clinical Division of Endocrinology and Metabolism of the Medical University of Vienna in preparation for bariatric surgery. The patient was a 49-year-old female who showed morbid obesity (BMI 61.6 kg/m<sup>2</sup>), hypertension, and substituted hypothyroidism. Preoperative work-up revealed CS due to an adrenal adenoma. Therefore, the patient underwent unilateral adrenalectomy followed by bariatric surgery 6 months later. **Conclusion:** Since undiagnosed CS might result in severe perioperative complications in a population already at increased risk, this case report underlines the importance of careful endocrine evaluation of morbidly obese patients. After all, even rare endocrine causes should be excluded.

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## Introduction

Although overweight and obesity are common in patients with Cushing's syndrome (CS), morbid obesity (class III obesity; BMI  $\geq 40$  kg/m<sup>2</sup> [1]) is extremely rare in this group. To date, no reports on obese patients with a BMI over 60 kg/m<sup>2</sup> who were diagnosed with CS have been published. Indeed, in a series of 433 morbidly obese patients screened for hypercortisolism in preparation for bariatric surgery at our outpatient clinic (age  $41 \pm 12$  years; BMI  $47 \pm 6.9$  kg/m<sup>2</sup>; 76% women), no one was diagnosed with CS [2].

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**Fig. 1.** **A** Photo of the patient's moon face and telangiectasias shortly after the adrenalectomy (September 2010). **B** Photo of the patient 1 year after gastric bypass (March 2012).



**Fig. 2.** **A** Photo of the patient's buffalo hump shortly after the adrenalectomy (September 2010). **B** Photo of the patient's back 1 year after gastric bypass (March 2012).

### Case Report

In June 2010, a 49-year-old female patient with morbid obesity (174 kg, 168 cm, BMI 61.6 kg/m<sup>2</sup>) was admitted to our institution to be prepared for bariatric surgery. She denied having an eating disorder but reported insomnia, fatigue, memory impairment, and extreme skin sensitivity to sun light. Other members of her family (2 sisters, mother, and grandmother) were also affected by obesity. She started to develop obesity at age 27 when she reached the weight of 135 kg (BMI 47.8 kg/m<sup>2</sup>) during pregnancy. Her blood pressure was reported to be normal until the age of 44. Despite multiple diets, she was unable to restore normal weight. She suffered from untreated hypertension and Hashimoto's thyroiditis, which had been treated with levothyroxine (Euthyrox®; Merck GmbH, Vienna, Austria), 125 µg, since 1992. In addition, she had a levonorgestrel-releasing intrauterine implant (Mirena®; Bayer Austria GmbH, Vienna, Austria) for birth control and reported regular menstrual bleeding. Apart from fat pads along the collar bone and on the back of the neck (buffalo hump) as well as a moon face with telangiectasias on the cheeks (fig. 1A, 2A), no typical features suggestive of CS such as purple striae or hirsutism were detectable. In preparation for bariatric surgery, an endocrine check-up was routinely performed in order to exclude an endocrine cause

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**Table 1.** Biochemical data in Liddle's Test.

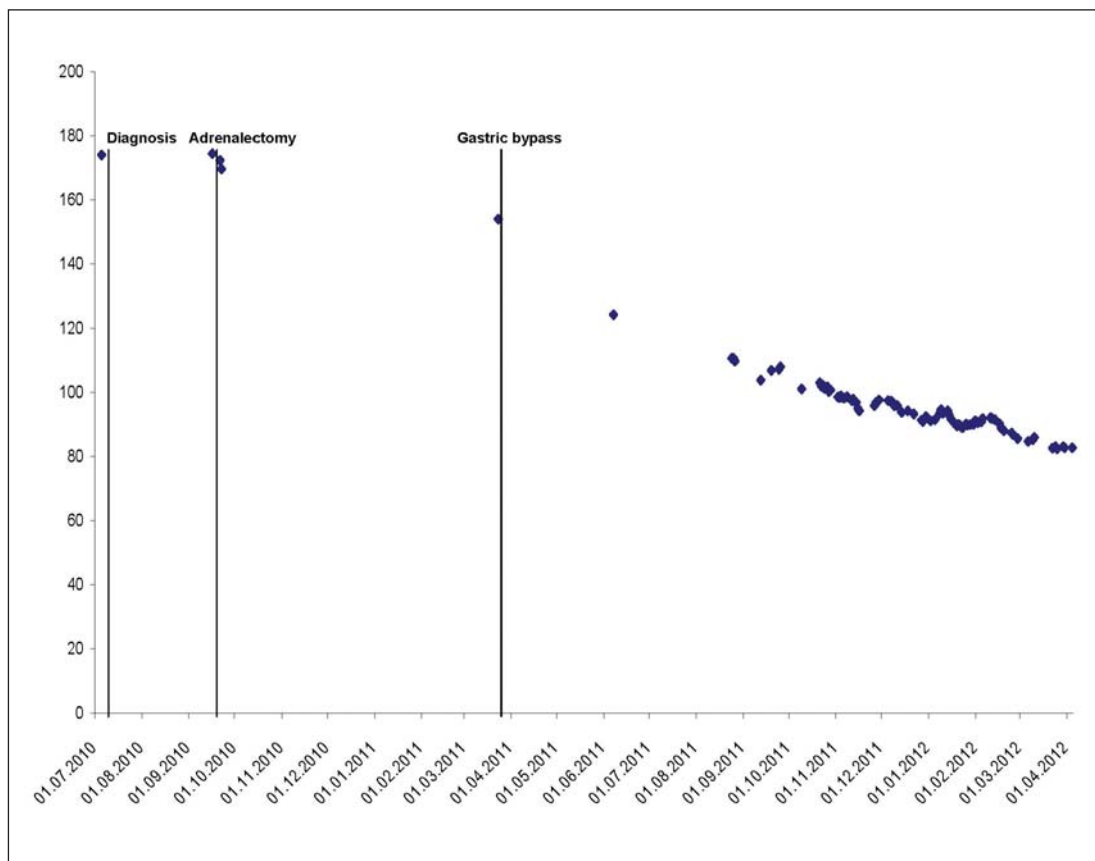
Day	Time	ACTH pg/ml	Serum cortisol µg/dl	U-cortisol µg/24 h (normal = 36–137 µg/24 h)
1	8 AM	<5	11.7	–
2	–	–	–	165.5
3	8 AM	<5	13.5	–
4	–	–	–	166.5
5	8 AM	<5	13.8	177.7

**Table 2.** Diurnal profile of cortisol 1 week after unilateral adrenalectomy.

Time	ACTH pg/ml (normal = 7–10 AM: <46 pg/ml)	Serum cortisol µg/dl (normal = 7.50–9 AM: 9.4–23.9 µg/dl; 4–8 PM: 2.3–11.9 µg/dl)
8 AM	27	6
12 AM	–	6.8
4 PM	–	3.4
11 PM	–	2.3

for the obesity. The diagnosis of CS was considered when no suppression of serum cortisol was observed following an administration of 1 mg dexamethasone overnight (13 µg/dl; normal: <1.8 µg/dl). Her blood pressure was 198/116 mm Hg and subsequently normalized by a triple therapy containing candesartan in combination with hydrochlorothiazide (Blopress Plus® 16/12.5 mg; Blopress® 16 mg; Takeda Pharmaceutical GmbH, Vienna, Austria) and amlodipine (Norvasc® 10 mg; Pfizer Corporation Austria GmbH, Vienna, Austria). Liddle's test was performed. After an oral administration of 0.5 mg and 2.0 mg dexamethasone every 6 h for 2 days, serum cortisol was not suppressed, exhibiting concentrations of 13.5 µg/dl and 13.8 µg/dl, respectively. Also, the urinary free cortisol did not decrease during Liddle's test (table 1). In addition, the plasma concentration of the adrenocorticotropic hormone (ACTH) was below the limit of detection, and thus an adrenal origin of the hypercortisolism conditioned by a CS was suspected. Eventually, magnet resonance tomography (MRT) revealed an adenoma (2.2 × 1.7 cm) in the left adrenal gland. In September 2010, a laparoscopic unilateral left adrenalectomy was carried out without complications at the Department of Surgery of the General Hospital. Histology confirmed the diagnosis of an adenoma. Postoperatively, substitution with hydrocortisone (Hydrocortone® 20 mg; 2–1–0; Auden Mckenzie, Middlesex, UK) was started and the patient was transferred back to our institution. Since hypertension improved, the antihypertensive therapy was reduced to candesartan (Blopress 16 mg). The diurnal cortisol concentrations sojourned in the lower range after suspending the substitution therapy for 1 day (table 2), indicating cure of the hypercortisolism.

The patient was discharged from the hospital with a substitution therapy based on hydrocortisone (Hydrocortone 20 mg; ½–½–0) which was decreased appropriately. One month after the adrenalectomy, another low-dose dexamethasone suppression test was conducted. The basal serum cortisol concentration was 7.8 µg/dl, and the plasma ACTH concentration was 30 pg/ml. Resulting from the administration of 1 mg dexamethasone overnight, a suppression of both cortisol and ACTH was observed (0.2 µg/dl and 5 pg/ml, respectively). The antihypertensive therapy was stopped 2 months after adrenalectomy since blood pressure had normalized. Normal bone density was assessed by densitometry: the T-score was between 0.2 in the lumbar spine and 0.5 in the femoral neck. Within 6 months, the patient spontaneously lost 20 kg (BMI 55 kg/m<sup>2</sup>) and subsequently underwent a laparoscopic omega-loop gastric bypass surgery at the Department of General Surgery without complications. One year later, she weighed 83 kg (BMI 29.4 kg/m<sup>2</sup>; fig. 1B, 2B, 3) and reported no depression or insomnia and an improvement of her quality of life. Her blood pressure ranged between low and normal (90/70 mm Hg) without medication. A body-lifting operation is planned as soon as her BMI stabilizes.



**Fig. 3.** Weight in kg (vertical axis) over time (horizontal axis).

## Discussion

There is little epidemiological information about the incidence and prevalence of CS. Studies conducted in Italy, Spain, and Denmark estimated that the annual incidence ranges from 0.7 to 2.4 people per million population [3–6]. Although the prevalence in the general population has been reported to be a fraction of a percent, recent studies found a much higher prevalence of CS in high-risk cohorts [3]: 8% in a group of 423 patients with treatment-resistant hypertension [7] and 9.4% of 294 patients with type 2 diabetes mellitus [8]. According to some authors, CS has to be suspected and consequently searched for among patients with uncontrolled high blood pressure or diabetes mellitus, metabolic syndrome, polycystic ovarian syndrome, osteoporosis, depression, or adrenal incidentaloma [9]. However, a screening strategy is generally only justified if it is supported by enough evidence of its efficacy and if the benefits will exceed the costs of unnecessary procedures [10]. Considering the enormous number of overweight and obese people worldwide (respectively 1.5 billion and over 500 million adults in 2008 [11]), screening all accordant patients for CS would overwhelm the resources of national health systems. On the other hand, early recognition of CS may prevent physical long-term consequences and reduce mortality associated with untreated CS.

As a direct consequence of the obesity epidemic, a growing number of obese patients seek bariatric intervention [12]. An undiagnosed CS in patients undergoing bariatric surgery increases the risks of postoperative thromboembolic events [13] and of higher bone loss

resulting from delayed CS diagnosis compared to patients with simple obesity [14]. Moreover, Fleseriu et al. [15] reported the death of a patient with undiagnosed CS due to severe malnutrition induced by the malabsorptive intervention [16]. Therefore, obese patients listed for bariatric surgery should undergo a preoperative endocrinological screening, although the prevalence for the disease in this risk group is low. In fact, CS was found in only 0.8% of 783 obese persons (174 males, BMI  $46.8 \pm 8.5$  kg/m<sup>2</sup>; 609 females, BMI  $45.2 \pm 7.7$  kg/m<sup>2</sup>) aged 18–65 years, who underwent evaluation before bariatric surgery [17]. Moreover, in the above mentioned 433 patients of our outpatient clinic, no one was affected by CS [2].

Although weight gain and abdominal fat accumulation are typical features of CS, most patients suffering from the disease do not show morbid obesity, as can be seen from the characteristics of the European Register on Cushing's Syndrome (ERCUSYN) Study Group: the mean BMI of enrolled CS patients in 23 European countries was  $31 \pm 7$  (range 17–56) kg/m<sup>2</sup> [18].

The very low prevalence for CS in morbidly obese patients might be due to the fact that CS patients have a four times higher mortality caused by cardiovascular complications such as coronary artery disease, congestive heart failure, and myocardial infarction [6]. On the basis of these data and of those of other studies on the fatal outcome of untreated CS [19], we suppose that the probability to reach a BMI over 60 kg/m<sup>2</sup> without experiencing an adverse event is low. In the case reported here, the extremely high BMI might be conditioned by multiple factors, like genetic predisposition for obesity which was worsened by pregnancy and hypothyroidism (the latter probably diagnosed with a certain delay) and added to the weight increase related to CS.

The improvements of our patient concerning BMI and blood pressure after adrenalectomy (before bariatric operation) were expected: according to a study on 50 patients suffering from ACTH-independent hypercortisolism, clinical recovery from obesity and hypertension after adrenalectomy was observed in 59.6% and 57.5% of the cases, respectively [20].

The issue on how long the patient really suffered from CS before diagnosis remains unresolved. Considering that she reported to have been normotensive until the age of 44 despite persisting obesity, we could speculate about a CS onset 5 years before diagnosis.

Other reported symptoms such as insomnia, fatigue, memory loss, and obesity are not primarily suggestive of CS and quite common among the general population; they can depend on many factors (e.g., stress, life events, genetic predisposition etc.). Also, signs like buffalo hump, moon face, skin sensitivity to sun light, and telangiectasias can be easily confounded with an obesity pattern or individual characteristics of the patient.

## Conclusion

Although screening for CS cannot be applied to all patients affected by simple obesity because the incidence of the latter is much greater, the present case suggests that CS is a rare but possible diagnosis in morbidly obese persons. In order to allow an early diagnosis and to prevent postoperative complications, patients seeking bariatric surgery and presenting with symptoms possibly attributed to CS (e.g., hypertension, diabetes and metabolic syndrome) should routinely undergo an endocrine work-up including a dexamethasone suppression test.

## Disclosure Statement

The authors declared no conflict of interest.

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