

Hyperprolactinemia in a Patient with Sheehan's Syndrome

Sheehan Sendromlu Bir Hastada Hiperprolaktinemi

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Abstract

Lactation failure is the first and the commonest manifestation of Sheehan's syndrome. We report the long-term follow-up of a patient with Sheehan's syndrome who presented with hyperprolactinemia rather than prolactin deficiency. A young woman developed Sheehan's syndrome after her 5th delivery, which was associated with severe postpartum hemorrhage. She presented with central hypothyroidism, secondary adrenal insufficiency and growth hormone deficiency with preservation of gonadotroph function and complete empty sella on magnetic resonance imaging. In addition, she had hyperprolactinemia, which did not get corrected after thyroid hormone replacement. This is the first reported case of hyperprolactinemia in a patient with Sheehan's syndrome, in whom hyperprolactinemia persisted despite the adequate replacement for central hypothyroidism. *Türk Jem 2010; 14: 47-9*

Key words: Sheehan's syndrome; hyperprolactinemia; postpartum hemorrhage; Empty sella.

Özet

Laktasyonun yetersizliği Sheehan sendromunun ilk ve en yaygın belirtisidir. Bu çalışmada prolaktin yetersizliği değil, hiperprolaktinemi olan bir Sheehan sendromlu hastanın uzun süreli takibi sunulmaktadır. Orta yaşlı bir kadında, beşinci çocuğunu doğurduktan sonra postpartum kanamaya bağlı Sheehan sendromu gelişmiştir. Gonadotrop fonksiyonun korunduğu ve manyetik rezonans görüntüleme tamamen boş bir sella saptanan hasta santral hipotiroidizm, sekonder adrenal yetersizlik ve büyüme hormonu eksikliği bulguları vermekteydi. Ayrıca tiroid hormon replasmanı ile düzelmeyen hiperprolaktinemi de vardı. Bu vaka, santral hipotiroidizm tedavisi için uygun replasmana rağmen hiperprolaktineminin devam ettiği Sheehan sendromlu bir hasta ile ilgili olarak bildirilen ilk hiperprolaktinemi vakasıdır. *Türk Jem 2010; 14: 47-9*

Anahtar kelimeler: Sheehan sendromu, hiperprolaktinemi, postpartum kanama, boş sella

Introduction

Sheehan's syndrome refers to the occurrence of varying degrees of hypopituitarism after parturition (1). The disorder is rare in Western countries but continues to be seen in some countries such as India and Turkey (2,3). It usually unfolds as complete anterior pituitary failure, but some of the functions may be preserved. Preservation of gonadotroph function resulting in subsequent pregnancy has most often been reported in the literature (4). Lactation failure is considered as the earliest manifestation of Sheehan's syndrome and is seen in most of the patients (5). Preservation of lactotroph function or presence of hyperprolactinemia is exceedingly rare and

have been reported before the availability of modern imaging tools as magnetic resonance imaging (MRI) (6). We report a young woman, who after developing Sheehan's syndrome, continued to lactate; the investigations demonstrated hyperprolactinemia, which did not normalize after thyroxine therapy.

Case Report

A 37-year-old woman delivered her 5th child at a local hospital via full-term vaginal delivery, which was followed by postpartum hemorrhage (PPH) continuing for several hours. She was not transfused because of lack of such facility at the local hospital. Post partum, she lactated normally and resumed menstrual

cycles three months later, but developed oligomenorrhea. She also noticed cold intolerance, lethargy, constipation, decrease in breast size, and dizziness. With these complaints, she was evaluated in endocrine ward in June 2003. Physical examination revealed features of hypothyroidism; she was pale, had dry coarse skin and delayed relaxation of deep tendon reflexes. She had a pulse rate of 64 beats per minute and supine blood pressure of 110/60mmHg, without any postural drop. She had sparse axillary and pubic hair without any mucosal and cutaneous hyperpigmentation. Her visual fields were normal on confrontation. In view of symptoms of hypothyroidism dating back to her last delivery, which was associated with PPH, she was investigated for possible Sheehan's syndrome. Hemogram revealed anemia of microcytic hypochromic type with normal counts. Plasma glucose was 76mg/dl and serum electrolytes, liver and kidney function tests were normal. Routine chest X-ray, abdominal ultrasound and electrocardiogram were normal. Basal hormone estimations taken in the morning in fasting state revealed a low total thyroxine (T4) and triiodothyronine (T3) with an inappropriate mild increase in thyroid-stimulating hormone (TSH) suggesting central hypothyroidism, low basal (8 AM) serum cortisol suggestive of hypoadrenalism with normal follicle-stimulating hormone (FSH) and luteinizing hormone (LH), and elevated prolactin (PRL) (table 1). Diagnosis of Sheehan's syndrome was made on the basis of severe PPH followed by partial hypopituitarism. Patient was put on replacement therapy and subsequently discharged on thyroxine 100 µgms per day, prednisolone 5 mgs/day and was kept on regular follow-up. Three years later, the patient stopped menstruating at the age of 40 years, and her serum PRL continued to be elevated in spite of normal T4. Keeping in view the rarity of the disorder and elevated serum PRL on several occasions, the patient was again admitted in 2008 for more detailed investigations. Prednisolone was stopped for four days and she was subjected to insulin tolerance test (ITT) as described (3). Samples were taken for glucose, growth hormone (GH), cortisol and PRL in the basal and stimulated state. Hormone estimations revealed low and nonstimulable GH and cortisol. PRL continued to be elevated in the fasting

state and did not increase further during hypoglycemia. Serum LH and FSH levels were elevated. All hormone assays were performed with specific radioimmunoassay. MRI revealed the sella filled with cerebrospinal fluid and stalk touching the base with a normal posterior pituitary bright signal on T1-weighted image. Contrast-enhanced MRI revealed a small rim of pituitary less than 2 mm in thickness suggestive of completely empty sella (Fig 1).

Discussion

The present patient had developed postpartum hemorrhage after her last delivery at the age of 37 years. She continued to lactate normally, resumed menstruation within three months after parturition, though remained oligomenorrhic for 3-4 years, and thereafter entered menopause. After investigations, the patient was confirmed to have central hypothyroidism, secondary adrenal insufficiency and GH deficiency. Serum PRL was elevated on repeated testing, while dynamic testing did not demonstrate any further increase in PRL levels. MRI confirmed presence of an atrophic anterior pituitary and empty sella. The fact that this patient developed amenorrhea and hypoestrogen state at the age of 40 years and showed increasing trend of serum LH and FSH levels suggests preservation of gonadotroph axis. Sheehan's syndrome, since its original description is considered when either complete or partial anterior pituitary failure develops, usually follows a postpartum hemorrhage. Hypopituitarism is believed to be due to ischemic necrosis of the anterior pituitary secondary to postpartum hemorrhage (1,5). Role of autoimmunity is suggested by demonstration of antipituitary and/or anti-hypothalamic antibodies (7). Preservation of one or more of the anterior pituitary hormone secretions can occur. Sparing or recovery of gonadotroph

Table 1. Hormonal parameters over the three years

Hormone (Plasma)	Units	Values 2003	Values 2008	Normal values
T3	ng/ml	0.5	1.30	0.7-2.5
T4	µg/dl	1.0	9.39-	5.5-13.5
TSH	µIU/ml	11.24	0.42	0.5-6.5
LH	IU/L	12.22	6.54	3-12
FSH	IU/L	14.83	28.64	2-6.6
Estradiol	Pg/ml	-	11	11-65
Prolactin*	µg/L	50.52	35.52	>2
GH*	µg/L	<0.25	<0.25	>3
Cortisol*	µg/dl	1.96	<1.00	>20

T3, Tri-iodothyronine; T4, thyroxine; TSH, thyroid stimulating hormone; FSH, follicle stimulating hormone; LH, Luteinizing hormone; GH, growth hormone. *Peak values after insulin tolerance test. Hormone assays performed with specific radioimmunoassay



Figure 1. Contrast enhanced MRI of pituitary T1 weighted image, Sagittal view showing pituitary filled with CSF and stalk touching the base of the floor against a thin rim of pituitary suggestive of empty sella (Arrow)

function and consequent pregnancy has been reported in some cases (4). GH and PRL-producing cells are mostly confined to the lower and lateral regions of the pituitary gland and are most susceptible to damage following ischemic necrosis (5). Because of this, an absence of PRL rise after thyrotropin-releasing hormone (TRH) is considered to be the most sensitive screening test in patients with Sheehan's syndrome (8).

Hyperprolactinemia in patients with Sheehan's syndrome has been reported, but is extremely rare. Vaughn et al., in 1980, described a 30-year-old woman, who developed symptoms suggestive of hypopituitarism eight weeks after vaginal forceps delivery without any postpartum hemorrhage and failed to resume menstrual cycles. Hormonal investigations revealed hypopituitarism in the form of GH deficiency, central hypothyroidism, secondary adrenal insufficiency, secondary hypogonadism with hyperprolactinemia; the skull x-ray and standard sellar computed tomography (CT) were normal (9). Stacpoole et al., in 1983, reported a 20-year-old woman, who developed postpartum hemorrhage after her only pregnancy and was transfused with seven units of blood. Fifteen months later, she presented with amenorrhea, galactorrhea and symptoms of hypocortisol state. Investigations revealed hyperprolactinemia and ACTH deficiency with normal function of the rest of the pituitary hormone-producing cells including thyrotrophs. Imaging in the form of CT and pneumoencephalography demonstrated evidence of primary empty sella. Patient was put on prednisolone replacement therapy and her symptoms improved, but hyperprolactinemia persisted (10). Whether the above-mentioned patient had autoimmune hypophysitis could not have been ascertained at that time since the first patient of autoimmune hypophysitis was diagnosed ante mortem in 1980 (11). Isolated ACTH deficiency in association with hyperprolactinemia in the context of pregnancy and delivery is commonly seen in patients with autoimmune hypophysitis (12). Kelestimur in 1992 reported a 55-year-old woman, whose last delivery, 20 years before, had been complicated by massive vaginal bleeding. Patient had a normal lactation, but had not resumed menstrual cycles. Investigations revealed central hypothyroidism, secondary adrenal insufficiency, central hypogonadism and GH deficiency. In addition, the patient also had hyperprolactinemia associated with normal-sized pituitary on CT. Hyperprolactinemia was postulated to be due to severe hypothyroidism as serum PRL normalized with thyroxine replacement (6). Other than the above reference, central hypothyroidism is not considered a cause of hyperprolactinemia. Also majority of patients with Sheehan's syndrome do not have hyperprolactinemia in spite of severe central hypothyroidism. In the present patient, hyperprolactinemia was not due to hypothyroidism because, PRL level did not normalize despite the adequate correction of central hypothyroidism. The cause of elevated PRL in our patient is not clear and many explanations could be offered. Macroprolactinemia, a common finding in patients with hyperprolactinemia, is a theoretical possibility in the present patient; however, polyethylene glycol precipitation was not performed in view of mild hyperprolactinemia (13). Also, we did not give her any agent for controlling her hyperprolactinemia and the patient is still under observation. Autoimmune hypophysitis ultimately can give the picture of

empty sella on pituitary imaging and cannot be ruled out at present, although GH deficiency is considered to be less common in lymphocytic hypophysitis and pituitary stalk was not thickened in the present patient (12,14). The possibility of a prolactinoma undergoing apoplexy, as has been reported previously (15), also seems less likely, because the patient did not have any menstrual disturbances, galactorrhea or infertility prior to conception. Possibility of spared lactotrophs getting disinhibited from hypothalamic inhibition or a small prolactinoma located in the pituitary remnant cannot be ruled out with the present day imaging techniques.

In summary, a case of Sheehan's syndrome associated with hyperprolactinemia is reported. The present case scenario is unique in that the patient had hypopituitarism because of Sheehan's syndrome, and high prolactin levels did not normalize after adequate thyroxine replacement. We, at present, want to highlight the extreme rarity of the condition and believe that this is the first reported case of hyperprolactinemia in a patient with Sheehan's syndrome in whom hyperprolactinemia persisted despite the adequate replacement for central hypothyroidism.

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