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A Unique Case Report of Acromegaly in Post-Partum Woman

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Abstract: ***Here we report a case of a female who was diagnosed with acromegaly post-referral for prolonged postpartum amenorrhea. A 36-year-old female patient, gravida 2 para 1, had underwent normal transvaginal delivery and breastfeeding had been discontinued a year post delivery. Soon after, spontaneous menstruation failed to restart. Subsequently, she was referred to our general hospital for complain of prolonged amenorrhea with galactorrhoea and complains of enlarged tongue and lips. On hormonal investigation it was revealed that patient hadsevere hypogonadotropic hypogonadism (luteinizing hormone 1.23 mIU/mL, follicle-stimulating hormone 4.45mIU/mL), along with a moderate increase in serum prolactin levels (53.2 ng/mL).Her growth hormone was 60 ng/ml. Magnetic resonance imaging (MRI) of the head was performed, to rule out organic abnormality in the central nervous system could be a cause of amenorrhea.MRI revealed mass lesions extending from the pituitary fossa to the suprasellar area with similar signal intensity as the gray matter. Bi-temporal hemianopsia was observed on campimetry. After brief examination, the patient was diagnosed with acromegaly.***

Keywords: acromegaly, amenorrhea, postpartum

1. Introduction

Acromegaly is a hormonal disorder which causes certain characteristic facial features with variety of metabolic disorders caused by the excess production of growth hormone (GH) from pituitary adenoma tumour. It can be diagnosed by characteristic features and diagnostic criteria established for patients suspected of having the disease.

Pituitary adenomas which exceed 10 mm in size are termed as macroadenomas and those smaller than 10 mm in size are termed as microadenomas. Microadenomas show prevalence of 14.4% in autopsy studies, while 75% of cases of GHproducing pituitary adenomas are reported to be macroadenomas.[1]Clinical features of high levels of GH are soft tissue swelling with visible enlarged hand, feet, nose, lips and ears. Patient with acromegaly shows features of mandibular overgrowth, brow ridge, forehead protrusion, changes in voice tone, hypertrichosis and hyperpigmentation.[1]

Recently we had encountered a female patient who was diagnosed with acromegaly and presented with prolonged amenorrhea as the first symptom post normal transvaginal delivery.

2. Case Report

A 36-year-old married female, gravida 2 para 1 (one previous artificial abortion), presented to our university general hospital with amenorrhea at one year seven months'post-delivery, with planning of second child. She had no relevant past or family medical history.

She had conceived spontaneously without any complications during her pregnancy. She had delivered a healthy female infant at 39 weeks of gestation. Intrapartum blood loss was reported to be within the normal range. The baby was breastfeed for a year followed by weaning through bottle-feeding.

As the patient failed to experience spontaneous menstruation after the cessation of breastfeeding.

She came to our hospital for investigating her unusual enlargement of face and prolonged amenorrhea. Milk secretion was observed when her nipples were manually pressed even after 7 months of weaning. These findings were obtained through a brief history and a thorough medical examination.

On transvaginal ultrasound no abnormalities in the uterus or ovaries were detected. Ovaries were not polycystic. Laboratory investigation data of blood analysis at patient's first visit were as shown in Table 1.

Table 1: Laboratory Data

White blood cells	49oo /µL	Estradiol	13 pg/mL	Calcium	10.1 mg/dL
Red blood cells	$4.8*10^6$/µL	FSH	4.45mIU/mL	Mg	2.1 mg/dL
Hemoglobin	9.3 g/dl	LH	1.23mIU/mL	IP	5.7 mg/dL
Hematocrit	30.5	PRL	53.2 ng/mL	ALP	404 U/L
Platelet	1.5 lakh	TP	7.7 g/dL	LAP	40 U/L
Neutophils	64%	Alb	4.6 g/dL	GTP	16 U/L
Eosinophils	4%	T-Bil	0.7 mg/dL	ChE	426 mg/dL

Lymphocytes	27%	AST	14 IU/L	Cholesterol	193 mg/dL
PT	14 secs	ALT	15 IU/L	Triglyceride	280 mg/dL
PT-INR	1	BUN	10.4 mg/dL	LDL Cholesterol	124 mg/dL
APTT	30 secs	Cr	0.43 mg/dL	FBS	96 mg/dL
Fibrinogen	300 mg/dl	CRP	0.03 mg/dL	HbA1c (NGSP)	6.20%
D-dimer	0.2μg/dl	LDH	140 U/L		
Free thyroxine	2.7 pg/mL	Na	143 mEq/L		
Free triiodothyronine	0.9 ng/mL	K	4.1 mEq/L		
TSH	1.64μU/mL	Cl	104 mEq/L		

Alb, albumin; ALP, alkaline phosphatase; ALT, alanine aminotransferase; APTT, activated partial thromboplastin time; AST, aspartate transaminase; BUN, blood urea nitrogen; ChE, cholinesterase; Cl, chloride; Cr, creatinine; CRP, C-reactive protein; FBS, fasting blood sugar; FSH, follicle-stimulating hormone; Hb, hemoglobin; INR, international normalized ratio; IP, inorganic phosphorus; K, potassium; LAP, leucine aminopeptidase; LDH, lactate dehydrogenase; LDL, low-density lipoprotein; LH, luteinizing hormone; Mg, magnesium; Na, sodium; NGSP, National Glycohemoglobin Standardization Program; PRL, prolactin; PT, prothrombin time; T-Bil, total bilirubin; TP, total protein; TSH, thyroid-stimulating hormone; γ-GTP, γ-Glutamyl transpeptidase.

No abnormality was detected in circulating blood cell counts or coagulation profile of the patient. The serum level of inorganic phosphorus was 6.0 mg/dL and the alkaline phosphatase (ALP) level was 385 U/L, both elevated beyond the normal range. In addition, the serum triglyceride level was high (280 mg/dL).

As the patient showed hypogonadotropic hypogonadism with amenorrhea and because of the slight hyperprolactinemia, magnetic resonance imaging (MRI) was performed to check her central nervous system and pituitary regions.

Through MRI a tumorous lesion in the pituitary fossa, extending to the suprasellar area with similar signal intensity as the gray matter was detected. The actual position of pituitary gland had shifted to the right cephalic side of the mass. The tumor was seen to enhance nonuniformly by gadolinium in T1-weighted images, and the optic chiasm showed compression and had shifted upward (Fig. 1a). Goldmann visual field perimetry demonstrated a pattern of bitemporal hemianopsia (Fig. 1b).

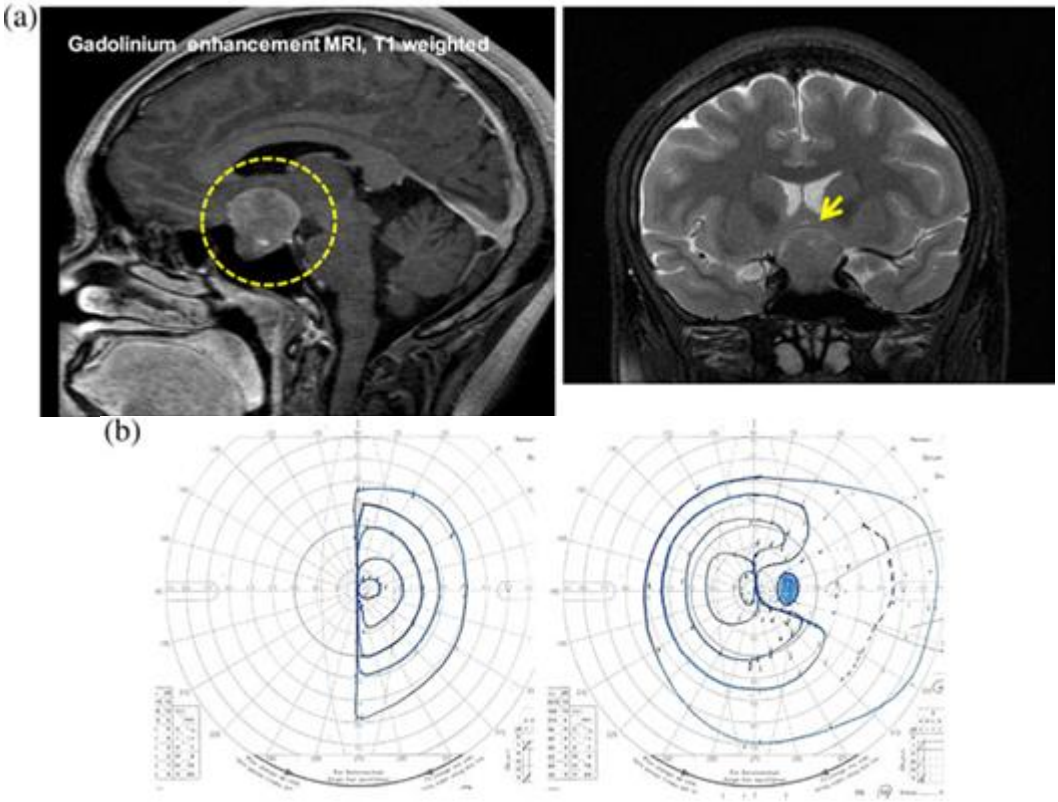

Figure 1: (a) Magnetic resonance imaging with gadolinium enhancement (T1-weighted). Yellow circle indicates the heterogeneously enhanced macroadenoma in the sella turcica. Yellow arrow indicates the optic chiasm compressed by the tumor (b) Visual field test (Goldmann visual field perimetry).

Patient had bitemporal hemianopia as a result of compression of the optic chiasm by the tumor. Fundoscopic examination suggested compressive neuropathy of the left optic nerve.

The basal levels of serum LH and FSH were low, although the gonadotropin response to gonadotropin-releasing hormone (GnRH) was normal, but the time taken to reach the peak values were delayed for both LH as well as FSH.

The baseline GH level was 60 ng/mL (the normal upper limit for GH is < 3.0 ng/mL; the inter-assay coefficient method is employed in our pathology laboratory for the determination of hormone concentrations)[2,3].

An exaggerated response to GH-releasing hormone (GRH) was found, with a peak value of 175.7 ng/mL. The serum level of insulin-like growth factor binding protein-1 (IGF-1) was extremely high (1060 ng/mL). The excessive GH serum level was not suppressed by a 75 g oral glucose tolerance test (OGTT). Impaired glucose tolerance was revealed by means of the 75 g OGTT, suggesting a condition of insulin resistance.[4,5]

After consulting endocrinologists and neurosurgeons, the patient was diagnosed with acromegaly. She later reported that her foot was enlarged and she was unable to wear her existing shoes and difficulty in wearing a ring on her finger.

Due to disturbances in her visual field, the patient underwent surgery to remove the pituitary tumor (transsphenoidal surgery: Hardy's method) post sequential intramuscular administration of octreotide, a somatostatin analogue.[6,7]

The histological diagnosis was suggestive of GH-producing pituitary adenoma in which 90% of the cells were diffusely immunostained by the GH antibody. 2 months post-operative, the serum GH level decreased to the normal range (2.5–5 ng/mL).

Patient also experienced spontaneous menstruation at 4 months postoperatively. And, she was able to wear her ring smoothly. Her facial features altered, which appearedto be slenderer and delicate. She was able to conceive successfully based on our advice on timing and gave birth to a healthy baby 2 years after trans-sphenoidal surgery.

3. Discussion

This report elaborates on a female patient who presented with prolonged amenorrhea which lasted for a year and seven months after her first delivery. Spontaneous menstruation did not recommencetill 7 months after weaning. As the patient's serum LH and FSH levels were reduced, we suspected hypogonadotropic hypogonadism.

Clinical signs of galactorrhea indicated hyperprolactinemia and prompted examination of hypothalamic–pituitary axis for a pituitary disease, viz. prolactinoma. Similarly, Sheehan syndrome can be considered in a patient with post-partum amenorrhea with low serum gonadotropin levels. This disorder was ruled out as there was a negative history of severe blood loss during delivery and normal TSH and thyroid hormone levels.

A moderate increase in PRL levels in this female patient did not indicate the need for MRI of the head; however, it was conducted to exclude the possibility of altered GnRH release which could result from an altered hypothalamic–pituitary axis caused by a brain tumor.

To confirmation the diagnosis of idiopathic hypogonadotropic hypogonadism MRI of the head is advisable. Accordingly, MRI findings helpsto achieve an accurate diagnosis and manage the patient appropriately.

Acromegaly is a relatively a rare disorder. Its incidence has been reported to be at 3–4 individuals per million, with a prevalence rate of 60 individuals per million.[8] An elevated level of GH post epiphyseal closure causes hypertrophy and/or deformity in bone, cartilage and soft tissues. Furthermore, it can lead to advancement of the growth of tumors.

Pituitary gigantism occurs when the disease manifests before epiphyseal closure. Etiology of more than 95% of cases of acromegaly is pituitary tumors arising from GH-secreting somatotrophs. Rare possible cause is commonly encountered tumors which are composed of two distinct cell types i.e somatotrophs and lactotrophs. These cells express prolactin. Such bimorphoustumorsmay cause acromegaly with moderately elevated serum prolactin levels.[9]

The clinical features of acromegaly include characteristic facial features, such as protrusion of the mandible, eyebrow arch or cheek bones, enlargement of the nose and lips and macroglossia. Hence, these patients may experience occlusal discrepancies or difficulty in wearing their finger rings or shoes.

Headaches, paresthesia due to carpal tunnel syndrome, occurrence of type 2 diabetes mellitus and hypertension are major complications of this disease.[10] Due to excess GH secretion, serum levels of phosphate and APH (ALP) are also typically elevates, as was marked in the present case.

The chief causes of amenorrhea in patients with GH-producing adenoma are hypogonadism and hyperprolactinemia. From amongst the hormone-secreting cells within the anterior pituitary, the reserve of the gonadotrophs that produce gonadotropins is limited. Hypogonadism can easily occur when more than 50% of the pituitary gland is damaged by tumor progression.

The development of prolactinomas, in addition to GH-secreting tumor or compression of the pituitary stalk or hypothalamic region, can induce secondary hyperprolactinemia. Prolactinemia is reported to be prevalent accompanying symptom in approximately 30–40% of female patients who were diagnosed with acromegaly.[11] It is difficult for patients to appreciate the enlargement of their hands or feet because the change is gradual. Therefore, doctors who do not specialize in endocrinology or internal medicine often lead to unexpected diagnosis of acromegaly.

Analyses of circulating LH, FSH and E2 are chosen to evaluate ovarian function. In addition, prolactin and TSH levels, as well as thyroid hormones, are useful because they provide an overview of pituitary function and are strongly involved in reproductive function. In this case, we could not perform an MRI because of the hypogonadotropic status with the presence of slight prolactinemia.

However, if the patient reports with complain of problems in the visual field or swelling of the hands or feet, we would have considered a diagnosis of acromegaly earlier. Our

experience reiterated the necessity of performing a detailed history and medical examination.

In addition, assessment of GH and IGF-1 serum levels con prove to be valuable for screening acromegaly at the first visit in a patient with amenorrhea. GH secretion is influenced by circadian rhythms, IGF-1 –produced by subsequent GH release.

Selective transsphenoidal surgical resection is the treatment of choice for well-circumscribed somatotroph cell adenomas, and approximately 60% of patients with macroadenomas could be cured, depending on the medical center facilities and experience of the neurosurgeon.[12]

However, it should be noted that visual disturbances caused by the tumor typically improved post resection, anterior pituitary dysfunction is prevelant in in 60–70% of patients who underwent sphenoidal surgery[13] and new hypopituitarism condition develops in up to 20% of patients. This reflects operative damage to the surrounding normal pituitary tissue.[13,14]

Our patient was periodically followed up by an endocrinologist, where the serum levels of gonadotropins and prolactin had remained within the normal range post-surgery. The patient visited to our hospital with complaint of amenorrhea at one year seven months post-delivery of her first child and was diagnosed with acromegaly.

However, it remains unclear as to when the disease could first manifest in this patient. As she conceived her first child spontaneously, we could not exclude the possibility of GH hypersecretion which already existed before her first pregnancy. Though fertility is commonly impaired in acromegaly, reproductive potential is preserved if only the tumor mass does not destroy the gonadotropin lineage. It has been reported that pregnancy in acromegalic women has a normal course leading to normal delivery, with normal babies.[15]

We also encountered a patient with acromegaly who presented with complaint of prolonged post-partum amenorrhea. Although a slight increase in serum prolactin levels can be followed up, a pituitary tumor could be considered in such patients with extremely reduced levels of serum gonadotropins. A thorough medical examination and interview are crucial for prompt diagnosis and treatment.

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