



Two Adult Patients with Ectopic Neurohypophysis and Panhypopituitarism Due to Absent Pituitary Stalk

Hipofiz Sapı Yokluğuna Bağlı Hipofizer Yetmezliği ve Ektopik Nörohipofizi olan İki Erişkin

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Abstract

We report two cases of 27-year-old and 19-year-old female patients with ectopic neurohypophysis and panhypopituitarism due to absent pituitary stalk. They were admitted to the endocrinology clinic with short stature, growth retardation and primary amenorrhea. Basal hormones revealed secondary hypothyroidism, adrenal insufficiency, hypogonadism and growth hormone insufficiency. Peak cortisol response to the short synacthen test (SST) was normal but was inadequate to insulin tolerance test. The other dynamic pituitary function tests showed panhypopituitarism. Magnetic resonance imaging of the pituitary gland revealed an ectopic posterior pituitary tissue and absent pituitary stalk. We administered hormone replacement therapy. As this disorder is usually encountered in the pediatric age group, we report here two adult patients with ectopic posterior pituitary tissue, absent pituitary stalk and panhypopituitarism. *Turk Jem 2014; 18: 143-146*

Key words: Ectopic neurohypophysis, panhypopituitarism, absent pituitary stalk

Özet

Hipofiz sapı yokluğuna bağlı total hipofizer yetmezliği ve ektopik nörohipofizi olan 27 ve 19 yaşlarında iki olguyu sunuyoruz. Bu hastalar endokrinoloji kliniğine boy kısalığı, gelişme geriliği ve primer amenore şikayetleri ile başvurdu. Bazal hormonların değerlendirilmesi ile sekonder hipotiroidi, adrenal yetersizlik, hipogonadizm ve büyüme hormonu eksikliği tespit edildi. Kısa synacten testinde pik kortizol cevabı normalken insülin tolerans testinde yetersizdi. Diğer dinamik hipofiz fonksiyon testlerinde total anterior hipofiz hormon yetersizliği vardı. Hipofiz bezinin manyetik rezonans görüntülemesinde hipofiz sapının olmadığı ve posterior hipofiz dokusunun ektopik yerleştiği görüldü. Hormon replasman tedavisine başlandı. Bu rahatsızlık genellikle çocuk yaş grubunda tespit edilmesine rağmen biz ektopik posterior hipofiz dokusu, hipofiz sapı yokluğu ve total anterior hipofiz hormon yetersizliği olan iki erişkin hastayı sunuyoruz. *Turk Jem 2014; 18: 143-146*

Anahtar kelimeler: Ektopik nörohipofiz, total hipofizer yetmezlik, hipofiz sapı yokluğu

Introduction

Ectopic posterior pituitary tissue results from defective neuronal migration during embryogenesis (1). Isolated growth hormone (GH) deficiency or multiple pituitary hormone deficiency can be associated with pituitary stalk transection syndrome (2). Imaging characteristics of this syndrome are hypoplasia of the adenohypophysis, lack of pituitary stalk whose visibility is assessed after administration of contrast material and ectopic posterior pituitary gland (3,4,5). Our cases were adult patients with stalk transection who had ectopic neurohypophysis and panhypopituitarism.

Case Reports

Case 1

A 27-year-old female patient presented with primary amenorrhea and growth retardation. The patient was the product of an uncomplicated normal vaginal delivery. Her height was 146 cm and her weight was 40 kg; she had a systolic arterial pressure of 100 mm Hg and diastolic pressure of 80 mmHg. There was no axillary or pubic hair; and breast development was Tanner stage 1. Her bone age was consistent with the age of 15. Pelvic ultrasonography showed a hypoplastic uterus. Basal hormones of the patient were found to be as follows: cortisol: 3.28 µg/dL (8-

25), PRL: 7.0 ng/mL (4.0-15.2), free T3: 1.97 pg/mL (1.71-3.71), free T4: 0.5 ng/dL (0.70-1.48), TSH: 1.8 µIU/mL (0.3-4.9), FSH: 0.8 µIU/mL (1.5-12.4), LH: 0.1 µIU/mL (1.7-8.6), E2: 5.0 pg/mL (12.5-166), IGF-I: 6.87 ng/mL (219-644).

Short synacthen test (SST), insulin tolerance test (ITT), thyrotropin releasing hormone (TRH) and luteinizing hormone (LH)-releasing hormone (LHRH) stimulation tests were performed in order to evaluate pituitary functions. Cortisol and GH responses were evaluated by ITT. While there was cortisol response to SST, cortisol response to ITT was not sufficient (Table 1).

Magnetic resonance imaging (MRI) revealed that dimensions of the sella were smaller than normal dimensions. Other abnormalities, including hypoplastic adenohypophysis, transected stalk, ectopic neurohypophysis, milimetric neurohypophysial tissue inferior to stalk were also observed on MRI (Figure 1).

The patient had no clinical or laboratory findings suggesting a pathology associated with neurohypophysis. As a result of the dynamic tests, the patient was diagnosed with panhypopituitarism; and a replacement therapy was initiated with prednisolone 2.5 mg, L-thyroxine 25 µg and estrogen/progesterone.

Case 2

A 19-year-old female patient had been diagnosed with GH deficiency and hypothyroidism at another health center that she applied four and a half years ago due to growth retardation. The patient was the product of an uncomplicated full-term pregnancy with normal vaginal delivery. Treatment with GH and L-thyroxine resulted in a height gain of 13 cm in four years. GH treatment was ceased 6 months ago as no further height gain was observed. L-thyroxine treatment has been continued. The patient never had menstruation. There was no axillary and pubic hair growth and the patient had no breast development.

Her height and weight were 130 cm and 32 kg, respectively. Her laboratory findings were as follows: chromosome analyses: 46XX, bone age: 13 years. Pituitary MR revealed pituitary gland measuring 8x8x3 mm (APXMLXKK), sella and pituitary gland smaller than normal, neurohypophysis was not present in its regular anatomic localization and placed ectopically (Figure 2). Pelvic MR showed a hypoplastic uterus measuring 2x1 cm.

Baseline hormonal values were found to be as follows: Free T3: 2.3 pg/mL, free T4: 1.13 ng/dL, TSH: 2.01 µIU/mL, IGF-1: 2.40 ng/mL (232-385), Prolactin: 6 ng/mL, FSH: 0.386 µIU/mL, LH: 0.1 µIU/mL, E2: 5 pg/mL, Cortisol: 8.7 µg/dL SST, ITT and LH-RH stimulation tests were performed in order to evaluate pituitary functions (Table 1). Cortisol and GH responses were evaluated using ITT. While there was sufficient response to SST, there was no cortisol response to ITT.

Functions of the neurohypophysis were observed to be normal. The patient was diagnosed as having panhypopituitarism and a treatment protocol including prednisolone 2.5 mg, estrogen/progesterone, and GH was administered and continued with L-thyroxine.

Discussion

Pituitary gland develops as a result of a fusion of the adenohypophysis, which is of ectodermal origin, and neurohypophysis, which is of neuroectodermal origin, during embryonic period (1). Hypoplastic pituitary gland is defined as crescentic glandular tissue seen at the floor of the sella, with a maximum measurable height of 2 mm (6). Impaired downward migration of neurohypophysis as a result of genetic defect, stalk

Table 1. Insulin tolerance test (ITT), thyrotropin releasing hormone (TRH), luteinizing hormone (LH)-releasing hormone (LH-RH) and Short synacthen test (SST) results

		Normal	0 min.	30 min.	60 min.	90 min.	120 min.
Case 1	(SST) Cortisol (µg/dL)	8-25	3.38	13.85	18.33	21.45	23.07
	(ITT) Cortisol (µg/dL)	8-25	2.94	11.26	12.95	9.32	6.71
	Blood glucose (mg/dL)	70-100	31	42	55	66	77
	GH (ng/mL)		<0.02	<0.02	<0.02	<0.02	<0.02
	TSH (µIU/mL)	0.5-4.4	1.16	10.22	19.55	19.63	17.30
	PRL (ng/mL)	4.4-15.2	5.52	13.13	10.54	8.51	7.61
	FSH (µIU/mL)	1.5-12.4	0.66	1.21	1.42	1.44	1.42
	LH (µIU/mL)	1.7-8.6	0.1	0.1	0.1	0.1	0.1
Case 2	(SST) Cortisol (µg/dL)	8-25	9.01	16.66	22.99	24.98	26.55
	(ITT) Cortisol (µg/dL)	8-25	3.37	10.25	7.84	5.40	4.57
	Blood glucose (mg/dL)	70-100	31	27	12	47	62
	GH (ng/mL)		0.25	0.19	0.13	0.23	0.31
	FSH (µIU/mL)	1.5-12.4	0.26	0.43	0.52	0.55	0.57
	LH (µIU/mL)	1.7-8.6	0.1	0.1	0.1	0.1	0.1

injury and perinatal trauma may cause fusion defects. In such patients, pituitary deficiency can be observed, as hormones creating stimulant effects of hypothalamus cannot reach the pituitary gland (7). Mutations in transcription factors responsible for pituitary ontogenesis such as HESX1, LHX3, LHX4, PITX2, POU1F1, PROP1, and SIX6 have been shown in those having congenital pituitary deficiency. Other than the above mentioned factors, a new mutation, namely OTX2 mutation, has been identified in a case having ectopic neurohypophysis, hypoplastic adenohypophysis and panhypopituitarism (8). Transection of the pituitary stalk can occur during an abnormal delivery. The fixed head of the fetus and breech presentation due to small maternal pelvis induce traction and transection of the pituitary stalk, but rarely brain trauma which may be caused by major events such as traffic accident (9). Some of the patients present with growth retardation due to hypothalamic and pituitary deficiency, others are diagnosed with acute adrenal deficiency (10,11). This syndrome is the most commonly diagnosed in childhood, whereas some of the patients are diagnosed in adulthood (12). Our cases presented with growth retardation and primary amenorrhea in adulthood. Isolated GH deficiency or multiple pituitary hormone deficiency may be present in pituitary stalk transection syndrome (2). The first one of our cases had low free T4 and normal TSH levels along with response to TRH test. There is one case report similar to ours in the literature (11). The patient had low free T4 and normal TSH levels along with the response to TRH test. It has been suggested that TRH stimulation test has a low sensitivity to be used in routine clinical practice. There may be considerable overlap between the basal TSH level of normal and patients with central hypothyroidism. The important principle to remember is that in the presence of

low free T4 or T3 levels in the circulation, the demonstration of even a normal basal TSH concentration in plasma is suggestive of TSH deficiency. Circulating TSH has multiple molecular forms or isoforms due to variations in the oligosaccharide structures. Due to the immunoreactive, but less bioactive TSH, patients with transection of the pituitary stalk may mimic normal thyroid axis albeit with secondary hypothyroidism. In addition, low levels of cortisol as well as decreased GH secretion could contribute to further increase in TSH release in these patients. There is no "gold standard" range of TSH values to develop for TRH stimulation test, but there is an immediate release of TSH rising to peak levels approximately 20-30 min after TRH injection, usually reaching values 5-10 fold higher than the basal value (13). The classic response of hypothyroid patients with intrinsic pituitary disease is a flat or suboptimal rise following TRH. The classic response of the hypothalamic variety of hypothyroidism is a normal but slightly delayed (60 min peak) TSH response following TRH. One factor that is recognized as an important determinant of the TSH response to TRH is the GH secretory status of the patient. Cobb and coworkers have reported that children with GH failure often demonstrated TSH responses to TRH that were greater than normal, and often prolonged (14).

Pituitary stalk transection syndrome is characterized by, initially, short stature due to GH deficiency, later, sequential insufficiency of several other pituitary hormones, and finally, ACTH deficiency in adulthood (10). Our cases were diagnosed with panhypopituitarism by dynamic tests in adulthood and replacement therapy was initiated. Case 2 was initially diagnosed with GH deficiency and hypothyroidism. Hypogonadism and secondary adrenal deficiency were diagnosed six year later.

Ectopic neurohypophysis is a condition where "bright spot" that has to be located in the posterior pituitary site of the sella is located at another site. In our cases, neurohypophyseal tissue was not located at the expected anatomical site. Moreover, along with absence of the stalk, the adenohypophyseal tissue was hypoplastic. It has been observed that most patients with ectopic neurohypophysis had no diabetes insipidus (4). In our cases, diabetes insipidus has not occurred in the presence of ectopic pituitary at the floor of the third ventricle, because vasopressin secretion was preserved from the transected part of the stalk. On the other hand, patients without a pseudo-posterior lobe often develop diabetes insipidus due to autolysis of vasopressin-producing cells (15).

Pituitary MR revealed no pituitary stalk in our patient and the neurohypophysis was ectopic. Through a progression from idiopathic GH deficiency to multiple hypophyseal hormone deficiency, the stalk becomes thinner, and this shift can be observed in post-contrast MR images. Partial preservation of the hypothalamo-hypophyseal portal vessels presents with an enhancing stalk, or a progressive disease presents with a non-visual stalk (16). History of the patient included pituitary deficiency. Dynamic tests were performed and replacement therapy was initiated after the patient had been diagnosed with panhypopituitarism. MR findings and the results of the tests suggested ectopic posterior pituitary gland and concomitant panhypopituitarism in our cases

Conflicts of Interest

There are no conflicts of interest.

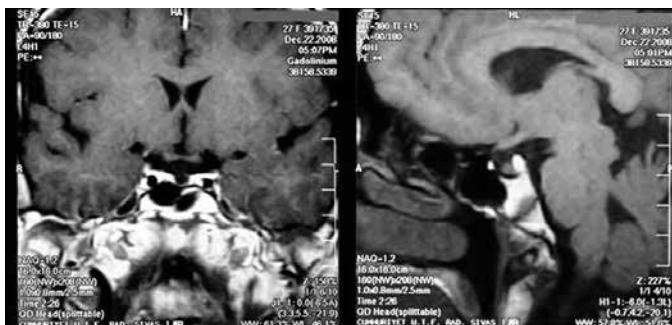


Figure 1. Hypoplastic adenohypophysis, transected stalk, ectopic neurohypophysis, image of a millimetric neurohypophyseal tissue inferior to stalk (case 1)

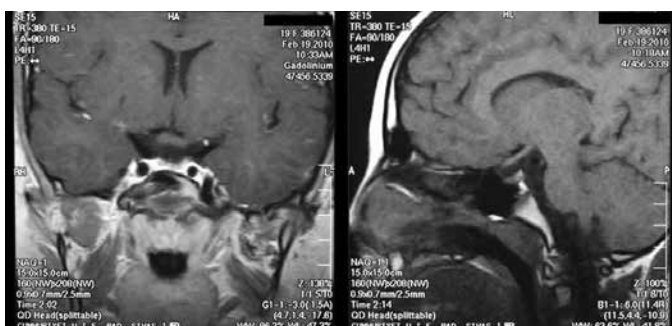


Figure 2. Hypoplastic adenohypophysis, transected stalk, ectopic neurohypophysis, image of a millimetric neurohypophyseal tissue inferior to stalk (case 2)

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