Fanconi syndrome in an individual with hypopituitarism

Fankoni sendromu ve hipopituitarizm birlikteliği

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Abstract
Hypopituitarism is defined as partial or complete insufficiency of pituitary hormone secretion. The clinical manifestations of hypopituitarism are variable, often insidious in onset and dependent on the degree of hormone deficiency. In a patient with hypopituitarism we first identified Fanconi syndrome, a generalized tubular dysfunction. The interesting point of this case was various electrolyte imbalances. The diagnosis of hypopituitarism, and Fanconi syndrome was based on these abnormalities. Clinical improvement was obtained by prednisolone, thyroxine, calcitriol, and calcium supplements. In conclusion, in the existence of various electrolyte imbalances, hypopituitarism and Fanconi syndrome coincidence should be taken into consideration.
Key words: Fanconi syndrome, hypopituitarism, electrolyte imbalance

Özet
Hipopituitarizm hipofiz hormonlarının bir kısmının veya hepsinin sekresyonundaki yetersizlik olarak tanımlanmaktadır. Hipopituitarizm klinik görünümü hormon eksikliğinin derecesine bağlı olarak değişkendir ve sıklıkla sinsi olarak başlar. İlk kez hipopituitarizmli bir olguda yaygın tübüler fonksiyon bozukluğuna yol açan Fankoni sendromunun birlikteliğini gösterdik. Bu olgunun ilginç yönü çok farklı elektrolit bozukluğunun bir arada bulunmasıydı. Hipopituitarizm ve Fankoni sendromu tanıları bu bozukluklardan yola çıkılarak konuldu. Tedavide prednizolon, tiroksin, kalsitriol ve kalsiyum verilmesi ile klinik düzelme sağlandı. Sonuç olarak, birçok elektrolit bozukluğunun bir arada olduğu olgularda hipopituitarizm ve Fankoni sendromu birlikteliğinin olabileceği göz önünde tutulmalıdır.
Anahtar kelimeler: Fankoni sendromu, hipopituitarizm, elektrolit bozukluğu

Introduction

Hypopituitarism is a rare entity and the clinical features can be variable due to age, gender, rapidity of onset, and the pattern of pituitary hormone deficiencies. Clinical manifestations may be non-specific such as fatigue, anorexia, weakness, hypotension, cold intolerance due to adrenal, and thyroid deficiencies, or more indicative such as growth retardation, impotence and infertility due to growth hormone, and gonadotropine deficiencies. (1-4).

Dysfunction of the proximal tubule may be seen as an isolated defect, presented by bicarbonaturia; but is more commonly associated with generalized proximal tubular dysfunction called the Fanconi syndrome. In addition to bicarbonaturia, this syndrome may be associated with the one or more of the following: phosphaturia, aminoaciduria, glucosuria, uricosuria, and tubular proteinuria (5,6).

Here, we presented a case with hypopituitarism and Fanconi syndrome, this coincidence has not been reported yet in the English literature. The features of two rare clinical states can cause various biochemical abnormalities. The present of two entities in a case may cause difficulties in the diagnosis.

Case report

A 74-year old female was admitted to our clinic with fatigue, weakness, anorexia, lethargy, and headache. She had a history of hypertension, and dyspepsia. She had been using metoprolol 50 mg/day, valsartan 160 mg/day and hydrochlorthiazid 12,5 mg/day combination, acetylsalicylic acid 100 mg/day, trimetazidine HCl 60 mg/day, and hydrotalcite 1000 mg/day. White blood cell count was 4200, hemoglobulin was 11.5 g/dl and platelet count was 252000. Biochemistry results showed hyponatremia, hypokalemia, hypocalcemia with normal serum albumin level and hypophosphatemia. These results are

shown in Table 1. Serum parathyroid hormone level was high. Renal function was preserved; serum urea and creatinine levels were normal. Arterial blood pressures were 110/60 mmHg and there was no edema or dehydration in physical examination. Additional tests were performed to investigate the biochemical abnormalities. Free $T_{3,}$ free $T_{4,}$ and TSH levels were consisted with central hypothyroidism. Other pituitary hormone levels were found low (Table 1). Cortisol response to ACTH stimulation test was insufficient (cortisol levels were 1.49 µg/dl at the beginning, 9.1 µg/dl at 30. minutes, 10.6 µg/dl at 60. minutes, 12.5 µg/dl at 90. minutes, and 12.7 µg/dl at second hours). Anti-nuclear antibody was negative.

Hyperphosphaturia was detected in both spot and 24 hours urine samples. The daily urine excretion of calcium was low (Table 1). At the same time serum bicarbonate level was low and urine pH level was normal (Serum bicarbonate level was 19 mmol/L, arterial and urine pH were 7.37 and 7 respectively). There were no proteinuria and glucosuria with dipstick analyses of urine. Bence Jones proteinuria was negative. Among Fanconi syndrome diagnosis criteria, patient had hyperphosphaturia and bicarbonaturia. This relation was sufficient to put diagnosis.

The evaluation of hypothalamic-pituitary region by pituitary magnetic resonance imaging (MRI) revealed partial empty sella (Figure 1)

These biochemical abnormalities considered as panhypopituitarism and Fanconi syndrome might be co-incidence in this patient. The patient was treated by prednisolone, thyroxine, calcitriol and calcium supplements. After one month of the treatment, the levels of serum sodium, phosphate, potassium and calcium were in normal range.

Discussion

The term hypopituitarism describes the deficiency of one or more of the hormone deficiencies of pituitary gland. The clinical manifestations of hypopituitarism are variable, often insidious in onset and dependent on the degree of hormone deficiencies. Several biochemical abnormalities can be detected especially with the lack of ACTH and TSH (1-3).

Furthermore Fanconi syndrome, the generalized dysfunction of proximal tubule, can be the cause of several biochemical abnormalities. Acquired Fanconi syndrome can be related with intrinsic renal diseases (acute tubular necrosis, multiple myeloma, Sjogren's syndrome, transplant rejection), pharmaceuticals (cisplatin, ifosfamide, gentamicin, valporic acid, 6- mercaptopurine), other exogenous toxins (glue sniffing, heavy metals [mercury, lead, cadmium, uranium], maleic acid) and nutritional insufficiency (i.e. Kwashiorkor) (7). Our patient was so elderly to have congenital Fanconi syndrome. Even if we could not detect an acquired reason for this syndrome, we accepted her to have Fanconi syndrome due to unidentified acquired reason.

Deficiency of ACTH, the most serious form of anterior pituitary hormone deficits, results in secondary hypoadrenalism and AVP (Arginin vasopessin) increase, and therefore may cause hyponatremia. We suspected cortisol deficiency in this patient because of the clinical and biochemical findings such as hyponatremia, lethargy and fatigue. After biochemical analysis and ACTH stimulation test, deficiency of all anterior pituitary hormones was determined.

Nutritional inadequate due to anorexia and the treatment of hydrochlorothiazide can explaine hypokalemia in this patient. On the other hand hypopituitarism did not explain the hypophosphatemia and hyperphosphaturia. Detection of low plasma bicarbonate level with normal pH urine showed the tubular dysfunction. There were not any intrinsic renal diseases and history of drug use or being exposed to exogenous toxins which associated with tubular dysfunction as a reason of Fanconi syndrome in our patient. The mechanism of the improvement of Fanconi syndrome related abnormalities by the hypopituitarism treatment could not be explained.

In conclusion, although hypopituitarism and Fanconi syndrome are rare entities, various electrolyte imbalances in a patient should consider this coincidence.

Table 1. Biochemical and hormonal parameters of the case

Parameters	Levels of the case	Normal range
Serum sodium (mEq/L)	113	135-150
Serum potassium (mEq/L)	2,4	3,5-5,1
Serum calcium (mg/dL)	7,4	8,5-10,5
Serum phosphate (mg/dL)	1,6	2,7-4,5
Serum urea (mg/dL)	19,9	10-50
Serum creatinine (mg/dL)	0,6	0,2-1,2
Serum albumin (mg/dL)	4,1	3,5-5,0
Serum bicarbonate (mmol/L)	19	22-28
Urine calcium (mg/24h)	32	100-300
Urine phosphate (mg/24h)	644	< 100
TSH (µIU/mL)	0,85	0,27-4,20
Free T3 (pg/ mL)	0,999	1,82-4,62
Free T4 (ng/dL)	0,169	0,93-1,71
ACTH (pg/mL)	6,71	10-48
Cortisol (µg/dL)	3,54	10-23
GH (ng/mL)	<0,05	0,6-8,6
Prolactin (ng/mL)	0,095	3,4-24,1
LH (mIU/mL)	0,91	7,7-58,5
FSH (mIU/mL)	3,55	25,8-134,8
Estradiol (pg/mL)	10,6	<130
PTH (pg/mL)	437,3	15-65

TSH: thyroid stimulating hormone, T3: triiodothyronine, T4: thyroxine, ACTH: adrenocorticotropic hormone, GH: growth hormone, LH: luteinizing hormone, FSH: follicle-stimulating hormone, PTH: parathyroid hormone

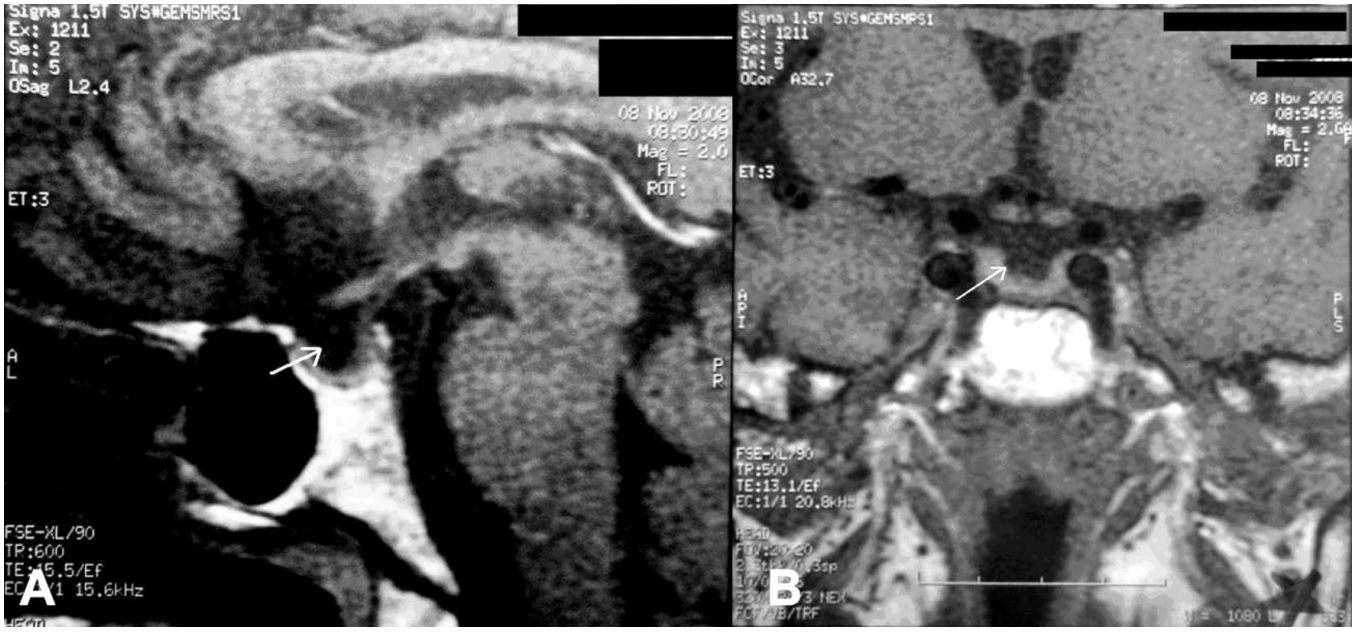

Figure 1. *Coronal (A) and Axial (B) MRI pictures of the patient with partial empty sella.*

Yazarlarla ilgili bildirilmesi gereken konular (Conflict of interest statement) : Yok (None)

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