



A case of posttraumatic acth deficiency that initial skin finding suggesting cushing syndrome

Başlangıç cilt bulguları cushing sendromunu düşündüren postravmatik ACTH eksikliği olgusu

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Abstract

Pituitary adrenocorticotrophic hormone (ACTH) deficiency is one cause of secondary adrenal insufficiency. Genetic factors, autoimmunity, infiltrative disease, cranial trauma may cause ACTH deficiency. Hyperpigmented skin lesions are expected in primary adrenal insufficiency while they are very rare in secondary adrenal insufficiency. Striae are characterized by linear smooth bands of atrophic appearing skin and pathogenesis is not understood. They are mostly associated with obesity, pregnancy, hypercortisolism. Striae are not an expected finding in hypocortisolemia. We presented a 34-year-old male patient that evaluated for striae on both axillas. He had head trauma and operation 12 years ago. Basal hypophysis hormone levels and dynamic tests were conducted. Basal cortisol and ACTH level were 0,18 ug/dl and <1,6 pg/ml, respectively. Adrenal gland had a suboptimal cortisol response in ACTH stimulation test. Conclusively, we diagnosed and followed a case of posttraumatic ACTH deficiency with hypocortisolemia that investigated with suspect of Cushing Syndrome due to striae on his skin

Keywords: Striae; Cushing Syndrome; Posttraumatic Acth Deficiency.

Öz

Hipofizer adrenokortikotropik hormon (ACTH) eksikliği sekonder adrenal yetmezlik nedenlerinden birisidir. Genetik nedenler, otoimmünite, infiltratif hastalıklar, kafa travmaları ACTH yetmezliğine neden olabilmektedir. Primer adrenal yetmezlikte hiperpigmente deri lezyonları beklenirken, sekonder adrenal yetmezlikte çok nadirdir. Strialar derinin gerilimine dik olarak yerleşmiş atrofik bandlardır ve patogenezi tam olarak açıklanmamıştır. Çoğunlukla obezite, gebelik, hiperkortizolizm ile ilişkilidir. Hipokortizolemide stria beklenen bir bulgu değildir. Bu yazımızda, her iki koltuktaki striaları nedeniyle değerlendirdiğimiz 34 yaşındaki erkek olguyu sunduk. Olgunun öyküsünde 12 yıl önce geçirdiği kafa travması ve ameliyat öyküsü mevcuttu. Bazal kortizol ve ACTH düzeyleri sırasıyla 0,18 ug/dl and <1,6 pg/ml idi. ACTH uyarı testinde, adrenal bezin kortizol cevabı suboptimaldi. Sonuç olarak, striaları nedeniyle Cushing Sendromu düşünerek araştırdığımız olguya, postravmatik ACTH yetmezliğine bağlı hipokortizolemi tanısı koyduk ve takibe aldık.

Anahtar Kelimeler: Stria; Cushing Sendromu; Postravmatik Acth Eksikliği.

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INTRODUCTION

Secondary adrenal insufficiency is defined as insufficient cortisol production in adrenal glands due to pituitary adrenocorticotropic hormone (ACTH) deficiency. ACTH deficiency is observed either in isolation or together with other pituitary hormone deficiencies. Autoimmunity, genetic factors, infiltrative diseases, infectious causes, metastases, pituitary destruction or traumatic brain injury due to any other reason are among the pathogenetic factors. The most distinctive difference between primary and secondary adrenal insufficiency is that hyperpigmentation occurs due to high ACTH levels in primary adrenal insufficiency, while no pigmentation is observed in the skin lesions that occur in ACTH deficiency (1).

Striae are atrophic band shaped lesions located vertically across the spread of the skin. They are scars that occur as a result of dermal connective tissue injury where newly formed collagen is formed in response to the local stress force on the skin. While its pathogenesis is not thoroughly defined, mechanical, hormonal, and genetic factors are known to play a role. The lesions are initially pink-red; then transform into grey-white color. Striae are known to be more prevalent among obesity, pregnancy, rapid weight change, and hypercortisolism/Cushing Syndrome (2-4).

In this paper, we presented a case that admitted to the dermatology with red-purple colored striae in the axilla. He was referred to the endocrinology department and was evaluated with a prediagnosis of hypercortisolism/Cushing Syndrome. After examinations, he was diagnosed with subclinical hypocortisolism associated with posttraumatic ACTH deficiency.

CASE REPORT

A 34-year-old male patient, referred to the endocrinology clinic for the evaluation of red-purple colored striae on both axilla. His medical history revealed skin lesions appeared approximately 4 months ago and spread over time, and occurred also on his abdomen. He has any chronic disease or drug therapy; but had cranial operation two times 12 years ago due to a head trauma, and an arterial embolization due to internal carotid artery aneurysm a year later.

On his physical examination, blood pressure was 120/80 mmHg; pulse was rhythmic and 75 beats/min; body temperature was 36.8°C; and body mass index was 21 kg/m². There were numerous red-purple colored striae on both axillas, which were parallel to one another and were 10-15 cm in length (Figure 1).

Additionally, there were a few striae on his abdomen, which were light pink in color and not as apparent as those on the axilla. Hematologic, biochemical, and hormonal tests were conducted on the blood samples. Hematologic and biochemical values are normal range. Basal hormone levels are presented in Table 1.



Picture 1. The appearance of striae in patient.

Table 1. Baseline hormone levels of patient.

Hormone (normal range)	Patient
TSH (0,34 - 5,86 uIU/ml)	0,83
Free T ₃ (2,5 - 3,9 pg/ml)	3,41
Free T ₄ (0,61 - 1,12 ng/dl)	0,67
FSH (1,2 - 19,1 mIU/ml)	3,08
LH (1,24 - 8,6 mIU/ml)	1,97
IGF-1 (135 - 449 ng/ml)	332,7
GH (0,003-0,971 ng/ml)	0,40
Prolactin (2-15 ng/ml)	14
ACTH (4,5 - 48 pg/ml)	<1,6 / <1,6
Cortisol (6,7 - 22,6 ug/dl)	0,18 / 0,17

Due to his medical history and basal hormone levels, dynamic tests of hypophyseal hormones [ACTH, thyrotropin releasing hormone (TRH) and luteinizing hormone releasing hormone (LH-RH) stimulation tests] were conducted. Basal TSH level is 2.86 uIU/mL, max: 10.43 uIU/mL in TRH stimulation test and basal LH level is 3.25 mIU/mL, max: 12.30 mIU/mL in LH-RH stimulation tests. However, in the standard ACTH stimulation test, adrenal gland could have a suboptimal cortisol response (basal: 0.22 ug/dL; max: 8.30 ug/dL). Insulin tolerance test, the golden standard in assessing hypophyseal-adrenal axis, was planned in order to investigate cortisol and growth hormone insufficiency. However, it could not be performed due to significantly low levels of basal cortisol, suboptimal cortisol response to the stimulation test, and lack of patient's consent.

Adrenal, pituitary, and cranial magnetic resonance (MR) of the case were obtained. There were no abnormalities on the adrenal gland MR. Pituitary size and signal intensity in neurohypophysis were considered normal. In his history of intracranial operations, blocked left internal carotid artery, chronic infarct related cystic encephalomalacic cavity in a very large area in the frontotemporoparietal region, and ischemic-gliotic lesions were observed.

In his evaluation by the neurology and neurosurgery departments, the current lesions were reported to be chronic alterations associated with previous head trauma and past operations; and no additional treatment was recommended. Striae were recommended to be re-evaluated by the dermatology department and were suspected to be idiopathic / physiologic, and cosmetic treatment recommendations were made.

Based on the laboratory and MR examinations, the case was considered a posttraumatic ACTH deficiency case that developed as a result of head trauma and intracranial operations. Due to the suboptimal cortisol response to the standard ACTH test, hydrocortisone treatment at a dose 10 mg /day was started and the case was follow-up. Additionally, he was informed about symptoms of possible cortisol insufficiency in case of stressful conditions and infectious diseases and what he should do if such conditions were to occur.

DISCUSSION

ACTH deficiency is a cause of secondary adrenal insufficiency characterized by lack or deficiency of cortisol production in adrenal glands. Cases of secondary adrenal insufficiency present with nonspecific complaints such as weakness, fatigue, loss of appetite, myalgia and hypoglycemia. Since mineralocorticoid deficiency does not occur, electrolyte imbalance symptoms are rarely observed. History of head trauma is one of the significant factors in the etiology of ACTH deficiency. Possible pathophysiologic mechanisms involved are direct injury by the trauma; increased intracranial pressure due to edema or hematoma; reduced cerebral perfusion pressure; or injury of the stalk or hypothalamus that can occur during the surgical intervention (1, 5).

Past cohort studies reported a prevalence of 15-90% for hypophyseal insufficiency following a traumatic brain damage. The vastly wide range of prevalence is interpreted to be because the pituitary hormone insufficiencies remain unnoticed at early stages after a head trauma; it depends on the intensity and type of the trauma; it is difficult to predict when the insufficiency will appear; and different dynamic tests and different criteria are used for the diagnosis at different centers.

While isolated or multiple pituitary hormone deficiency are observed due to traumatic brain damage, the most commonly reported hormone deficiency are those of growth hormone and gonadotropin. Though acute pituitary insufficiencies are reported more frequently following traumatic brain damage, medical literature also includes case reports of pituitary insufficiencies diagnosed years after the damage (6, 7). Saito et al. reported a case they diagnosed with posttraumatic hypothalamic hypopituitarism that presented 31 years after a traumatic brain damage, in a hypoglycemic coma and also had symptoms such as atrophic testes and alopecia (8). Karavitaki et al. also reported a case diagnosed with ACTH deficiency 9 months after brain damage (9).

Kokshoorn et al. from the Netherlands evaluated findings on 112 cases followed at least for a year after a head traumatic causing brain damage. The study was conducted at five different centers and the age of the cases ranged between 18-70 years. All patients underwent basal cortisol and ACTH measurements in the morning and were administered standard ACTH test. For the hypothalamus-pituitary-adrenal axis evaluation,

90 cases were administered insulin tolerance test and two cases were administered CRH test. Hypopituitarism was detected in 6 (5.4%) of the cases. There were two cases with adrenal deficiency, three cases with severe growth hormone insufficiency, and one case with hypogonadism (10). In another multi-center study, where 100 patients were evaluated to investigate the association of traumatic brain damage and subarachnoid hematoma with hypopituitarism, hypopituitarism symptoms were observed in 35% of the patients with traumatic brain damage, and in 37.5% of the patients with subarachnoid hematoma. ACTH deficiency was observed in 1% of these patients (11). In a review of literature on traumatic brain damage and pituitary hormone deficiency by Tanriverdi and Kelestimur in Turkey, it was reported that chronic pituitary insufficiency developed in about 15-20% of the cases with traumatic brain damage. While it is suggested in the review that more cases were affected with brain damage in the real life than actually detected, they also emphasized that epidemiologic studies on this matter are not sufficient. It was reported that isolated hormone deficiency were observed more frequently than multiple hormone deficiency following a traumatic brain damage, and that growth hormone was the more frequently affected hormone. In posttraumatic acute period of 1-4 days, cortisol, TSH and free T₄ measurements to evaluate ACTH deficiency, and repeat dynamic tests in addition to basal hormone measurements for ACTH and growth hormone deficiency on months 6 and 12 in the follow-up period were recommended. It was emphasized that hormonal follow-up of the cases should be re-evaluate every 5 years and the tests should be repeated at any time in case of a clinically suspicious condition (12).

In a case with ACTH in deficiency suspicion, it is necessary to firstly investigate the basal ACTH and cortisol levels, and then to conduct the ACTH stimulation test to evaluate if the cortisol level is low (1). On the other hand, insulin tolerance test is the golden standard for hypothalamus-pituitary-adrenal axis evaluation. This test can be administered to selected cases that can tolerate the possible severe hypoglycemia risk. We did not administer insulin tolerance test in the case. However, repeated measurements revealed that basal cortisol and ACTH values of the case were significantly low and no adrenal cortisol hormone response to ACTH stimulation was expected.

Pituitary imaging is necessary to demonstrate the possible lesions in pituitary hormone insufficiencies. While a normal pituitary form is expected in idiopathic ACTH deficiency, impaired anatomic structure findings are observed in secondary ACTH deficiency (5). No congenital abnormality or mass that could lead to ACTH deficiency was observed in MR of our case; while the defects seen on the images were considered to be associated with prior intracranial procedures he had undergone.

Striae are atrophic linear bands that form as a reaction to local stress on the dermal damage areas. They are more prevalent among females than males. Dermal

edema and some inflammatory transformations accompanied by perivascular lymphocytic infiltration may take place during the early phases of its development. Subsequently, epidermal atrophy and rete ridge loss develop and hair follicles and other appendages disappear (4).

In association with the influence of hormones such as estrogen and relaxin, striae are observed in 90% of the pregnant women. It has also been associated with Cushing disease, Marfan Syndrome, and exogenous steroid use (13). Physiologically, it can also be caused by rapid weight changes. Moreover, striae may develop secondary to topical steroid use. The striae observed on pregnant women and cases with endogenous hypercortisolism are darker than striae observed among obese people. While striae are localized predominantly around breasts, arms, thighs, abdomen, and lumbosacral region, they can also be seen in the face and flexor areas of cases with Cushing Syndrome and exogenous steroid use (4). Edematous striae are very rare and often occur as side effects of systemic glucocorticoid use.

In conclusion, striae are dermal lesions the physiopathology of which is not entirely elucidated, but the underlying cause should to be investigated when observed. Possible hypercortisolism /Cushing Syndrome should be excluded in these cases. The diagnosis of the case presented was initially investigated for suspected hypercortisolemia; but was found out to be a subclinical cortisol insufficiency associated with ACTH deficiency that developed secondary to prior traumatic brain damage. To our knowledge, cortisol insufficiency does not play a role in the development of striae, and coming across such an unexpected diagnosis in this case was an interesting experience for us. We decided to present this case in order to emphasize that ACTH deficiency may present with different clinical findings and these patients should be followed up for a long period of time following head trauma for possible pituitary hormone insufficiency.

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