A Case of Post-traumatic ACTH Deficiency Followed by Cushing Syndrome Prediagnosis

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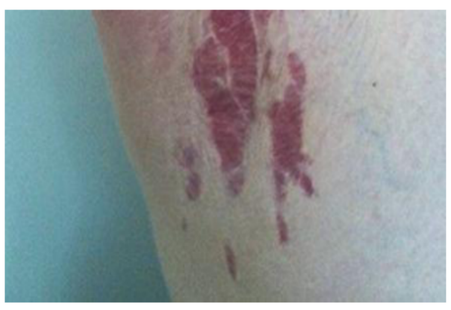
OBJECTIVES

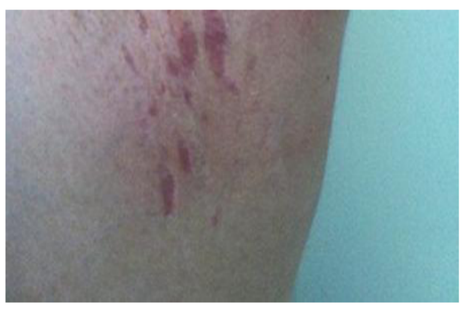
Secondary adrenal insufficiency is defined as insufficient cortisol production in adrenal glands due to pituitary adrenocorticotropic hormone (ACTH) deficiency. ACTH deficiency is observed either in isolation or together with other pituitary hormone deficiencies. Autoimmunity, genetic factors, infiltrative 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). Striaes 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

METHODS

A 34-year-old male patient, referred to the endocrinology clinic for the evaluation of red-purple colored striae on both armpits. His medical history that the 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 twice 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 36.8ºC; and body mass index was 21 kg/m^2. There were numerous red-purple colored striae on both armpits, 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 armpits.
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. 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 encephalomalasic 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.

Graphs and tables





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

RESULTS

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).

CONCLUSIONS

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 hypercortisolemi/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 observations and that patients should be followed up for a long period of time following head trauma for possible pituitary hormone insufficiency.

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