Turk Toraks Derg 2013; 14: 158-60 DOI: 10.5152/ttd.2013.40

CASE REPORT / OLGU SUNUMU

A Case of Panhypopituitarism with an Addisonian Crisis Activated by Rifampicin

Rifampisin Tedavisinin Aktive Ettiği Addison Krizi Olan Panhipopituitarizm Olgusu

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Abstract

Addisonian crisis is an acute and life-threatening complication of adrenal failure. A 44-years old female case presented with Addisonian crisis following a two-week anti tuberculosis treatment because of tuberculosis lymphadenitis. Panhypopituitarism was detected at investigations for aetiology. Acceleration of cortisol metabolism by rifampicin treatment was blamed for the Addisonian crisis.

KEY WORDS: Rifampicin, Addisonian crisis, tuberculosis

Özet

Addison krizi, adrenal yetmezliğin akut gelişen hayatı tehdit eden bir komplikasyonudur. Kırk dört yaşında kadın olgu, tüberküloz lenfadenit tanısı ile başlanılan anti-tüberküloz tedaviden iki hafta sonra addison krizi ile başvurmuştur. Etyolojiye yönelik yapılan incelemelerde panhipopituitarizm saptanmıştır. Addison krizi nedeni olarak rifampisin tedavisinin kortizol metabolizmasını hızlandırması sorumlu tulumuştur.

ANAHTAR SÖZCÜKLER: Rifampisin, Addison krizi, tüberküloz

Received/Geliş Tarihi: *09.01.2013* ***Accepted/Kabul Tarihi:*** *07.04.2013* ***Available Online Date/Çevrimiçi Yayın Tarihi:*** *14.06.2013*

INTRODUCTION

Rifampicin, which is used to treat tuberculosis, increases endogenous cortisol clearance in addition to its acceleration of the metabolism of many drugs in the liver. Therefore, it is known that rifampicin can cause Addisonian crises in patients with a limited adrenal reserve [1]. This paper presents a case of Addisonian crisis that developed after rifampicin treatment in a patient with undiagnosed secondary adrenal failure.

CASE REPORT

A 44-year-old female presented to the otorhynolaryngology clinic with a right upper cervical swelling for 2 months. Cervical ultrasonography showed conglomerated lymph nodes which have undistinguishable hili at the right cervical chain. The largest was 25x22 mm in size. Excisional biopsy from these lymph nodes was consistent with caseous granulomatous inflammation. This case report was written with the patient's consent.

The patient consulted the chest disease clinic after histopathological diagnosis but no pulmonary complaint was found in systemic investigation. Thorax computed tomography (CT) showed a few lymph nodes (calcified or not) in the thoracic compartment which were not pathological sizes in the mediastinal lymphatic compartment, significant volume loss in left upper lobe of lung, traction bronchiectasis, a 6 mm calcified nodule, cystic bronchiectasis and cavitations in the collapsed lung region (Figure 1). Upon microbiologic evaluation of the sputum, acid fast bacilli (AFB) gave negative results three times, sputum culture for tuberculosis was negative, and cutaneous purified protein derivative (PPD) test was 12 mm. In laboratory evaluations, the erythrocyte sedimentation rate (ESR) was 30 mm/hour, and haematogram and biochemistry results were normal. The standard anti-tuberculosis treatment including isoniazide (INH), rifampicin (RIF), pyrazinamide (PZN), and ethambutol (EMB) was started. Two weeks after initiation of the treatment, she presented to the emergency room with malaise, severe nausea and vomiting, and clouding of consciousness. On physical examination, her blood pressure was 80/50 mmHg, pulse was 120/minute, body temperature was 37.5°C, and skin and mucous membranes were dry and pale. Prerenal azotemia (BUN: 59, Cr: 2.0) and hyponatremia (Na: 115 mEq/L) were detected. Liver function tests were normal. Fluid and electrolytes were regulated in the intensive care unit. Renal function tests normalised during follow-up (urea: 24, creatinine: 1.0) but hyponatremia (Na: 108 mEq/L) persisted. Thyroid function tests were consistent with secondary hypothyroidism (free T3: 1.68 pg/mL, free T4:0.43 ng/dL and TSH: 1.95 mIU/mL), so other tests were performed to evaluate other anterior pituitary hormones. The results of the laboratory examination were as follows:

Na: 121 (135-150) mEq/L, K: 2.9 (3.5-5) mEq/L, Free T3: 1.6 (1.71-4.51) pg/mL, Free T4: 0.4 (0.7-1.48) ng/dL, TSH: 0.19 (0.35-4.94) µIU/mL, Cortisol 2 (5-25) µg/dL, Adrenocorticotropic hormone (ACTH): <5 (10-70) pg/mL.

This case is presented as an e-poster 34th National Congress of Respiratory TUSAD (6-10 October 2012 İzmir, Turkey).
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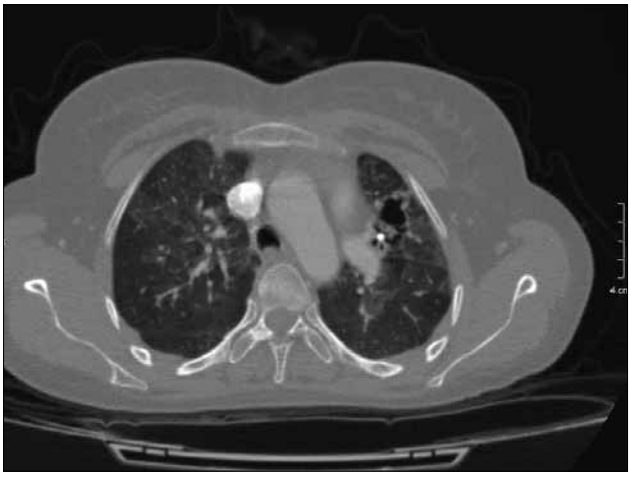

Figure 1. Thorax BT showed a few lymph nodes (calcified or not) at thoracic compartment which weren't at pathological sizes in mediastinal lymphatic compartment, significant volume loss in left upper lobe of lung, traction bronchiectases, a 6 mm calcified nodule, cystic bronchiectasis and cavitations in collapsed lung region

Follicle stimulating hormone (FSH), luteinising hormone (LH) and oestradiol (E2) were compatible with hypogonadotropic hypogonadism. FSH: 5 (21.7-153) mIU/mL, LH: 1.6 (11.3-50) mIU/mL, E2: 10 (12.5-166) pg/mL, prolactin: 20 (2.7-26) ng/mL without response after insulin hypoglycaemia. Hypogonadotropic hypogonadism and secondary adrenal failure were detected.

Steroid (methylprednisolone) and thyroid hormone replacements were added to the anti-tuberculosis treatment. The patient recovered and electrolytes were normalised during follow-up. Hypophysis magnetic resonance imaging (MRI) to determine the aetiology of pituitary failure revealed cerebrospinal fluid (CSF) herniation at the location of adenohypophysis and parenchyma of adenohypophysis had a linear pattern (Figure 2).

After a week of aetiological research, anti-tuberculosis treatment including rifampicin (10 mg/kg/day) with oral prednisolone (5 mg) and thyroid hormone (100 mg) was started. Liver function tests were normal at the time of Addisonian crisis, so that rifampicin was added to the anti-tuberculosis treatment. When rifampicin was re-administered, no symptoms of adrenal crisis were thereafter again observed. During the anti-tuberculosis treatment, corticosteroid replacement therapy was continued. Radiological and clinical improvement was observed in the patient after two months and anti-tuberculosis treatment was continued. including INH and RIF. There was no cervical lymphadenopathy upon physical examination. Also, weight gain and a decrease in ESR were seen. Anti-tuberculosis treatment was completed at sixth months due to resolution of symptoms and there has been no follow-up for the last six months.

DISCUSSION

Hypopituitarism (failure of the pituitary gland) is a clinical syndrome due to the insufficient production and release of one or more pituitary hormones. Deficiency of all pituitary hormones is known as panhypopituitarism. The mortality rate of patients with hypopituitarism is 1.2 to 2.2 times that of normal subjects. Hypopituitarism generally progresses slowly except in conditions like hypophysis apoplexy and Sheehan's

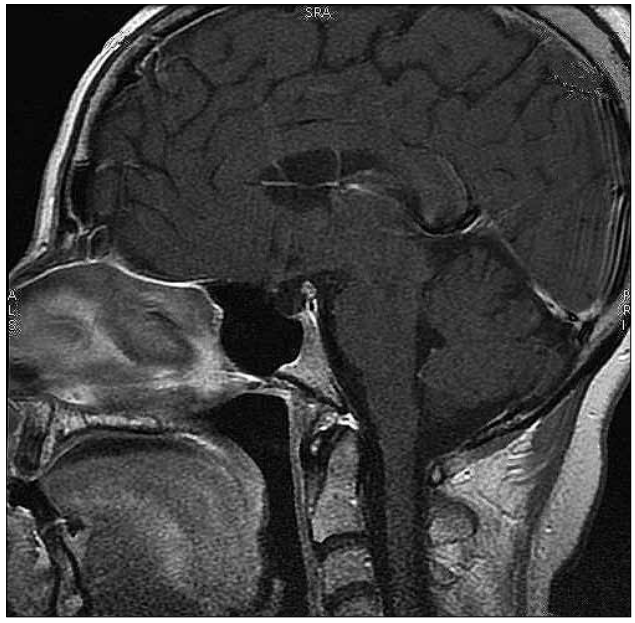

Figure 2. In MRI adenohypophysis had a linear pattern

syndrome. Subclinical forms may easily be overlooked. Diagnosis is made with the detection of low hormone levels both in the pituitary gland and in target organs [2].

Patients with secondary adrenal failure due to hypopituitarism have nonspecific symptoms such as chronic fatigue, malaise, anorexia, and weight loss. Nausea, vomiting, and abdominal pain may also be observed. Blood pressure is low in many patients but only postural hypotension may be detected in some.

Our patient had nonspecific complaints such as malaise and fatigue, which were thought to be associated with tuberculosis. However, nausea, vomiting, and hypotension developed after anti-tuberculosis treatment and laboratory evaluation revealed hyponatremia. Hormone levels were seen because of refractory hyponatremia and examination for anterior pituitary abnormality detected panhypopituitarism. In pituitary MRI, adenohypophysis was in a linear pattern.

Rifampicin is included in the standard anti-tuberculosis treatment regime. Rifampicin is known to induce liver enzymes and increase cortisol metabolism due to increased cytochrome p450 activity [1,3]. Our patient had secondary adrenal failure due to undiagnosed panhypopituitarism when anti-tuberculosis treatment was initiated, which presented as Addisonian crisis. In the literature, there are many similar reports of Addisonian crisis and Addison's disease induced by rifampicin treatment [4,5].

Addisonian crisis is the acute and life threatening complication of adrenal failure. It may develop in a patient with previous chronic adrenal failure or may be the presenting sign in a previously undiagnosed patient. Triggering factors may be infections, surgical procedures, cessation of glucocorticoid treatment, and not increasing glucocorticoid dose in the presence of stress factors. We believe that the factor that triggered the Addisonian crisis in our case was rifampicin treatment (which increases cortisol clearance) in the presence of secondary adrenal failure due to undiagnosed pituitary insufficiency.

Disseminated tuberculosis causing bilateral adrenal enlargement and Addison's disease has rarely been reported. Adrenal involvement is a rare manifestation of tuberculosis. The clinical picture clearly shows that 80-90% of the damage occurs within the bilateral adrenal cortex.

Tuberculosis may affect many of the endocrine glands, including the hypothalamus, pituitary and thyroid, but the most commonly involved endocrine organ is the adrenal gland [5,6]. However, in this case, tuberculosis was not disseminated and adenohypophysis was found in a linear pattern following pituitary MRI.

Our patient was followed in the intensive care unit after emergency room admission. Fluids and electrolytes were regulated and glucocorticoid treatment was initiated after samples had been taken. Because hormonal assessments were consistent with panhypopituitarism, levothyroxine was added to the treatment regime after glucocorticoid replacement. She recovered and nausea and vomiting disappeared at follow-up. Vital signs and serum sodium concentration were normalised. Maintenance treatment was planned and anti-tuberculosis treatment was continued. She was informed of the adrenal failure and its symptoms, and was recommended to carry an information card with her; follow-up visits were arranged, and the patient was discharged. We hope that our experience might help fellow physicians in their future diagnoses.

Conflict of Interest
No conflict of interest was declared by the authors.

Peer-review: Externally peer-reviewed.

Informed Consent: Written informed consent was obtained from patients who participated in this case.

Author Contributions
Concept - F.F.; Design - F.F., T.M.; Supervision - F.F.; Funding - F.F., T.M.; Materials - D.Ç., F.F., T.M.; Data Collection and/or Processing - F.F., T.M.; Analysis and/or Interpretation - F.F.; Literature Review - F.F.; Writer - F.F.; Critical Review - F.F.; Other - F.F.

Çıkar Çatışması
Yazarlar herhangi bir çıkar çatışması bildirmemişlerdir.

Hakem değerlendirmesi: Dış bağımsız.

Hasta Onamı: Yazılı hasta onamı bu olguya katılan hastalardan alınmıştır.

Yazar Katkıları
Fikir - F.F.; Tasarım - F.F., T.M.; Denetleme - F.F.; Kaynaklar - F.F., T.M.; Malzemeler - D.Ç., F.F., T.M.; Veri toplanması ve/veya işlemesi - F.F., T.M.; Analiz ve/veya yorum - F.F.; Literatür taraması - F.F.; Yazıyı yazan - F.F.; Eleştirel İnceleme - F.F.; Diğer - F.F.

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