Tertiary Adrenal Insufficiency in An Asthmatic Patient on Steroid Treatment

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SUMMARY

Steroid treatment in asthma patients leads to many side effects. Cushing Syndrome is more common than adrenal insufficiency as a side effect of systemic steroid treatment. We presented the case of tertiary adrenal insufficiency secondary to steroid treatment.

A 61 years old female asthmatic patient who had systemic and inhaler steroid treatment for approximately 30 years was admitted to the hospital with the symptoms of dyspnea, nausea and vomiting. The patient was very thin (43 kg) and had dark pigmented face and legs. Both plasma cortisole level (0.39 µg/dL) and ACTH level (< 5 pg/mL) were very low. A short synacthen stimulation test revealed a rising in basal cortisole levels.

Therapeutic glucocorticoid administration is the most common cause of adrenal insufficiency. Symptoms like nausea and vomiting can be misdiagnosed because of the adverse effects of drugs usually used in the treatment of asthma and adrenal insufficiency may not be diagnosed if it is not suspected.

KEY WORDS: Bronchiale asthma, steroid, adrenal insufficiency

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ÖZET

STEROİD TEDAVİSİ ALAN ASTIMLI BİR HASTADA TERSİYER ADRENAL YETMEZLİK

Astım hastalarındaki steroid tedavisi birçok yan etkiye sebep olur. Sistemik steroid tedavisinin yan etkisi olarak Cushing sendromu adrenal yetmezlikten daha sıktır. Yaklaşık 30 yıldır şiddetli astım nedeniyle oral ve inhaler glukokortikoid tedavi alan 61 yaşında bayan hasta bulantı ve kusma şikayetleri ile hastanemize başvurdu. Hasta kaşektik (43 kg) görünümdeydi. Yüzünde ve bacaklarında hiperpigmente cilt lezyonları vardı. Plazma kortizol düzeyi (0.39 µg/dL) ve ACTH (< 5 pg/mL) düzeyi normalden çok düşüktü. Kısa "synacthen" stimülasyon testi yapıldıktan sonra kortizol düzeyi artış gösterdi.

Tedavi amaçlı glukokortikoid verilmesi adrenal yetmezliğin en sık nedenlerinden biridir. Bulantı ve kusma gibi semptomlar yanlış tanı konulmasına neden olabilir; çünkü astım tedavisinde kullanılan ilaçlar sıklıkla benzer yan etkilere neden olur. Hastadan şüphelenilmezse adrenal yetmezlik tanısının konulamayacağını bilmek bu açıdan önemlidir.

ANAHTAR KELİMELER: Bronşiyal astım, steroid, adrenal yetmezlik

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INTRODUCTION

Tertiary adrenal insufficiency is the most common cause of adrenal insufficiency (1). The results of withdrawing long-term exogenous corticosteroids are well documented as causing tertiary adrenocortical insufficiency due to prolonged ACTH suppression (2,3). Glucocorticoid treatment is widely used as a first-line therapy for the treatment of asthma (4). Due to cortisole excess many asthmatic patient acquire a cushingoid appearance and become Cushing syndrome (5). Adrenal insufficiency is seen less frequently. Not all patients show the clinical and electrolyte evidence of mineralocorticoid deficiency of adrenal insufficiency so any asthmatic patient receiving prolonged inhaled or oral glucocorticoid therapy presenting with nonspecific symptoms like nausea and vomiting should be suspected as adrenal insufficiency. Here we report an asthmatic patient with tertiary adrenal insufficiency.

CASE

A 61 years old female patient was admitted to the hospital with dyspnea, nausea and vomiting. Her appearance was thin. The patient was in an acute asthmatic attack and had been on oral and inhaler steroid treatment for asthma approximately 30 years. Her drug therapy on admission was budesonide and salbutamol inhalers. In the last three months her dyspnea complaint had been more severe and she had been admitted to several emergency services where was given iv steroid therapy. On admission her temperature was 36.2°C, blood pressure was 110-60 mmHg, respiratory rate was 24/minute and pulse rate was 88/minute. Her weight was 43 kg. There were brown colored skin lesions on face, on the dorsal of her hands and leg (Figure 1,2). There were sibilance roncuses bilaterally in physical experiment and the respiratory sounds were diminished. Blood biochemical levels, including electrolytes and hematological examination were all normal range. Chest X-ray was normal. There was grade 1 hepatosteatose in abdominal sonography. Arterial blood gases revealed as pH 7.481, $PaCO_2$ 24.3 mmHg, PO_2 103.3 mmHg, SaO_2 98.4%, HCO_3 18.3. On pulmonary function testing; FVC: 75%, FEV_1: 43%, FEV_1/FVC: 62, PEF: 31% and MEF25-75: 14%.

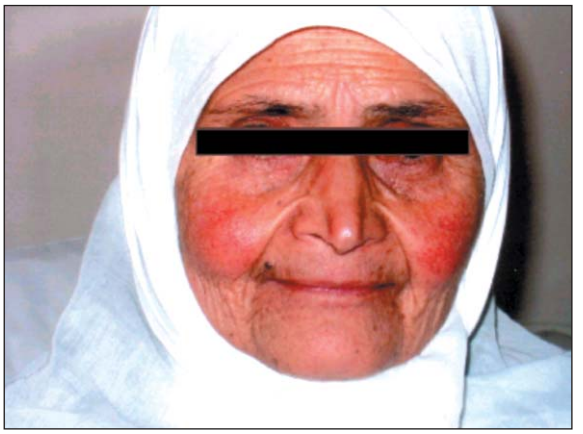

Figure 1. Brown coloured skin lesions on face.

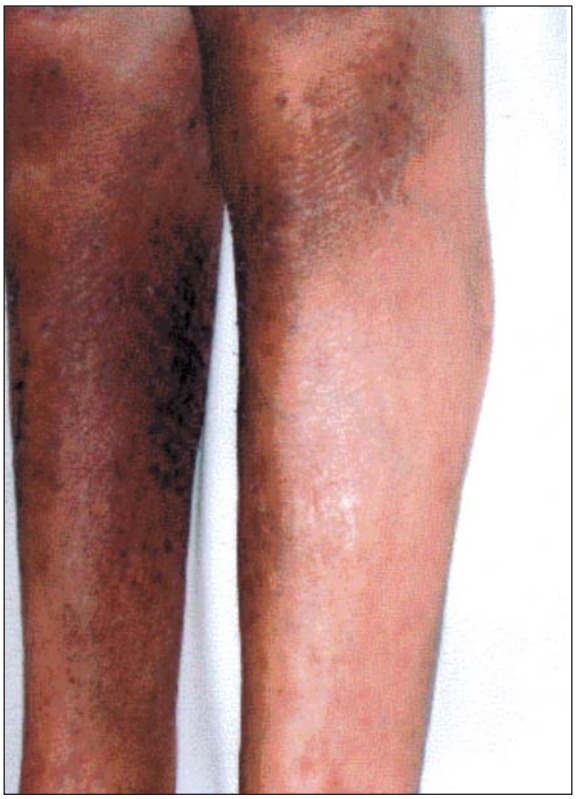

Figure 2. Brown coloured skin lesions on leg.

Theophylline, β2 mimetic, prednisolone 80 mg and tiotropium were started for the treatment of asthma. Adrenal insufficiency was suspected when nausea, vomiting and weakness became more serious after tapering steroid dose. Also the hyperpigmented lesions on the dorsal of her hand and legs rose the suspicion. These dark colored lesions were diagnosed as subcutaneous atrophy and it is supposed to be occurred after steroid therapy.

Plasma cortisole level was 0.39 µg/dL (normal range 8-22 µg/dL) and ACTH level was < 5 pg/mL (normal range 5-50 pg/mL) which were very low. A short synacthen stimulation test (250 µg tetracosactide intramuscularly) showed basal cortisole levels of 0.39 µg/dL rising to 26 µg/dL (normal increases are > 22 µg/dL). Hypophyseal magnetic resonance imaging was normal and all the other hormone levels were found in normal range. The patient was diagnosed as tertiary adrenal insufficiency due to oral and inhaler glucocorticoid therapy. The steroid dose was increased and the patient showed an excellent response.

DISCUSSION

Adrenal insufficiency may be a primary, secondary or tertiary process (1,2). Primary adrenal insufficiency occurs when there is an autoimmune, infectious, inflammatory disease or a cancer metastasis to the adrenal gland. Secondary adrenal insufficiency occurs due to diseases of the hypophysis. Tertiary adrenal insufficiency occurs due to hypothalamic depression caused by glucocorticoid therapy or in diseases effecting the hypothalamus. Tertiary adrenal insufficiency due to theuropatic glucocorticoid administration is the most common cause of adrenal insufficiency (1).

Tertiary adrenal insufficiency develops from hypothalamic-pituitary depression usually due to iatrogenic glucocorticoid therapy. Tiredness, weakness, nausea, vomiting, weight loss, diarrhea, hyponatremia, hypoglycemia are some of the symptoms which adrenal insufficiency should be suspected in a patient on steroid therapy. Hyperpigmentation is seen in primary adrenal insufficiency which is due to increased levels of ACTH. When adrenal insufficiency is suspected; plasma cortisole and corticotropine (ACTH) levels should be examined. Morning plasma cortisole concentrations of < 3 µg/dL are indicative of adrenal insufficiency and level over 19 µg/dL rule out the disease (2). In primary adrenal insufficiency plasma ACTH levels are always > 100 pg/mL. The short corticotropine stimulation test is then used to rule out primary adrenal insufficiency. Adrenal function is considered to be normal if the basal or post-corticotropine plasma cortisole levels is at least 18 µg/dL. To differentiate secondary and tertiary adrenal insufficiency insulin induced hypoglycemia test should be done. In normal individuals and in patients with tertiary adrenal insufficiency due to the use of glucocorticoids the plasma cortisole concentration increases to at least 20 µg/dL. In secondary and tertiary adrenal insufficiency caused by a hypothalamic disease there will be no increase in cortisole levels. We couldn't apply insulin induced hypoglycemia test to the patient since she was over 50 years old. Adrenal suppression has been described in many children and in few adult patients being treated with high dose inhaled corticosteroids (2,4-6). In their report, Karalus et al noted that adrenal suppression was greatest in patients taking oral steroid therapy compared with inhaler steroid users (7).

Cushing's syndrome is more frequent than adrenal insufficiency. In contrast adrenal failure is seen less frequently and may have an insidious onset. Our patient had been using oral and inhaler corticosteroids for a long period and had presented with nausea and vomiting. These nonspecific symptoms and the hyperpigmented lesions on her hand and feet made us suspect of primary adrenal insufficiency but later these lesions were diagnosed as subcutaneous atrophy.

Physicians should be aware that symptoms of adrenal insufficiency like nausea and vomiting which may be misdiagnosed as the adverse effects of drugs (eg. teophilin) frequently used for the treatment of asthma.

Although early symptoms of adrenal crisis are nonspecific such as nausea, vomiting, fatigue, blurred vision, electrolyte imbalance, without appropriate treatment, shock, coma and death may occur, hence adrenal crisis requires immediate diagnosis and appropriate treatment. Any asthmatic patient who is on corticosteroid treatment and describes suggestive symptoms of adrenal insufficiency hypotalamopituitary axis functions should be evaluated. Our case highlights the importance of suspecting adrenal insufficiency in any asthmatic patient on steroid treatment.

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Yazışma Adresi

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