doi: 10.5262/tndt.2013.1003.14

Adrenal Insufficiency in a Patient with End Stage Renal Disease due to Secondary Amyloidosis

Sekonder Amiloidoza Bağlı Son Dönem Böbrek Hastalıklı Bir Olguda Adrenal Yetmezlik

ABSTRACT

Amyloidosis is a group of disease characterized by the extracellular deposition of the fibrils called amyloid in various organs. Progressive organ dysfunction is seen in the systemic form. It may infiltrate various endocrine glands but rarely causes endocrine dysfunction. In this report, we describe a case of symptomatic adrenal failure complicated with infection in a patient with end-stage kidney disease due to secondary amyloidosis.

KEY WORDS: Addison disease, Adrenal failure, Amyloidosis

ÖZ

Amiloidoz, amiloid adı verilen fibrillerin çeşitli organlarda ekstrasellüler nitelikte birikmesiyle karakterize bir grup hastalığı tanımlamaktadır. Sistemik amiloidozda ilerleyici organ disfonksiyonu görülmektedir. Birçok endokrin organda amiloid depolanması görülebilmekle birlikte nadiren endokrin disfonksiyona neden olmaktadır. Bu olgu sunumunda, sekonder amiloidoza bağlı son dönem böbrek hastalıklı bir hastada infeksiyonla komplike olan semptomatik adrenal yetmezlik tanımlanmıştır.

ANAHTAR SÖZCÜKLER: Addison hastalığı, Adrenal yetmezlik, Amiloidoz

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Received : 09.07.2012
Accepted : 07.08.2012

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INTRODUCTION

The amyloidoses comprise a heterogeneous group of diseases in which proteins aggregates into characteristic fibrils with some unique properties (1). The prevalence of the disease varies in the world. In the developing countries, secondary amyloidosis (AA amyloid) is more frequent than primary amyloidosis (AL type), because of the higher burden of chronic infectious diseases such as tuberculosis and osteomyelitis. In some parts of the world, familial Mediterranean fever, a genetic disorder, accounts for a major part of secondary amyloidoses. Secondary amyloidosis is seen more frequently in our country than many others owing to the high frequency of familial Mediterranean fever and tuberculosis. In some kidney biopsy reports, it has been documented to be as high as 12% (2).

The kidney is the most commonly affected organ in patients with secondary amyloidosis. In clinical practice, renal involvement most often presents as proteinuria or nephrotic syndrome. However, primary amyloid deposition can be limited to the vessels or tubules and such patients present with progressive renal failure. Apart from the kidney, the liver, spleen and heart are frequently involved in systemic amyloidosis. Amyloid infiltration may be seen in endocrine glands but it does not always cause dysfunction. Primary adrenal insufficiency rarely occurs in amyloidosis, but if it occurs, life-threatening complications may develop. In this report, we describe a patient that presented as symptomatic adrenal failure due to amyloidosis and was on a regular hemodialysis programme.

CASE REPORT

A 52-year-old man on a regular hemodialysis programme due to end-stage renal disease presented to emergency department of our hospital with fever and generalized sei-

zure during hemodialysis. He was on a hemodialysis programme for three years because of amyloidosis due to bronchiectasis (Figure 1). In the medical history, there was no diabetes, hypertension or seizure. There was no history of vomiting, diarrhea or drug addiction. He was febrile for two days and plasma glucose level was detected as 30 mg/dL during seizure. After intravenous replacement of 30% dextrose, the seizure disappeared. His vital signs were as follows; blood pressure 80/40 mmHg, heart rate 110 beats/minute, respiratory rate 22/minute, body temperature 39.9 °C. Bilateral ronchi, a permanent right jugular catheter, skin hyperpigmentation was noted on his physical examination. Other examination findings were within the normal range. Complete blood count revealed a leukocyte count of 10800/mm^3 with a platelet count of 363.000/mm^3. His hematocrit was 39% with a hemoglobin level of 13.5 g/dL. Erythrocyte sedimentation rate was 20 mm in the first hour. Biochemical investigations disclosed the following: blood glucose level 94 mg/dL, serum sodium 133 mmol/L, potassium 3.9 mmol/L, calcium 8.1 mg/dL , phosphorus 4.1 mg/dL, magnesium 2.01 mg/dL , urea 52 mg/dL, creatinine 5.04 mg/dL, total protein: 48 g/L, albumin 23 g/L, ALT 25 IU/L, AST 41 IU/L, C-reactive protein was 16.1 mg/L (normal range 0.00-1.00). On his chest radiogram, bronchiectasis and jugular catheter was noted. He was hospitalized due to suspicion of catheter infection with sepsis, and empirical antibiotic treatment was started after blood cultures were obtained. Because of the history of seizure with hypoglycemia and hypotension, early morning serum cortisol sample was taken and revealed a result of 1.56 µg/dL. Corticotropin stimulation test with 250 mcg synachten intramuscularly was applied and results are shown in Table I Serum ACTH and DHEA-S were detected as 378 pg/mL (normal range 6.0 –56.7 pg/ml) and 13.4 µg/dL (normal range 4.8-40), respectively. Serum TSH, free T3 and free T4 were within the normal range. The patient was diagnosed as having primary adrenal failure and prednisolone 7.5 mg/day was started. After starting steroid treatment, his systolic blood pressure prosecuted within 90-110 mmHg intervals. Vancomycin treatment was started because of the detection of *Enterococcus feacium* in blood culture. There was no fever and no bacteria were detected in two control blood cultures. The patient was discharged with steroid replacement at the end of the 14 days of the antibiotic treatment.

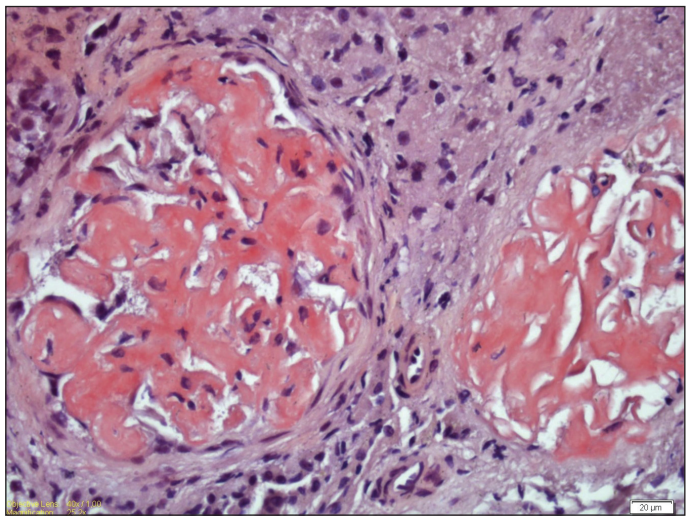

Figure 1: *Glomerular amyloid deposition, light microscopy with Congo-red x40.*

Table I: Results of Corticotropin stimulation test (250 mcg synachten, im).

0-minute serum cortisol	7.57 µg/dl
30-minute serum cortisol	8.94 µg/dl
60-minute serum cortisol	10.79 µg/dl
6-hour serum cortisol	9.36 µg/dl
24-hour serum cortisol	7.13 µg/dl

DISCUSSION

Amyloid infiltration of endocrine glands can be seen in cases of systemic amyloidosis more commonly than thought previously. In the literature, the most frequent organs infiltrated by amyloid are the thyroid glands and testis (3-4). Asymptomatic amyloid deposition in thyroid glands was reported in %30-80 of the patients (5). Although amyloid deposition in adrenal glands was demonstrated in pathology specimens, symptomatic primary adrenal failure was rarely reported (6-8). In a study investigating a total of 374 patients with secondary amyloidosis, adrenal amyloid deposition was detected in 41% of the patients using whole body amyloid scintigraphy (9). In the same study, it is reported that only five patients required glucocorticoid replacement. This situation may be explained by the requirement of the extensive adrenal cortex damage to produce clinical symptoms (10-11).

Diagnosis of the adrenal failure is very critical to prevent life-threatening complications. Some symptoms and signs of the adrenal failure (such as nausea, vomiting, metabolic acidosis, hyperkalemia and hypotension) may be ascribed to uremia and autonomic neuropathy which can be seen in systemic amyloidosis. End stage renal disease due to secondary amyloidosis is reported 11% at the time of the diagnosis (9). Progression to end stage renal disease is reported nearly 23%, changing with some risk factors (9). The frequency of the adrenal involvement in the patients with end-stage renal disease due to secondary systemic amyloidosis is not known exactly. The diagnosis of the adrenal failure in these patients can be very difficult because of the high frequency of hypotension and the masking effect of hemodialysis on the electrolyte and metabolic disturbances. Furthermore, low cortisol response to corticotropin without clinically evident adrenal failure was observed in nearly 50% of the patients with systemic amyloidosis (12-14). In these studies, some of the patients had end-stage renal disease. Although a simple test

can be enough for the diagnosis of adrenal failure, this is not the case in end-stage kidney disease patients with secondary amyloidosis. Thus, clinicians should consider both clinical and laboratory findings carefully to diagnose adrenal failure in this group of patients. Perhaps, it is more important to remember the disease.

In secondary systemic amyloidosis, abnormal response to corticotropin represents a dilemma as to whether adrenal failure exists or not unless symptoms or signs related with disease are present. Hypotension and hypoglycemia are important clues for suspicion for adrenal failure. The patient in this case had no frequent hypotension episodes during hemodialysis seasons. It may be speculated that our patient already had subclinical adrenal failure due to adrenal amyloid infiltration, and symptoms developed with a stress factor, infection, causing decrement of adrenal reserve to a critical level.

In our country, Familial Mediterranean fever (FMF) is the leading cause of secondary amyloidosis (15,16). Connective tissue disorders and chronic lung diseases are other common etiological causes (16,17). Control of underlying inflammatory disorders can result in prevention and regression of secondary amyloidosis (1). Colchicine is an effective treatment for FMF both in preventing amyloid formation and regression of amyloid deposition, especially when started early in the course of the disease (1,17,18).

In conclusion, we presented a patient with secondary systemic amyloidosis who developed adrenal failure, a clinical condition rarely reported in the literature. The endocrine system is frequently involved in systemic amyloidosis, but it rarely causes endocrine dysfunction. Clues for adrenal failure can be masked with hemodialysis in patients with end-stage renal disease. As in the present case, adrenal failure should be kept in mind in all patients with systemic amyloidosis, and special attention and evaluation should be done to prevent untoward results.

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