Amiodarone Induced Thyroid Dysfunction In a Patient Who Underwent Aortic and Mitral Valve Replacement: Case Report

Aort ve Mitral Kapak Replasmanı Yapılan Bir Hastada Amiodarona Bağlı Gelişen Tiroid Disfonksiyonu

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ABSTRACT Amiodarone is well recognized benzofuranic-derivative as an anti-arrhythmic drug containing a high dose of iodine with considerable potential to cause thyroid dysfunction. Amiodarone is often used to treat both ventricular and atrial arrhythmias. Its cardiac side effects are less frequent than those associated with other antiarrhythmics. It has potentially marked effects on thyroid physiology. The present patient was a 66-year-old woman who developed thyroid dysfunction and was given amiodarone as an anti-arrhythmic agent for cardiac arrhythmia after open heart surgery.

Key Words: Amiodarone, thyroid dysfunction, open heart surgery

ÖZET Amiodaron iyi bilinen benzofuranik derivesi bir anti-aritmik ilaçtır ve içerdiği yüksek iyot konsantrasyonu nedeniyle tiroid disfonksiyonu oluşturma potansiyeli fazladır. Amiodaron hem ventriküler hem de atriyal aritmilerin tedavisinde sıklıkla kullanılır. Kardiyak yan etkileri diğer antiaritmiklere göre daha az sıklıkla ortaya çıkar. Tiroid fizyolojisi üzerine potansiyel belirgin bir etkisi mevcuttur. Burada 66 yaşında açık kalp cerrahisi sonrası antiaritmik ilaç olarak amiodaron verilen ve cerrahiden sonra tiroid disfonksiyonu geliştiren kadın bir olgu sunulmuştur.

Anahtar Kelimeler: Amiodaron, tiroid disfonksiyonu, açık kalp cerrahisi

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Amiodarone is an iodine rich anti-arrhythmic agent which may lead to either hypothyroidism or hyperthyroidism during long term therapy and approximately 50% of patients on amiodarone treatment present with abnormal thyroid function.[1] Both thyrotoxicosis (AIT - amiodarone induced thyrotoxicosis) and hypothyroidism (AIH - amiodarone induced hypothyroidism) may develop during amiodarone therapy and these patients may have no thyroid dysfunction in their medical history. AIT is primarily related to excess iodine-induced thyroid hormone synthesis in an abnormal thyroid gland (type I AIT) or to amiodarone-related destructive thyroiditis (type II AIT).[2,3] This anti-arrhythmic agent has a structural resemblance to thyroid hormones with its 35% iodine content and amiodarone induced thyroid dysfunction is rarely manageable by discontinuation of the drug, partly due to the long terminal half life up to four months. Besides amiodaron particles are known to inhibit T4 to T3 conversion, they

work as inhibitors of nuclear receptors for thyroid hormones, exert cytotoxic effect and induce immune/inflammatory process in thyroid gland.[3-5]

CASE PRESENTATION

A 66- year-old female patient admitted to our hospital with rheumatic valvular heart disease. The patient was euthyroid in the preoperative period and she did not have any thyroid gland dysfunction in her medical history.

She was admitted to hospital with the complaints of dyspnea and cough. Echocardiography revealed mitral stenosis (mitral valve area:1.1cm^2, with 18 mmHg peak and 8mmHg mean gradient), mitral regurgitation (first degree), aortic stenosis (with 50 mmHg peak and 25 mmHg mean gradient), aortic regurgitation (second degree) and first degree tricuspid regurgitation. Ejection fraction was 65% and pulmonary artery pressure was 40 mmHg. Coronary angiography did not reveal any coronary artery stenosis, pulmonary artery pressure was found to be 45mm Hg (systolic) 20 mmHg (mean). Mitral and aortic valve replacement was performed. Prosthetic bileaflet valve with the size of 29 mm (ATS Medical, Inc. Model: 500DM29) for mitral position and 21 mm sized prosthetic bileaflet valve (ATS Medical, Inc. Model: 500FA21) for aortic position. The operation was performed with standart aortic and bicaval cannulation, moderate systemic and topical hypothermia. Mitral valve replacement was performed through a left atriotomy. Aortic cross clamp time and total cardiopulmonary bypass time was 110 minutes and 144 minutes, respectively. The cardiac rhythm was sinus after the procedure. The early postoperative period was uneventful and the patient was extubated at the eighth hour in ICU. Two ventricular tachycardia (VT) attacks occured in the postoperative follow up and amiodarone infusion was administered with 300 mgr loading and 900 mgr/24hrs infusion dosage. After a short period of normal sinus rhythm, atrial fibrillation and VT was seen again and cardioversion was performed (three times with 100-300j). The echocardiography revealed normal aortic and mitral prosthetic valve functions. Renal dysfunction with decreasing urine output was supported with hemodialysis. The patient was intubated because of shortness of breath and respiratory acidosis. The thyroid function tests revealed elevated total and free T4 levels with supression of TSH (T3: 0.912 ng/mL, T4: 14.40 µg/dL, TSH: 0.156 µIU/mL, fT3: 4.11 pmol/L, fT4: 49.65 pmol/L [Normal ranges: T3: 0.6-1.95 ng/ml, T4: 5-11.5 µg/dl, TSH: 0.27-4.2 µIU/mL, fT3: 3.95-6.8 pmol/L, fT4: 12-22 pmol/L]). Amiodarone infusion was stopped (after 8 days and total 3.6 gr) and the patient was followed up with atrial fibrillation.

DISCUSSION

Amiodarone is a potent class III anti-arrhythmic drug used for the prophylaxis and treatment of many cardiac rhythm disturbances, ranging from paroxismal atrial fibrillation to life threatening ventricular tachyarrhythmias. Dysthyroidism (hypo- or hyperthyroidism) occurs in 10 to 20% of the patients treated with amiodarone for arrhythmia.[6] The data on the amiodarone induced thyroid dysfunction in short-term treatment is sparse. Iervasi et al studied serum total and free thyroid hormone, reverse T3, and TSH levels in patients with cardiac arrhythmias during the first 10 days of treatment with a loading of amiodarone by iv infusion.[7] Total and free concentrations of T4 tended to progressively and significantly increase starting from the fourth day of therapy whereas total T3 decreased from the second day progressively throughout the study, TSH levels early and significantly increased starting from the first day of therapy. Clinically relevant thyroid dysfunction is not uncommon during amiodarone administration and requires careful diagnosis and treatment. Thyrotoxicosis type II has an explosive onset, and is difficult to predict. It may develop at any time during treatment, often accelerating in severity over only a few days. Type II thyrotoxicosis occurs in an apparently normal thyroid, and results from a direct toxic effect of amiodarone causing a subacute destructive thyroiditis with consequent leakage of preformed thyroid hormones into the circulation.

In this case we observed a decrease in total T3 and TSH levels. The levels of total and free T4 were in normal range on the fourth day of the

treatment. As we know that the patient did not have any thyroid dysfunction previously the changes in the thyroid function may be attributed to amiodarone therapy. To prevent further thyroid dysfunction and its complications, amiodarone was ceased. It is known that amiodarone-induced thyrotoxicosis differs from other forms of thyrotoxicosis and severe left ventricular dysfunction is associated with increased mortality in AIT.[8]

Amiodarone is a potent antiarhythmic drug which must be carefully used in cardiac surgery patients in the postoperative period in means of thyroid dysfunction. Although potential antiarrhytmic effects, amiodarone can cause serious arrhythmia due to elevated tyroid hormone levels.

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