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Case Report

Recurrent atrial fibrillation with fast ventricular rate in an elderly lady: old records reveal cause of the malady

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ABSTRACT

Amiodarone is an iodinated benzofuran derivative and is prescribed widely in management of arrythmias- ventricular and supraventricular alike. Excellent efficacy, minimal negative inotropic activity and less rate of ventricular pro arrhythmia makes it the choice of drug in heart failure. Side effects however, make it a drug to be used with caution and they range from pulmonary toxicity to thyroid dysfunction. 15-20% of patients treated with amiodarone are believed to develop some thyroid dysfunction. It can cause amiodarone induced hypothyroidism (AIH) or amiodarone induced thyrotoxicosis (AIT). AIT usually is seen in areas with low uptake of iodine and AIH in areas with sufficient iodine uptake. We report a case of 58-year-old lady with rheumatic heart disease who was started on amiodarone for atrial fibrillation and later presented with recurrent atrial fibrillation (AF) with fast ventricular rate (FVR) and diagnosed as AIT. The challenges in diagnosis and management are discussed.

Keywords: AIT, Amiodarone, Thyrotoxicosis, Atrial fibrillation

INTRODUCTION

Amiodarone is an iodinated benzofuran derivative and a widely prescribed anti-arrhythmic. Available in both, intravenous and oral preparations, most patients receive initial intravenous dose followed by maintenance dose which can vary from 200 mg to 600 mg. With structural similarity to thyroxine (T4), containing 37% iodine by weight, each 200 mg tablet contains about 75 mg of organic iodine and 8-17% of this is released as free iodine, hence treatment with 200 mg tablet can supply more than 100 times the daily iodine need.[1] Being highly lipid soluble, it concentrates in the adipose tissue, muscle, liver, lung and thyroid gland and has long elimination half-life of 14-120 days after prolonged therapy. Its major metabolite desethylamiodarone is qualitatively similar to amiodarone, but it's elimination half-life is longer.[2] Thyroid dysfunction is a known complication of amiodarone therapy and both hypothyroidism and hyperthyroidism can occur. Thyrotoxicosis due to the drug can be of two types- type 1 which develops in those with pre-existing or latent thyroid disorders and type 2 in those with normal thyroid. It is important to keep a high degree of suspicion of the above conditions in patients who have received amiodarone so that treatment is not delayed. Our case report highlights the case of a lady with rheumatic heart disease who was presenting with repeated episodes of atrial fibrillation (AF) with fast ventricular rate (FVR) inspite of optimisation of treatment and high degree of suspicion for amiodarone induced thyrotoxicosis led to diligent workup and diagnosis of type 2 amiodarone induced thyrotoxicosis (AIT).

CASE REPORT

A 58-year-old lady presented with complaints of palpitations and breathlessness to the emergency room and diagnosed to be having AF with FVR with heart failure.

She is a known case of rheumatic heart disease with mild mitral stenosis and moderate to severe mitral regurgitation with AF for which she was on medications including calcium channel blockers, beta-blockers, oral anticoagulants, diuretics and other supportive medications. Clinical examination revealed that the patient was in AF with heart rate of -160/min irregular, blood pressure (BP) of 126/80 mm of Hg and auscultation of chest revealed bilateral basal zone crepitations.

She was administered 2 doses of injection diltiazem (0.25 mg/kg and 0.35 mg/kg IV respectively) and tablet metoprolol XL 50 mg was also given. Once stable, she was shifted to the ward and came to be under our care. She had history of hospitalization 15 days back for AF with FVR and on evaluation, was newly diagnosed to have hyperthyroidism (TSH-0.10, free T4-43.81, free T3-5.30) for which she was started on neomercazole 20 mg 1-0-1 and screened for TRAb, which was negative. ECHO showed LA size of 50 mm and mitral valve thickening and showing diastolic doming with MVA-1.82 cm^2 (normal-4-6 cm^2). Despite increasing the dose of rate control drugs, heart rate did not reduce as expected. A need to evaluate for presence of factors leading to reduced response to medications was hence considered and review of all past records was done to see if patient had received amiodarone. It was revealed that patient had received oral amiodarone in the past for almost a year which was discontinued 6 months back. Prescription after that did not mention amiodarone in the prescription and patient also confirmed that she was not on amiodarone for the last 6 months. It is worth noting that patient was administered amiodarone infusion followed by oral amiodarone for 2 days during the hospitalization immediately before the present. In view of the above information, a diagnosis of amiodarone induced thyrotoxicosis was considered and evaluation was carried out including a repeat thyroid function test, thyroid ultrasonography (USG) and inflammatory markers; free T4 was 23.05 ng/dl, in view of which neomercazole dose was increased to 20 mg three times a day. Thyroid examination revealed enlarged gland with palpable nodule and IL6 was 1.74. Thyroid USG showed normal left lobe, bulky right lobe (2.7×2.9×4.9 cm) and showed well defined, smooth, marginated, wider than taller, spongiform lesion measuring 2.3×2.7×3.6 cm with few macrocalcifications within (TIRADS II). PSV was 11.6 cm/sec. In view of the above reports, AIT type 2 was considered. To confirm this, nuclear scan was advised, considering the cost of which, patient's relatives wanted to do it at a later date. After discussing with them, steroids were started at 1 mg/kg/ day and patient was discharged. Patient came for follow up at OPD and repeat TFT revealed free T4 of 20.17 and free T3 was 4.20. She was advised nuclear scan but they wanted to wait for few days. Patient however presented again with AF with FVR again within 3 days and at that time TSH was 0.97 uIU/ml, free T4 was 20.47 ng/dl and free T3 was 4.17. Patient was ready for nuclear scan this time and Tc uptake scan was done after stopping antithyroid drugs for 4 days prior to procedure. It revealed significantly reduced tracer uptake in both the lobes of thyroid gland with thyroid uptake of 99 mTc <1%. This confirmed the diagnosis of type 2 AIT. TFT was repeated the following week when patient came for follow up which TSH was 4.35, free T4 was 15.39. Steroids were continued at the dose of 0.5 mg/kg and patient asked to follow up. Patient reported improvement in her symptoms at follow up and final diagnosis was type 2 amiodarone induced thyrotoxicosis responding to anti-thyroid drugs and steroids.

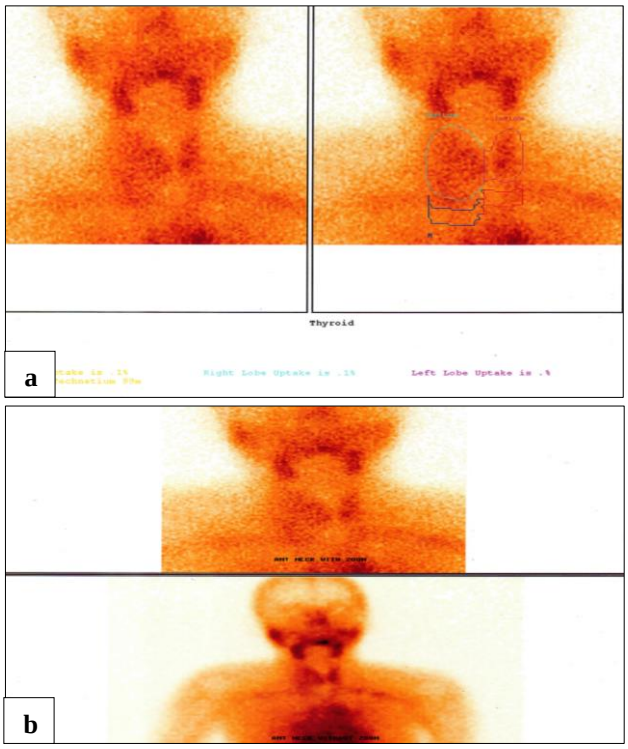

Figure 1 (a and b): Thyroid scan showing <1% uptake of 99 mTc suggestive of thyroiditis.

DISCUSSION

Thyroid dysfunction is a known complication of amiodarone therapy. A study estimated the incidence rate to be 14.1 per 100 person-years.[3] Another noted that 14-18% of patients treated with the drug develop thyroid dysfunction, either AIT or AIH.[4] AIT can be of two types. Type 1 AIT develops in those with preexisting or latent thyroid disorders and Type 2 in those with normal thyroid and is thought to be due to increased release of hormones resulting from inflammatory process- thyroiditis.[5] There may also be mixed types. As the treatment is different for both types, it is important to reach the correct diagnosis.

The diagnostic challenge to distinguish between the two can be overcome with detailed history (pre-existing thyroid disorder, positive drug history for use of amiodarone, dose and duration and time since discontinuation) detailed clinical examination (goitre, exophthalmos, peripheral signs of thyrotoxicosis) and work up (thyroid antibodies, thyroid ultrasonography, nuclear scan). Presence of fever and tenderness may

indicate thyroiditis, hence type 2 AIT. Goitre and exophthalmos, type 1 AIT.

The diagnosis, however is not straightforward due to many reasons. Firstly, cardiac manifestations of thyrotoxicosis may be absent due to intrinsic inhibitory effects of amiodarone on the heart.[6] Elderly patients may present with apathetic thyrotoxicosis and hence the diagnosis may be missed.[7] Clinical suspicion may not be high as patient may not be on the drug during presentation and may have received it in the past and it may be forgotten that adverse effects may continue to occur months after stoppage of the drug.[8] In addition, some may have a mixed type.

Inspite of the difficulty in distinguishing between the two, efforts should be made to find the type as each type has specific therapy and wrong therapy will result in ineffective or delayed responses as well as expose the patient to side effects of drugs. Treating clinicians should suspect AIT in patients who are or were on amiodarone who were stable but show signs of cardiac decompensation, worsening arrhythmia, recurrent atrial fibrillation, or angina. Diagnostic tools should be utilised without delay. Thyroid sonography is useful as it may show presence or absence of goitre (diffuse/nodular). Colour flow Doppler study is a valuable tool, as type 2 AIT will show absent hypervascularity (pattern 0) and type 1 AIT, increased vascularity (pattern 1 to 3) and blood flow velocity.[9-11] Thyroid RAIU (I131) is a nuclear study in which the uptake is more in type 1 AIT and can be normal, low normal or even increased sometimes in type 2 AIT, hence reducing its diagnostic value. Some studies have shown that RAIU misdiagnosed the type.[12] Inflammatory markers like C reactive protein, interleukin-6 have little diagnostic value due to their poor specificity. Radio nuclear scans (scintigraphy with Tc-99m, Tc-99m MIBI) are essential in distinguishing between the two types. as type 1 AIT will show increased uptake whereas type 2 will show reduced uptake.[13]

Patients should be tested for presence of thyroid antibodies (TgAb/TPOAb/TSI). They may be present in type 1 AIT depending on the underlying thyroid disorder. High levels of thyroglobulin antibodies and TPO antibodies have also been reported in 8% of type 2 AIT patients.[14] Those with mixed type of features, no response to antithyroid drugs alone, worsening after initial improvement and critically ill with no time to investigate are treated as mixed type with anti-thyroid drugs with/without potassium perchlorate and steroids.

Our patient had features of type 2 AIT as described in case report and was treated with antithyroid drugs and steroids, to which she responded.

What makes this case worth reporting is that our patient had rheumatic heart disease, the burden of which is still high in our country. It remains an important cause of AF in our country, where it is present in nearly one-third of the patients with AF.[15] We could not find any reported cases of AIT in a known case of RHD.

Importantly, among the drugs recommended for rhythm control in AF (amiodarone, dofetilide, dronedarone, flecainide, propafenone and sotalol), amiodarone is commonly used in our country due to the ease of availability. Among the drugs recommended for rate control (beta blockers, non dihydropyridine calcium channel blockers, digoxin and occasionally amiodarone), experience shows that amiodarone is still commonly used especially in patients presenting in failure and hemodynamic instability, worsening of rate, recurrent arrhythmias. This results in a lot of patients getting exposed to the drug, making them vulnerable to the side effects, even if used for short duration owing to its long half-life. Interestingly, these patients may present with recurrent or worsening arrhythmias which may be attributed to the underlying structural heart disease (large LA for example) and the diagnosis of AIT may be completely missed. To add to the problem, clinicians may add amiodarone when other drugs fail to control rate adding to the problem.

CONCLUSION

In conclusion, amiodarone induced thyrotoxicosis should be suspected in patients presenting with recurrent/ worsening arrhythmias despite being on drugs. A diligent search for evidence of use of amiodarone should be done, even if remote. Presence of RHD should not make clinicians attribute the worsening or refractory nature of arrhythmias to it. In suspected, not critically ill cases of AIT, detail workup to conclude the type of AIT should be made.

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