SEVERE AMIODARONE-INDUCED BRADICARDIA CONCEALS SICK SINUS SYNDROME: CASE REPORT

Irina Crăcană1, T.F. Vasilcu2*, Alexandra Mardare3, Ioana Dana Alexa1, D.T.M. Marcu2
University of Medicine and Pharmacy “Grigore T. Popa” - Iași
Faculty of Medicine
1. 1st Medical Department, Discipline of Internal Medicine, Nephrology and Geriatriy
2. 1st Medical Department, Discipline of Internal Medicine and Cardiology
3. Neurology Department
*Corresponding author. E-mail: teodor.vasilcu@gmail.com

SEVERE AMIODARONE-INDUCED BRADICARDIA CONCEALS SICK SINUS SYNDROME: CASE REPORT (Abstract). Sinus node dysfunction is one of the most common arrhythmias in elderly patients; it is usually associated with intermittent and variable symptoms, thus making it difficult to diagnose. We present the case of an elderly female patient with a personal history of atrial fibrillation treated for the last three years with amiodarone; she was admitted to the Geriatric Clinic for non-specific symptoms with onset two months previously for which she had already sought care in different medical services. Clinical examination showed severe bradycardia; ECG and Holter ECG on admission confirmed severe bradycardia, with a heart rate between 29 and 50 beats/min (bpm). Given her long-term treatment with amiodarone we looked for and found hyperthyroidism; the endocrine examination led to the diagnosis of mixed type Amiodarone-induced thyrotoxicosis and initiation of corticosteroid and antithyroid treatment. The evolution of cardiac arrhythmia was monitored with the help of several Holter ECGs performed after amiodarone washout and return to the euthyroid state, which revealed a tachycardia-bradycardia syndrome initially masked by the side effects of the unsupervised therapy with amiodarone, and properly treated by the implantation of a pacemaker. Keywords: SINUS NODE DYSFUNCTION, TACHYCARDIA-BRADYCARDIA SYNDROME, HYPERTHYROIDISM, AMIODARONE.

There are several normal age-related changes of the cardiovascular system, one of the most important affecting the conduction system with increasing fibrosis around the sinus node and loss of specialized cells and fibers. These changes, associated with a decreased response to sympathetic agonists would lead to a decreased peak heart rate and a significant decrease in heart rate variability, resulting in bradycardia, which may be further exacerbated by medication and ischemia (1). Older patients often have delayed conduction in the atrio-ventricular (AV) node, which would generate different types of AV blocks, that are usually without symptoms and could progress to complete AV block (2).

These significant changes in the anatomy and function of the conduction system of the aging heart explain the increased frequency of sick sinus syndrome, a group of arrhythmias presumably caused by a malfunction of the sinus node, including sinus arrest, sinus node exit block, sinus bradycardia and tach-
Severe amiodarone-induced bradicardia conceals sick sinus syndrome: case report

The manifestations of this disease are diverse, intermittent and often difficult to surprise on casual ECG (3), reason for which the epidemiological data are limited and the incidence of this disease in the general population remains unclear (4, 5). Syncope and/or fatigue are the cardinal symptoms in the bradycardia forms, and palpitations in the tachycardia forms, but it is not uncommon (especially in the elderly) that symptoms to be limited to dyspnea, reduced exercise capacity or mild cognitive impairment (sometimes interpreted as the onset of dementia syndrome) (6). In this context, Holter ECG monitoring remains the investigation of choice, identifying not only the accurate diagnosis but also the right moment for the implantation of pacemaker.

When confronted with fast atrial fibrillation, controlling the ventricular rate should be of the outmost importance, and the favorite antiarrhythmic drug is amiodarone (5). This trend led to a massive use of this drug in elderly patients, which was accompanied by a constantly increasing number of unwanted side effects, most frequently occurring at thyroid level. The lack of periodic and systematic control can be accompanied by serious clinical situations, such as severe bradycardia, that can be masked by nonspecific symptoms and thus easily overlooked and undertreated.

**CASE PRESENTATION**

We present the case of an 86 year old female patient admitted to the Geriatric Clinic for several non-specific symptoms, such as: dry and irritative cough, vertigo and generalized itching with nocturnal exacerbation. The onset of these symptoms was insidious about two months prior to this hospitalization, the patient having already sought care in different medical services. On admission she presented: facial erythema, scratching lesions on the posterior chest wall, rhythmic heart rate of 46 beats/min, and bilateral upper limb resting tremor. Her medical history revealed an episode of fast atrial fibrillation that had occurred three years earlier and was successfully treated with amiodarone, although the biochemical thyroid function tests indicated at that moment subclinical hyperthyroidism, with TSH concentration at the lower limit of normal range but with fT4 and fT3 concentrations within the normal range.

Our diagnosis was severe bradycardia, most probably due to thyroid dysfunction secondary to the long-term, unsupervised treatment with amiodarone. The biochemical tests revealed very low serum levels of TSH hormone (TSH = 0.01 pmol/l), high levels of fT4 (fT4 = 30.8 μUI/ L), and normal levels of fT3. ECG on admission confirmed sinus bradycardia (Figure 1); however, the 24-hour ECG monitoring showed sinus bradycardia alternating with idioventricular rhythm; the average heart rate was 35 bpm, range 29 to 50 bpm; the absence of any cardio-cerebral symptoms allowed the postponing of pacemaker implantation.

The endocrine examination confirmed the diagnosis of mixed type amiodarone-induced thyrotoxicosis, and a treatment with corticosteroids and antithyroid drugs was initiated.

The clinical course was favorable, as the patient reported the disappearance of dry cough and prurigo 48 hours after the discontinuation of amiodarone and the heart rate slowly ascended (up to 50 bpm). A 24-hour ECG monitoring 1 month after the discontinuation of amiodarone treatment showed an average heart rate of 45 bpm, range 39 to 100 bpm, which led us to suspect an underlying, unsuspected bradycardia-tachycardia syndrome.
syndrome. A third 24-hour ECG monitoring was done after 6 weeks of thyroid treatment, when thyroid function had already returned to normal; hence, we considered that this one would reflect the correct cardiac status of our patient. The result was very much the same as the previous one, thus confirming the diagnosis of bradycardia-tachycardia syndrome, for which a pacemaker was implanted.

DISCUSSION

The normal aging process of the heart includes fibrosis and loss of specialized cells and fibers of the conductive system, which would favor an increased incidence of sick node dysfunction. This condition can take many forms, including bradycardia-tachycardia syndrome. The diagnosis of this form can be difficult, as random ECG is more often normal. The bradycardia episodes are usually without any symptoms; the tachycardia episodes are associated with palpitations and the patient is wrongly diagnosed with only tachyarrhythmia and would receive an antiarrhythmic treatment, usually amiodarone. This drug should be carefully monitored, not only for the well-known side-effects, but also for the negative effect on the bradycardia episodes.

Numerous studies (7, 8, 9) show that low doses of amiodarone can be used safely in patients with fast arrhythmias and normal systolic function. However, the length of the treatment with amiodarone proved to be an independent risk factor in the prediction of adverse effects (4), mainly changes at the cardiovascular (im...
portant bradycardia), thyroid (hyper- and hypothyroidism), pulmonary and hepatic level (9, 10).

Still, the absence of cardiac symptoms (syncope, fatigue) and hyperthyroidism led to a delay in the diagnosis. This case also presented some of the less known side effects of amiodarone, that include nervous system disorders (paresthesia, pain and muscle weakness, tremor, walking and moving disorders, headache, vertigo), gastrointestinal disorders (nausea, taste alteration, constipation, lack of appetite) or skin disorders (itching, petechiae) (8) that can be easily interpreted as a concomitant chronic or aging-related disease.

CONCLUSIONS
Our case emphasizes the need for sustained monitoring of treatment with amiodarone; the multiple side effects (cardiovascular and thyroid) associated with the progression to a higher-degree AV block led to severe bradycardia, fortunately without cerebral and cardiac consequences.

The therapeutic decision, especially in tachycardia-bradycardia syndrome should be carefully considered; the patients that require antiarrhythmic therapy should be rigorously monitored, mainly those treated with amiodarone, and the 24-hour ECG monitoring should be the safest way for identifying the excessive secondary “bradicardization”.

REFERENCES