CASE PRESENTATION

Thyrotoxicosis and Heart Failure – a Case Report

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ABSTRACT

Introduction

Heart failure (HF) with reduced ejection fraction is a complex condition requiring comprehensive diagnostic work-up and management.

Case presentation

A 62-year-old male presented with resting HF and multiple syncopes. Medical history: former smoker, type 2 diabetes, advanced peripheral artery disease. Physical examination: congestive HF, obesity, discrete exophthalmia, grade 1 goitre, BP 110/70 mmHg, HR: 180 bpm. ECG: atrial fibrillation (AF), 180 bpm, RBBB, ST depression in anterolateral leads. CXR: pulmonary congestion, right pleural effusion. Blood analysis: D-dimer >5ng/ml, NTproBNP 12.900 pg/ml, hsTnI 550 ng/L, low TSH, fT3, fT4 4xULN. Cardiac echo: LVEF 20%, diffuse hypokinesis. HF symptom improvement with decongestion and rate control medication. Methimazole started on day 3. Intermittent conversion to sinus rhythm (SR) on day 7. ECG Holter (day 8-9): alternating moderate/high-rate AF and SR, 5-8 second sinus pauses and 1 syncope. LVEF 35% (day 9). Dual-chamber pacemaker implanted on day 10. Discharged on day 18. 2-months follow-up: LVEF 45%, NTproBNP 1.100 pg/ml, SR, HR 65-70 bpm, NYHA I HF.

Conclusion

Cardiac and non-cardiac aggravating factors can contribute to HF worsening. Unmasking these factors is essential, as specific treatments can markedly improve the patient's clinical status.

Keywords: heart failure, atrial fibrillation, thyrotoxicosis, syncope, pacing.

REZUMAT

Introducere

Insuficiența cardiacă (IC) cu fracție de ejecție scăzută reprezintă o patologie complexă ce necesită o abordare diagnostică și terapeutică exhaustivă.

Prezentare de caz

Bărbat, 62 de ani, se prezintă pentru IC de repaus și episoade sincopale recurente. Istoric: fost fumător, diabet zaharat tip 2, boală arterială periferică stadiul IV. Obiectiv: sindrom congestiv, obezitate, discretă exoftalmie, gușă grad 1, TA 110/70 mmHg, AV 180 bpm. ECG: FiA, 180 bpm, BRD, subdenivelare ST în derivațiile anterolaterale. RXCP: congestie pulmonară, lichid pleural drept. Analize: D-dimeri >5ng/ml, NTproBNP 12.900 pg/ml, hsTnI 550 ng/L, TSH scăzut, fT3, fT4 4xULN. Ecocardiografie: FEVS 20%, hipokinezie difuză. Fenomenele de IC s-au ameliorat sub medicație decongestionată și control AV. Metimazol inițiat în ziua 3. Conversie intermitentă la RS în ziua 7. Holter ECG (ziua 8-9): FiA cu AV medie / rapidă alternând cu RS, pauze sinusale (5-8 secunde) și o sincopă. FEVS 35% (ziua 9). Implantare de stimulator cardiac bicameral (ziua 10). Externare în ziua 18. La 2 luni: FEVS 45%, NTproBNP 1,100 pg/ml, RS, HR 65-70 bpm, IC NYHA I.

Concluzii

Multipli factori cardiaci și non-cardiaci pot contribui la agravarea IC. Identificarea acestora este esențială, dată fiind posibilitatea inițierii unor terapii specifice care pot ameliora semnificativ statusul clinic al acestor pacienți.

Cuvinte cheie: insuficiență cardiacă, fibrilație atrială, sincopă, cardiostimulare, tirotoxicoză.

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INTRODUCTION

Heart failure (HF) is a leading cause of hospitalization among adults, being associated with a poor quality of life, a high financial burden on the healthcare system and increased morbidity and mortality[1]. HF patients, both with preserved and reduced ejection fraction, may suffer from several different cardiovascular and non-cardiovascular pathologies that are involved in aggravating HF and their identification should be part of the diagnostic work-up as they may offer specific therapeutic opportunities[2].

CASE PRESENTATION

A 62-year-old male patient presented to the Emergency Department (ED) with progressive worsening of resting HF symptoms that appeared 2 months prior. He also reported multiple syncopes during the preceding year, not related to any specific setting, position or precipitating factor. He is a former smoker, has type 2 diabetes and stage IV peripheral artery disease (PAD) for which he underwent balloon angioplasty of the right superficial femoral artery and right toe amputation 6 months prior. The last known left ventricle ejection fraction (LVEF) was 50%, measured during the admission in the Vascular Surgery Department. His chronic medication included: aspirin, indapamide, ramipril, carvedilol, high dose atorvastatin, cilostazol, metformin, sitagliptin and basal insulin.

The physical examination in the ED identified overt signs and symptoms of resting congestive HF, grade I obesity, discrete exophthalmia, grade I goitre, BP 110/70 mmHg, HR: 180 bpm, SpO_2 94% without oxygen supplementation (98% on 3l/min mask O_2). ECG (Figure 1a): AF, 180 bpm, right bundle branch block (RBBB), left anterior fascicular block, descending ST depression in the anterolateral leads. The chest X-ray (CXR) revealed pulmonary congestion and a right moderate pleural effusion (Figure 1c), markedly different compared to the CXR performed 6 months prior (Figure 1b). ED blood analysis: high blood sugar (glycemia 236 mg/dl), D-dimer >5ng/ml, NTproBNP 12.900 pg/ml, hsTnI 550 ng/L. The measured LVEF on the transthoracic echocardiogram (TTE) was 20%, with diffuse hypokinesis, moderate functional mitral regurgitation (Figure 1d), severe tricuspid regurgitation, moderate-to-severe pulmonary hypertension – 50-55 mmHg estimated systolic pulmonary artery pressure (PAPs). A computed tomography (CT) pulmonary angiography was performed for excluding pulmonary embolism (Figure 1e). The coronary angiogram performed on the second day of admission revealed no obstructive coronary artery disease (CAD).

As the AF moment of onset was unknown (the patient did not report palpitations), the left atrium was dilated (50 ml/m^2) and no major hemodynamic instability was present, a rate control strategy was preferred. The HF symptoms slowly improved with decongestion (furosemide and spironolactone) and rate control medication (digoxin and carvedilol). Supporting the rate control strategy, the subsequent comprehensive blood analysis revealed very low TSH and increased fT3 and fT4 levels, consistent with hyperthyroidism. Given the clinical presentation, the endocrinologist established the thyrotoxicosis diagnosis of moderate severity and initiated antithyroid medication (methimazole) on day 3 (50 mg initially with a 10 mg decrease every 10 days and 2-month follow-up). The HbA1c level was 7.3%, the hemoglobin level was normal, and no iron deficiency was identified. Full dose low molecular weight heparin and high dose statin were administered during the admission.

Intermittent conversion to sinus rhythm (SR) (~40-50 bpm) was observed starting on day 7 (Figure 2a). The low sinus rate was considered independent of the antithyroid medication effect, but rather determined by the rate control medication. However, at that moment, the patient was receiving a low-intermediate carvedilol dose (6.25 mg b.i.d.) and the digoxin level was subtherapeutic (0.6 ng/ml). Thus, a possible sinus node dysfunction was taken into consideration. The ECG Holter monitoring performed on day 8-9 revealed alternating moderate / high-rate AF (max 174 bpm) and SR (mainly in the 50-55 bpm interval, lowest nocturnal 35 bpm), mean HR 60 bpm, as well as several 5-8 second sinus pauses immediately after AF conversion (Figure 2b). The patient presented one syncope during the monitoring, while sitting on the side of the bed, that quickly and spontaneously recovered, corresponding to an eight second pause recorded during the ECG Holter. The other pauses occurred while the patient was lying in bed and were reported as nausea and lightheadedness. The neurological and CT exams were normal.

Repeated TTE on day 9 revealed a significantly increased LVEF of 35%, assessed whilst in sinus rhythm. A dual chamber pacemaker was implanted on day 10, with no procedural complications. The hospital stay was uneventful afterwards.

The patient was discharged on day 18, with HF NYHA II symptoms, a NTproBNP level of 2.500 pg/

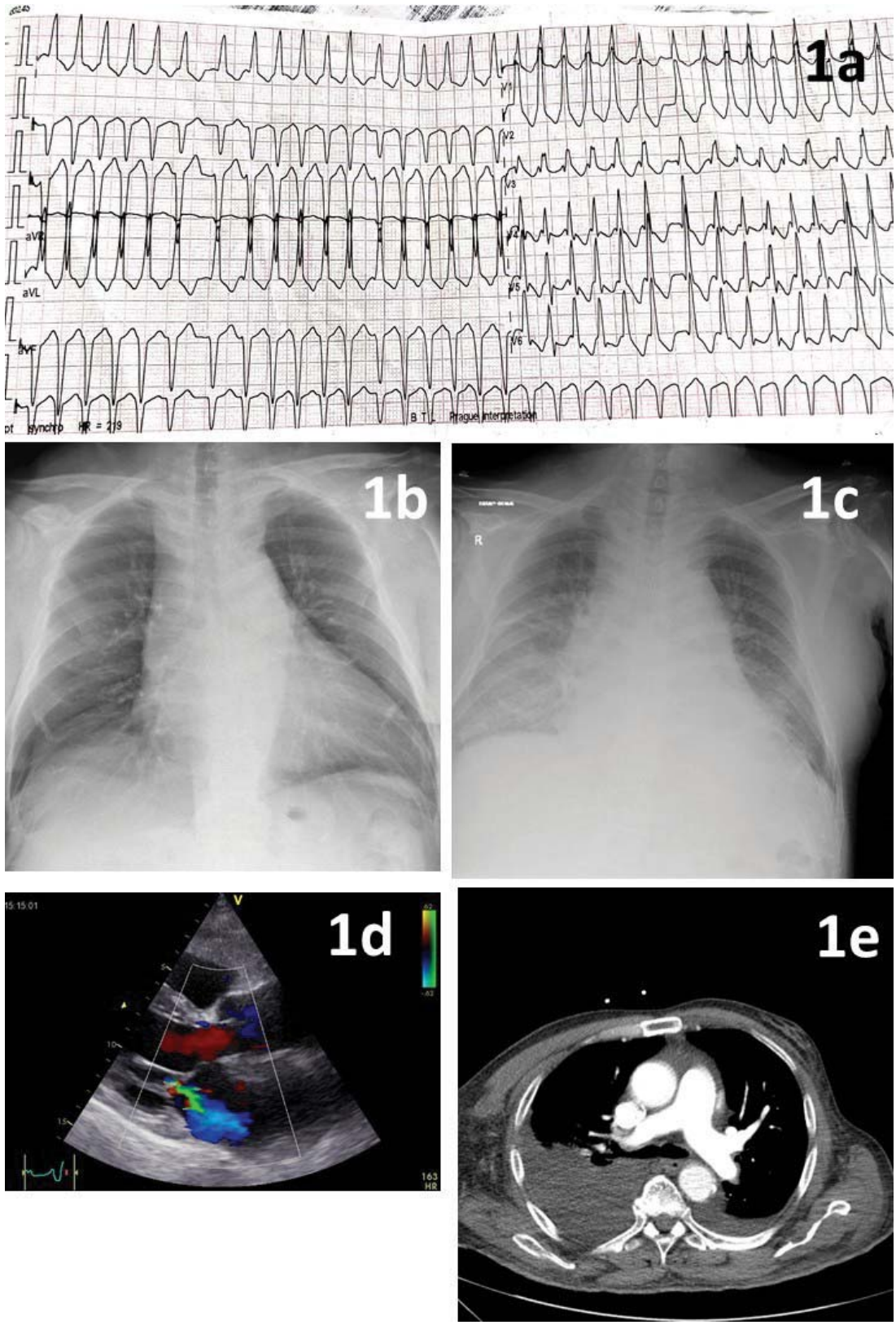

Figure 1. ECG and imaging. 1a – ECG: irregular rhythm (AF), HR ~ 180 bpm, borderline QRS length (120 ms), RBBB pattern, left anterior fascicular block, ST-T segment depression in the anterolateral leads. 1b – CXR 6 months prior – increased cardiac index, no congestion. 1c – CXR at admission – bilateral pulmonary congestion, apical vascular redistribution, and right pleural effusion, 1d – transthoracic echocardiography – moderate functional mitral regurgitation, dilated LA (50 ml/m2), no LVH, mild LV dilation (EDLVD 54 mm), 1e – CT pulmonary angiography – excludes PE, confirms the presence of moderate pleural effusion. Legend: ECG = electrocardiogram, AF = atrial fibrillation, HR = heart rate, RBBB = right bundle branch block, CXR = chest X-ray, LA = left atrium, LVH = left ventricular hypertrophy, LV = left ventricle, CT = computed tomography, PE = pulmonary embolism.

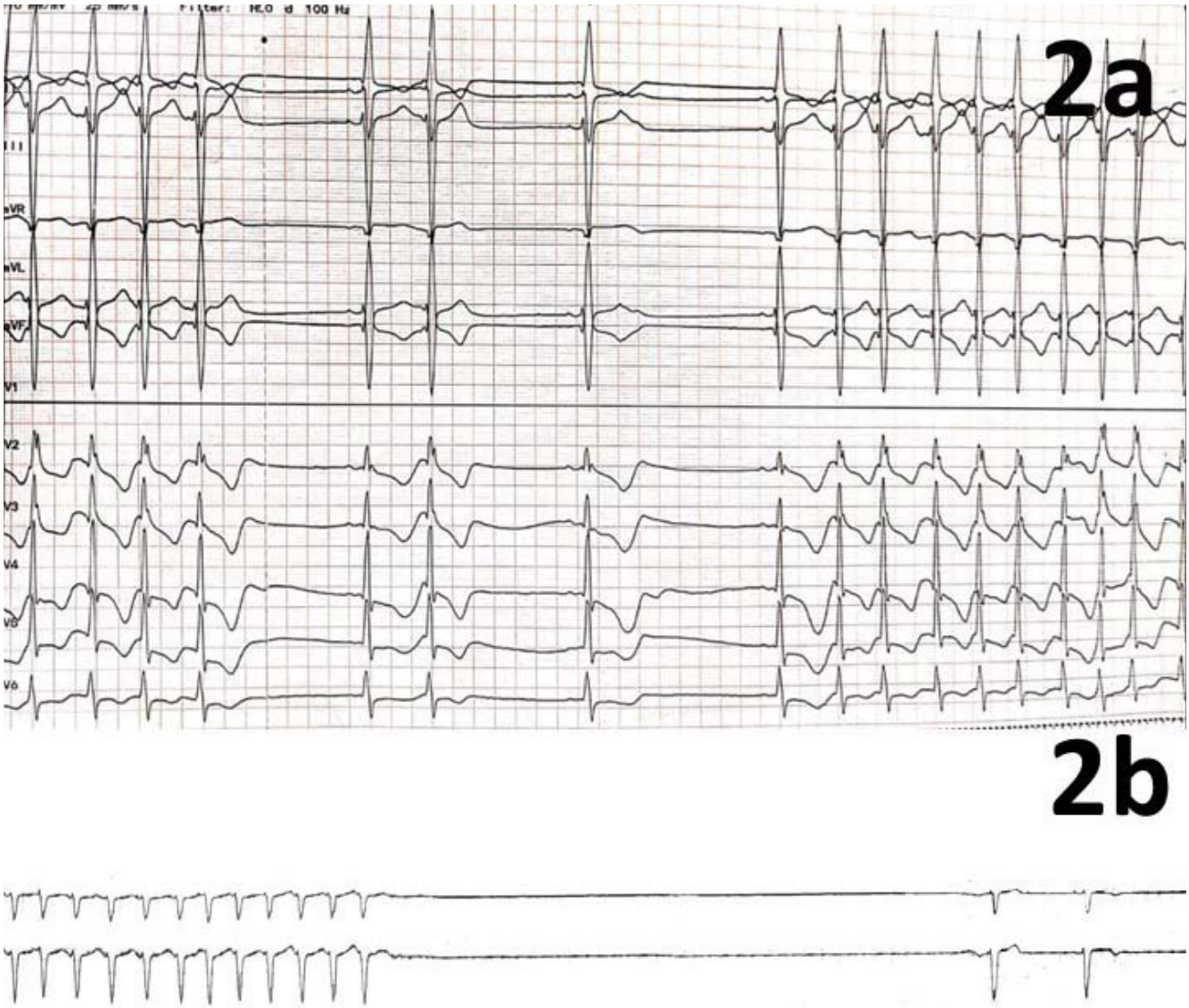

Figure 2. 2a - ECG – day 7 – intermittent conversion to SR with a slow HR (40-50 bpm). 2b - ECG Holter – day 8-9 – alternating moderate / high-rate AF and sinus rhythm, several 5-8 second post conversion symptomatic sinusal pauses (7 second pause pictured). Legend: ECG = electrocardiogram, SR = sinus rhythm, HR = heart rate, AF = atrial fibrillation.

ml, mean HR of 70 bpm (persistent alternating SR and AF – max 110 bpm). The discharge TTE showed a 35% LVEF, moderate mitral and tricuspid regurgitation and mildly elevated estimated PAPs (35 mmHg). Discharge medication included apixaban 5 mg b.i.d., carvedilol 12.5 b.i.d., digoxin 0.25 mg o.d. (5/7), furosemide 40 mg o.d., ramipril 5 mg o.d., spironolactone 50 mg o.d., atorvastatin 80 mg o.d., methimazole 10 mg t.i.d., metformin 1000 mg b.i.d., dapagliflozin 10 mg o.d. and 20U of basal insulin o.d.

At 2-months follow-up, the patient reported class I NYHA HF symptoms, having a LVEF of 45%, mild mitral regurgitation, NTproBNP level of 1.100 pg/dl and a self-measured HR of 65-70 bpm. The pacemaker interrogation revealed persistent SR in the preceding month and 15% ventricular pacing. Digoxin was stopped. The TSH level was slightly lower than the normal interval (0.32 vs 0.34 μUI/ml), but fT3 and fT4 levels were normal. Antithyroid peroxidase antibody levels were increased (2xULN) and the thyroid echography revealed multinodular diffuse disease. A thorough endocrinological follow-up was recommended for further management in a tertiary center.

DISCUSSION

We presented the case of this 62-year-old male patient with concomitant symptomatic sinus node disease, manifested as bradycardia-tachycardia syndrome, and hyperthyroidism leading to high-rate AF and severe LVEF depression.

Thyroid dysfunction should be actively searched in HF patients[2], as hyperthyroidism affects cardiovascular hemodynamics, initially leading to high-output HF and, in late stages, dilated cardiomyopathy[3]. Moreover, between 10% and 25% of hyperthyroid patients have AF[4], usually persistent rather than paroxysmal[5]. Undiagnosed or poorly controlled high-rate AF contributes significantly to HF symptoms through the development of tachycardia-induced cardiomyopathy (TIC) and left ventricle dysfunction.

In our case, the lack of typical symptoms for high-rate tachycardia, low LVEF and dilated left atrium rather suggested longer-standing AF, as opposed to paroxysmal and/or recent onset AF. These characteristics were used in the clinical decision to refrain from any cardioversion attempt, with or without prior transesophageal echocardiography, either drug induced or electrical, as no hemodynamic compromise was present and due to the known low cardioversion success and SR maintenance rates in this scenario. Enforced by the presence of hyperthyroidism, a rate control strategy was recommended[2], using a betablocker and digoxin, whilst amiodarone use was avoided.

Despite the obvious link between the high-rate AF, low LVEF and HF symptoms, a full diagnostic work-up of potential concomitant HF aggravating factors should be conducted. In essence, TIC is still an exclusion diagnosis, usually made after demonstrating the recovery of left ventricular function with normalization of heart rate in the absence of other identifiable etiologies and is usually reversible[6].

The increased D-dimer levels in the presence of RBBB and resting shortness of breath necessitated PE exclusion. The presence of increased troponin levels, diabetes and advanced peripheral artery disease in our case were associated with a high likelihood of obstructive CAD, one of the main causes of HF[1]. Computed tomography coronary angiography, if available, could play a role in diagnosing obstructive CAD, but irregular and/or elevated heart rate are known limiting factors of its accuracy[7]. Thus, an invasive coronary angiogram was preferred. Moreover, rates of up to 69.5% of concomitant asymptomatic CAD in PAD patients have been reported in the literature[8]. Surprisingly, no evidence of CAD was observed in this case, despite the patient's high-risk cardiovascular profile and advanced PAD.

One of our main challenges in this case was establishing the optimal type of pacing therapy. As intermittent conversion to SR was observed after initiating antithyroid and rate control drugs, SR would most probably have been maintained in the long-term after the normalization of the thyroid function and the expected LVEF improvement. The presence of long symptomatic sinus pauses, identified whilst receiving a low-intermediate betablocker dose, with subtherapeutic levels of digoxin, were considered as being consistent with an intrinsic sinus node dysfunction (sick sinus syndrome / bradycardia-tachycardia syndrome) and less likely to be completely drug-induced. However, pacing solely to permit the maintenance or increase of bradycardia inducing drugs in the absence of a conventional pacing indication would rather not have been recommended[2].

At least a dual chamber pacemaker was indicated in this case, as opposed to single-chamber atrial pacing, due to the high risk of developing high grade atrioventricular conduction disturbances in the presence of RBBB9, and to prevent atrioventricular dyssynchrony in the case of single-chamber right ventricle pacing.

The short-term improvement of the LVEF during the hospital stay from 20% to 35% observed in this case was mainly related to the partial rate and rhythm control. Additionally, the reduced stroke volume in tachycardia or variable R–R interval of atrial fibrillation may lead to LVEF underestimation[10]. However, long-term LVEF recovery mechanisms are more complex. The majority of adequately managed patients with TIC present LVEF recovery within 6 months[11], but cases of complete LVEF recovery within 24 hours after rhythm control have been reported[12]. Ventricular reverse remodeling and mitigation of the changes in cardiomyocyte and mitochondrial morphology accompanied by a macrophage-dominated cardiac inflammation reported in these cases[13] could play an important role in LVEF recovery. Myocardial scar burden identified by cardiac magnetic resonance (CMR) imaging may have a prognostic role in patients with TIC. For instance, in the case of AF patients and TIC undergoing ablation, the presence of late gadolinium enhancement on CMR imaging was strongly associated with the lack of LVEF recovery[14] and was a powerful predictor of mortality[15].

The LVEF gradual improvement (from 20% to 45% at 2 months) and HF symptom resolution after HR

control excluded our patient from a primary prevention implantable cardioverter-defibrillator or resynchronization therapy indication. Cardiac resynchronization, as opposed to right ventricle pacing, would have been indicated either first hand (in the absence of potentially reversible LV dysfunction) or as an upgrade (if the LV dysfunction persisted, regardless of NYHA class or AF absence / presence, in the latter case provided a strategy to ensure bi-ventricular capture was in place or maintenance of SR was expected)[16,17].

Digoxin at discharge on top of the beta-blocker was considered indicated, as the recurrence of moderate/high-rate AF episodes was very probable in the short term. Once evidence of optimal rhythm and rate control were available at 2 months follow-up, with no recorded AF episodes, digoxin was stopped, given its inadequate risk-benefit profile in this setting.

Finally, even if TIC is often considered benign, recurrent HF with uncontrollable tachyarrhythmia and sudden death were observed after recovery from cardiac dysfunction. A substrate for HF and/or life-threatening arrhythmia might persist, and careful, long-term follow-up seems required in these patients[18].

CONCLUSION

Thyroid dysfunction should be actively sought in HF patients, as its effects are usually reversible by specific treatment which markedly improve the patient's clinical status. Complex cases need a tailored management approach with close collaboration in a multidisciplinary team and therapeutic decisions should consider the potential reversible causes of LV dysfunction.

Compliance with ethics requirements:

The authors declare no conflict of interest regarding this article. The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national law. Informed consent was obtained from all the patients included in the study.

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