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CASE REPORT (English version)

Pulmonary hypertension in a patient with hyperthyroidism

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Summary

Recent studies have shown consistent association between cardiovascular abnormalities and hyperthyroidism, calling attention on benignity of the condition which generally responds well to thyroid disease treatment.
In this article we describe the case of a female patient with hyperthyroidism treated with radioiodine, which developed pulmonary hypertension, atrial fibrillation and valvular changes, showing significant improvement with methimazole therapy.

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Keywords: Pulmonary hypertension - Hyperthyroidism - Methimazole

Introduction

Pulmonary arterial hypertension (PAH) (Group 1, Venice Classification 2003) is defined based on the following hemodynamic criteria[1]: mean pulmonary artery pressure (MPAP) > 25 mm Hg at rest or > 30 mm Hg in exercise, pulmonary capillary wedge pressure or left atrial pressure <15 mm Hg, and pulmonary vascular resistance > 3 mm Hg • L-1 • s-1 or 240 dyne • s-1 • cm^{-5}. Currently there is an updated classification (Dana Point, USA, 2008) that includes idiopathic pulmonary arterial hypertension, formerly named primary, in Group 1, being: hereditary ($BMPR_2$, ALKI, endoglin), induced by drugs/toxins, related to systemic-pulmonary artery shunt and to hypertension due to persistence of fetal pulmonary circulation pattern[2]; introducing new hemodynamic parameters of values for pulmonary artery pressure, where: normal < 21 mm Hg; boundary between 21 and 25 mm Hg, and evidenced pulmonary hypertension > 25 mm Hg[3,4].
There are several indications about the relationship between its pathogenesis and vasoconstriction phenomenon[1,5]. The increased muscle tone is probably due to a major factor: the imbalance between the production of vasodilators (prostacyclin and nitric oxide -NO-) and vasoconstrictors (endothelin and thromboxane), due to endothelial dysfunction[5,6]. Another important factor may be an alteration of the potassium channel voltage-dependent in smooth muscle cells, which's inhibition would activate calcium channels, leading to the influx of this ion and to vasoconstriction[7].
The potential of severe pulmonary hypertension associated with hyperthyroidism is not yet clearly defined. Auto-immunity associated with endothelial damage, and increased metabolism of intrinsic pulmonary vasodilators, are proposed as the main mechanisms[1].
Also, other cardiac abnormalities related to hyperthyroidism are: arrhythmias (e.g. atrial fibrillation -AF-) and valvular abnormalities (e.g. mitral and tricuspid regurgitation, mitral valve prolapse, etc.)[8,9].
We describe a patient who showed clinical signs of hyperthyroidism in treatment, and who developed PAH, atrial fibrillation, and valvular dysfunction after radioiodine therapy.

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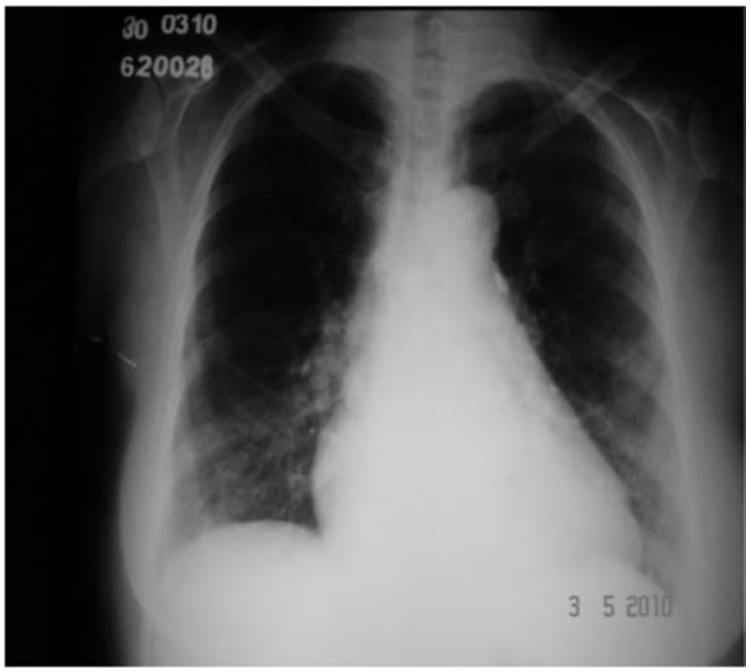

Figure 1. Front view chest X-ray showing an enlarged heart and elongated aorta.

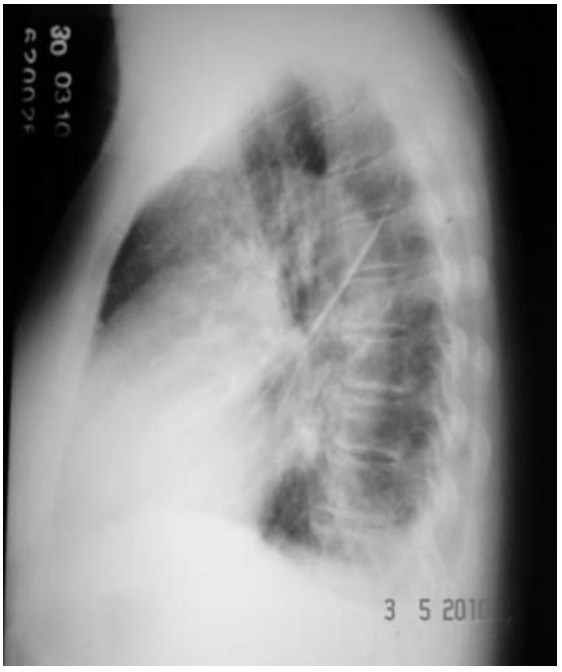

Figure 2. Side view chest X-ray showing retrosternal space reduction by increasing right ventricle, elongated aorta, and dorsal spondylosis.

Case report

We report the case of a female patient, Caucasian, 56 years old, single, born in São Gonçalo, resident of Barreto, Rio de Janeiro (Brazil), who was consulting at external Endocrinology Service of the Antonio Pedro University Hospital (*Hospital Universitário Antônio Pedro* -HUAP-), Niterói, Rio de Janeiro, Brazil. During a routine visit on March 31st 2010, the patient showed generalized edema, cold and hard, associated with complaint of fatigue due to efforts, that emerged two months after therapy for hyperthyroidism with radioactive iodine (according to the patient, symptoms emerged after treatment, worsening progressively since then). Chest X-ray obtained the day before (March 30th 2010 - Figures 1 and 2) showed enlarged heart, elongated aorta, decreased retrosternal space by increased right ventricle (RV) and dorsal spondylosis. We performed an electrocardiogram (Figure 3) which showed atrial fibrillation of undetermined time.

That same day she was admitted to the Endocrinology Nursing of HUAP. On April 9th 2010 we performed an echocardiogram that showed biatrial enlargement, enlarged RV (hypertrophy and dilation), mild mitral regurgitation and severe tricuspid by Doppler, and pulmonary artery systolic pressure (PASP) of 86 mm Hg. Patient evolved with clinical decompensation, showing dyspnea at rest and orthopnea, associated with intermittent and refractory atrial fibrillation,

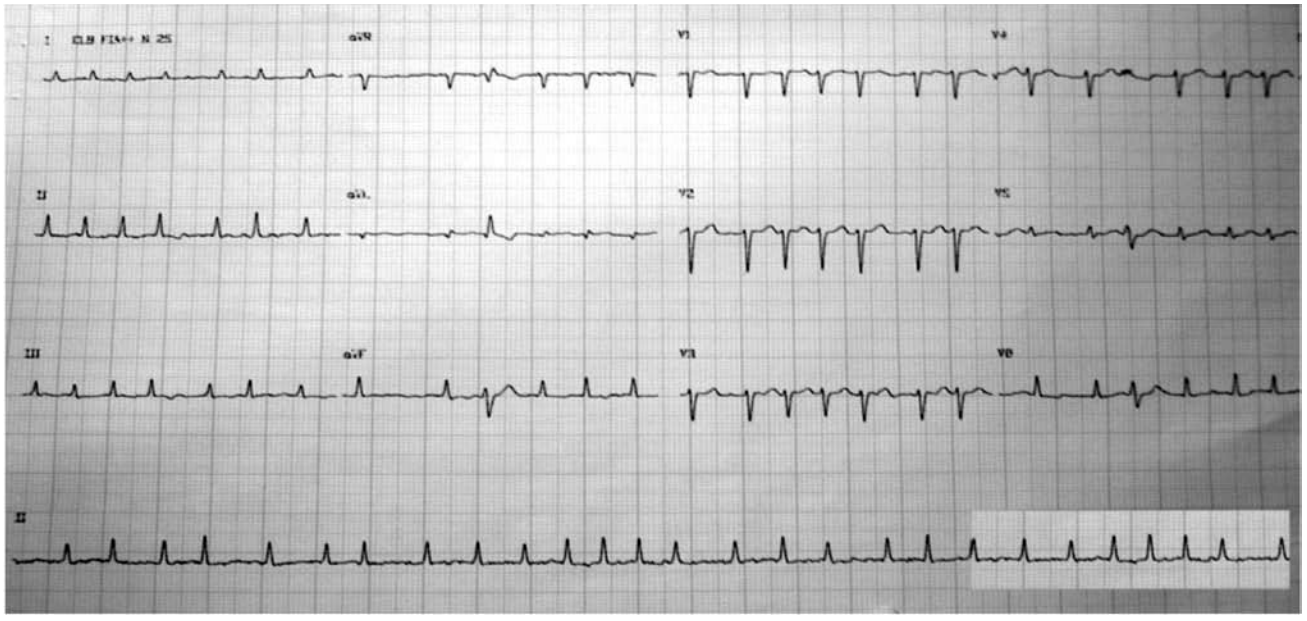

Figure 3. Admission electrocardiogram showing atrial fibrillation and supraventricular extrasystole.

reason why she was referred to Coronary Care Unit (CCU) on April 12th 2010.

At CCU admission patient showed heart rate (HR) of 130 bpm, irregular heartbeat, propulsion of right ventricle at palpation and hyperphonetic 2nd heart sound (P2 > A2), lung auscultation with crackles in the third of both hemithorax, and lower limbs edema.

We diagnosed PAH associated to hyperthyroidism and we started supportive treatment with methimazole. Patient evolved with good response, showing clinical and echocardiographic improvement. The examination held on May 3rd 2010 revealed the following results: right atrial volume 56.83 ml (index: 33.42), left atrial volume: 55.9 ml (index: 32.88); relationship E/E' of 7, and PSAP of 49.76 mm Hg (Figures 4 to 12), being derived to nursing, and later discharged with ambulatory monitoring.

Discussion

Studies show an association between hyperthyroidism and various cardiac abnormalities (e.g. AF, PAH, atrioventricu-

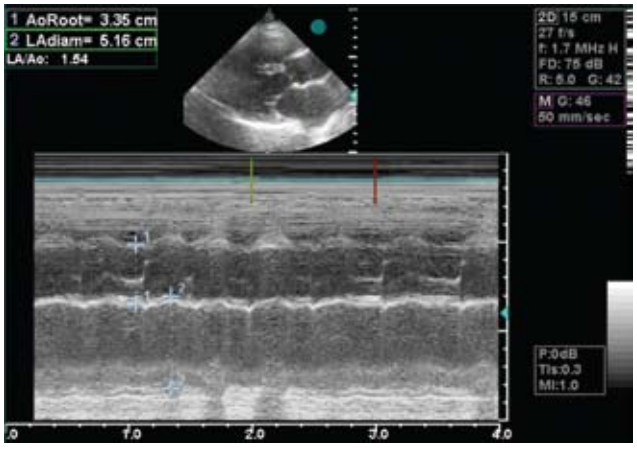

Figure 4. Predischarge Doppler echocardiography (May 30, 2010).

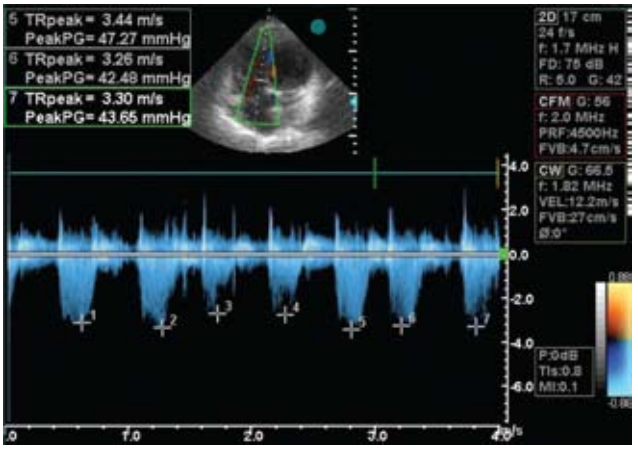

Figure 5. Predischarge Doppler echocardiography (May 30, 2010).

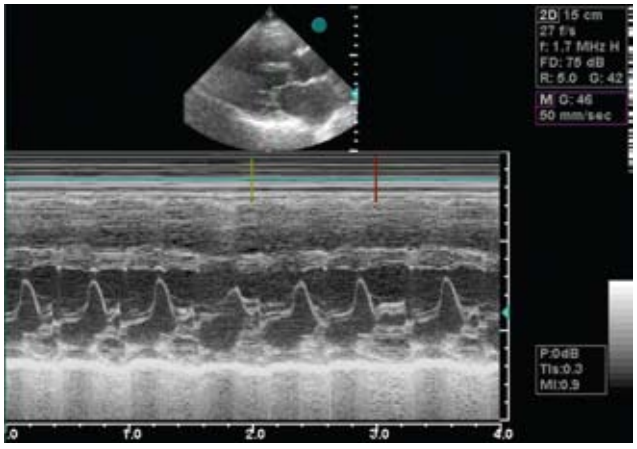

Figure 6. Predischarge Doppler echocardiography (May 30, 2010).

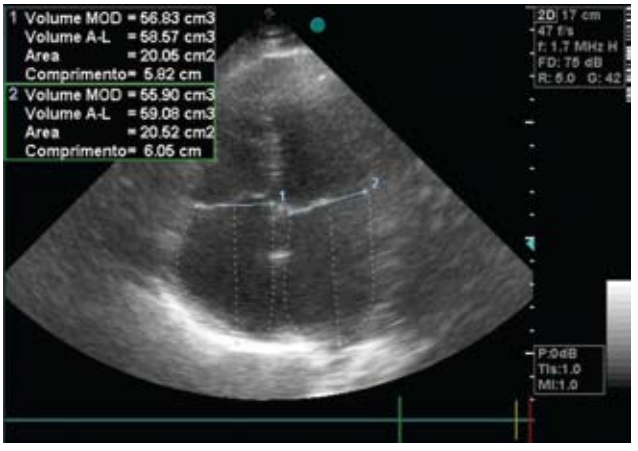

Figure 7. Predischarge Doppler echocardiography (May 30, 2010).

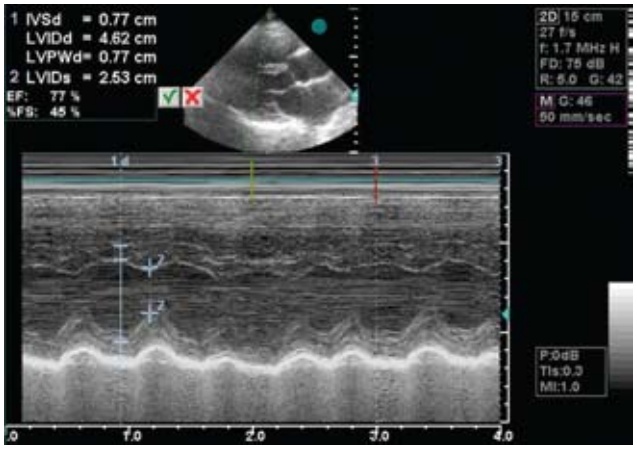

Figure 8. Predischarge Doppler echocardiography (May 30, 2010).

Modo M

Parâmetro	Valor	m1	m2	m3	m4	m5	m6	Método
M-mode Measurements:								
IVSd	0.77 cm	0.77						Medi
LVIDd	4.62 cm	4.62						Medi
LVPWd	0.77 cm	0.77						Medi
LVIDs	2.53 cm	2.53						Medi
LA diam	5.16 cm	5.16						Últim
AoRoot	3.35 cm	3.35						Últim
M-mode Calculations:								
EF Teich	76.62 %			EFcub	83.58 %			
LA/Ao	1.54			Ao/LA	0.65			
LVd Mass	112.7 g			LVd MassPENN	127.1 g			
LVd MassInd	66.40 g/m2			LVd MI PENN	74.86 g/m2			
LVVd Teich	98.10 cm3			LVVs Teich	22.94 cm3			
SV Teich	75.16 cm3			SI Teich	44.28 ml/m2			
%FS	45.24 %			LVVdCub	98.32 cm3			
LVVsCub	16.15 cm3			SVcub	82.17 cm3			

Figure 9. Predischarge Doppler echocardiography (May 30, 2010).

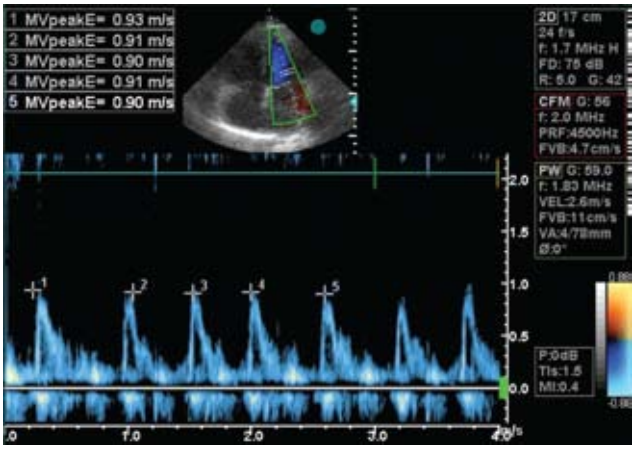

Figure 10. Predischarge Doppler echocardiography (May 30, 2010).

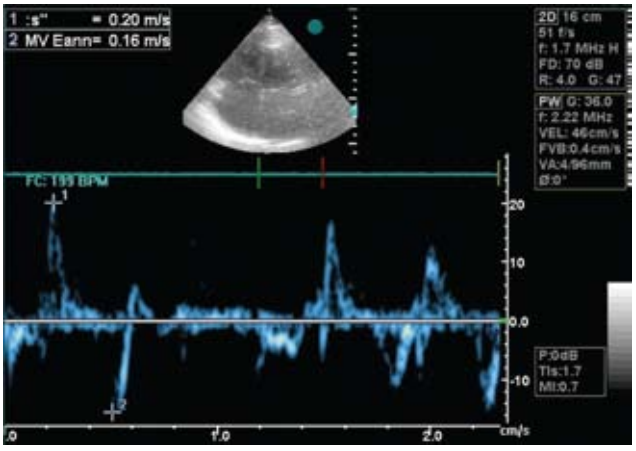

Figure 11. Predischarge Doppler echocardiography (May 30, 2010).

	Doppler							
Parâmetro	Valor	m1	m2	m3	m4	m5	m6	Método
Doppler Measurements:								
:s	0.19 m/s	0.19						Últim
:s"	0.20 m/s	0.21	0.21	0.20				Últim
MV:								
MVpeak E	0.91 m/s	0.93	0.91	0.90	0.91	0.90		Medi
MV Eann	0.13 m/s	0.13	0.11	0.12	0.16			Medi
TV:								
TRpeak	3.14 m/s	3.35	2.72	2.77	3.44	3.26	3.30	Medi
TRpeakPG	39.76 mmHg	44.84	29.66	30.64	47.27	42.48	43.65	Medi
Doppler Calculations:								
MV E/Eann	6.96			RVPs			44.76 mmHg	

Figure 12. Predischarge Doppler echocardiography (May 30, 2010). Shown as the inferior vena cava has a less than 50% collapse in inspiration and a diameter smaller than 1.6 cm, adding 10 mm Hg to the value of 39.76 mm Hg, resulting in a pulmonary artery systolic pressure of 49.76 mm Hg.

lar regurgitation)[8]. Some of the proposed possibilities to explain this association were increased cardiac output and increased pulmonary vascular resistance[8]. PAH potential attributable only to thyrotoxicosis is not clearly defined, being most cases mainly related to hyperthyroidism of autoimmune etiology (Graves disease)[1]. However, other studies show the similarity of PAH in groups with positive or negative autoantibodies[8]. Therefore we propose direct hormonal action as an agent of genesis of PAH in patients with hyperthyroidism[6,7].

Neither was demonstrated PAH correlation in reference to sex, age, cause of hyperthyroidism, presence of cardiac or systemic symptoms and duration, heart rate and hormone levels.

Treatment with methimazole showed a faster response compared to surgical treatment, regarding reduction of pulmonary arterial pressure and regression of cardiac disorders, being its action proposed for the production of L-NANE (methyl ester Ng-nitro-L arginine, an analogue of arginine), causing acute inhibition of synthesis of NO[7]. Patient groups treated with methimazole had lower pulmonary pressure than the group without drug. Therefore it is proposed that methimazole would influence on growth and maturation of vascular cells, and on the channel Ca^{++} ATPase, increasing the pulmonary vasodilator metabolism and reducing vasoconstriction metabolism; factors also implicated in a possible pathogenesis of PAH[1,7].

Conclusion

Taking into account the frequency of hyperthyroidism and indications of hormonal action on the cardiac system, especially in regards to pulmonary pressure, this situation should always be considered when treating a patient with hyperthyroidism (including those with AF and atrioventricular regurgitation, which have higher levels of pulmonary pressure)[8], particularly when radioactive iodine treatment is proposed since there is a high hormonal release due to cell destruction.

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