Case report

Right ventricular reverse remodelling in Idiopathic Pulmonary Arterial Hypertension diagnosed during pregnancy: Is it possible?

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Abstract

We present a case of a 36-year-old woman who developed a severe form of Idiopathic Pulmonary Arterial Hypertension (IPAH) during pregnancy and after emergency delivery. The management of IPAH during or after pregnancy is complex. Due to the severity of her IPAH, an upfront triple combination therapy, including i.v. epoprostenol, was started. The rapid institution of this treatment regimen allowed a complete right ventricular reverse remodelling after 1 year of therapy, leading to a down-titration until complete suspension of epoprostenol from the treatment regimen.

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1. Introduction

Pulmonary Arterial Hypertension (PAH) is a progressive and devastating disease characterized by an increase in pulmonary vascular resistances (PVRi), causing right ventricular (RV) failure and death if not adequately treated.

Idiopathic Pulmonary Arterial Hypertension (IPAH) predominantly affects women of reproductive age. The disease could be diagnosed occasionally during pregnancy, with a high maternal and fetal mortality risk reported.

The management of IPAH during or after pregnancy is complex. Recent international Pulmonary Hypertension (PH) guidelines recommend initial combination therapy, including i.v. prostanoids, for high risk patients (pts) but few data are available on upfront triple combination therapy after delivery. Long-term response after discharge is largely unknown in these pts.

When epoprostenol is begun for a complete therapeutic approach, its withdrawal during follow-up is almost impossible, due to its potent and lifesaving role.

We present a case of complete 1-year RV reverse remodelling that allowed a down-titration until complete suspension of epoprostenol from the treatment regimen.

2. Case report

A 36-year-old woman in the 34th gestational week of her first pregnancy presented to the emergency department with progressive severe dyspnea on exertion. She had no major illnesses and her mother died when she was 2 years old for a non-specified cardiopathy. Regular cardiac follow-up during pregnancy was normal until the 7th month.

She presented in sinus tachycardia (heart rate 135 beats per minute), with systemic hypotension (arterial blood pressure 75/40 mm Hg) and tachypnea (respiratory rate 35/min). On chest auscultation there were minimal bi-basilar rales and a grade IV holosystolic murmur.

Routine biochemistry, including auto-immunity screening, was normal except for NT-proBNP (11.000 pg/ml), with systemic hypotension (arterial blood pressure 75/40 mm Hg) and tachypnea (respiratory rate 35/min). On chest auscultation there were minimal bi-basilar rales and a grade IV holosystolic murmur.

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Due to persistently poor clinical conditions, sildenafil 20 mg TID was initiated and rapidly up-titrated to 80 mg TID. On day-1, epoprostenol was not available in Emergency Unit. Despite sildenafil treatment, poor hemodynamic response was evident (PAP s/d/m 80/35/50 mm Hg, PAWP 9 mmHg, CI 3.06 L/min/m², PVRi 3.26 WU). On day-2 and after a multidisciplinary meeting, continuous i.v. infusion of epoprostenol (rapidly up-titrated to 15 ng/kg/min within 72 h from initiation) was started. Oral bosentan (62.5 mg BID) was added to back ground therapy on day-7. Significant hemodynamic response (PAP s/d/m 80/35/50 mm Hg, PAWP 9 mmHg, CI 3.3 L/min/m², PVRi 12 WU) was recorded after 10 days of treatment regimen. The lady was discharged after 1 month of hospitalization with sildenafil 20 mg TID, bosentan 125 mg BID and epoprostenol 15 ng/kg/min (through a Groshong catheter). The dosage of sildenafil was down-titrated due to National Prescription Policy. Low doses of diuretics were maintained (50 mg/24h). Pre-discharge echocardiographic parameters were: RV diameter 42 mm, TAPSE 19 mm, RV/LV 1.4, sPAP 68 mm Hg.

Due to the progressive normalization of non-invasive parameters (NT-proBNP, 6 minute walk distance, echocardiographic parameters) after 3 months of triple combination therapies, epoprostenol was progressively reduced by 1 ng/kg/min every 4 weeks and finally stopped after 1 year of treatment. Hemodynamic assessment after epoprostenol withdrawal showed PAP s/d/m 31/11/20 mm Hg, PAWP 10 mm Hg, CI 3.06 L/min/m², PVRi 3.26 WU. Echocardiographic parameters were: RV diameter 30 mm, TAPSE 22 mm, RV/LV 0.9, sPAP 33 mm Hg.

At present, after 2 years from epoprostenol withdrawal, she is still on combination therapy with sildenafil 20 mg TID and bosentan 125 mg BID. All non-invasive parameters are stable and she is in WHO class I with a quite normal functional activity. Her son is growing up healthy.

3. Discussion

During pregnancy, blood volume increases up to 50% of the normal value. In normal subjects, adequate cardiac output is maintained through increase in heart rate and reduction of PVRi. This physiologic adaptation lacks in patients with PAH, for whom pregnancy is associated with a further increase in PAP and progressive RV dysfunction and dilatation. For this reason, pregnancy is contra-indicated in women suffering from PAH. With the introduction of specific PAH drugs, peri-partum mortality has decreased from 38% to 25%, but still remaining significantly high both for mothers and for babies [1].

One of the major prognostic determinants in patients with PH is RV dysfunction. Long-term pressure overload in IPAH patients induces progressive RV remodelling, including myocardial hypertrophy, ventricular dilatation, tricuspid regurgitation and early diastolic ventricular septal bowing [2]. In literature, there are some data on RV reverse remodelling in chronic thromboembolic pulmonary hypertension treated with thromboendoarterectomy or balloon pulmonary angioplasty [3] and in IPAH after lung transplantation [4]. The upfront use of a combined triple therapy with phosphodiesterase-5 inhibitors, endothelin-1 receptor antagonists and protonoids has been recently described in patients with severe PAH in WHO class III-IV [5]. This approach has been associated in some cases with normalization of RV function and PVRi. For this reason, the authors suggested its use, especially in extremely critical conditions.

We performed the same approach of Sitbon et al. in a pregnant woman that presented with a severe RV shock at time of delivery. Despite the initiation of epoprostenol as second treatment regimen (after only 1 day of delay), the rapid institution of the upfront triple combination therapy with bosentan, sildenafil and epoprostenol allowed a complete RV reverse remodelling after 1 year of epoprostenol therapy, leading to a quite normalization of clinical status (WHO class I), echocardiographic [Fig. 1], biohumoral and hemodynamic parameters. With a normalized RV function, epoprostenol could be down-titrated and sometimes withdrew, improving patient compliance to IPAH specific therapies.

In conclusion, we suggest that in very compromised pregnant at time of diagnosis, an upfront triple combination therapy could lead to a complete early RV reverse remodelling, improving significantly the survival time.

References

[1] E. Bédard, K. Dimopoulos, M.A. Gatzoulis, Has there been any progress made on pregnancy outcomes among women with pulmonary arterial hypertension? Eur. Heart J. 30 (3) (2009 Feb) 256–265, http://dx.doi.org/10.1093/eurheartj/ehn597.
[2] S.A. Van Wolferen, I.T. Marcus, A. Boonstra, et al., Prognostic value of right ventricular mass, volume and function in idiopathic pulmonary arterial hypertension, Eur. Heart J. 28 (2007) 1250–1257, http://dx.doi.org/10.1093/eurheartj/ehl477.
[3] S. Fukui, T. Ogo, Y. Morita, et al., Right ventricular reverse remodelling after balloon pulmonary angioplasty, Eur. Respir. J. 43 (2014) 1394–1402 doi: 1183/ 09031936.0012914.
[4] M.T. Kasimir, G. Seebacher, P. Jaksh, et al., Reverse cardiac remodelling in patients with primary pulmonary hypertension after isolated lung transplantation, Eur. J. Cardiothorac. Surg. 26 (4) (2004 Oct) 776–781.
[5] O. Sitbon, X. Jais, L. Savale, et al., Upfront triple combination therapy in pulmonary arterial hypertension: a pilot study, Eur. Respir. J. 43 (6) (2014 Jun) 1681–1697, http://dx.doi.org/10.1183/09031936.00116312.