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Scientific letter

Pregnancy and Pulmonary Arterial Hypertension: A Case Report

Embarazo e hipertensión arterial pulmonar: presentación de un caso

Dear Editor:

Physiological changes during pregnancy and peri-partum period can lead to hemodynamic stress with right ventricular (RV) failure, bleeding and thrombotic complications. Although maternal survival has improved with advances in PAH therapy and multidisciplinary approach, pregnancy is still not recommended.[1–4]

The authors present a case of successfully managed PAH pregnancy in a 28-year-old woman from Guinea Bissau, *gravida 1 para 0*. In 2014, she was admitted for acute pulmonary thromboembolism. Investigation established the diagnosis of Systemic Lupus Erythematosus (SLE)/Sjögren Syndrome and Antiphospholipid Syndrome (APS). After pulmonary emboli resolved, Right Heart Catheterization (RHC) with mean Pulmonary Artery Pressure (mPAP) 66 mmHg, Pulmonary Vascular Resistance (PVR) 25 Wu and Cardiac Index (CI) 2.2 L/min/m^2 diagnosed her as PAH Group 1.4.1. Sildenafil 25 mg tid, prednisolone 7.5 mg id, hydroxycloroquine 250 id, azathioprine 100 mg id and warfarin were initiated.

In 2017, she was referred to our Pulmonary Hypertension Reference Center. She was in functional class II and in the six-minute walk test (6MWT) walked 240 m with severe dessaturation (minimum SpO_2 59%). Further evaluation was negative. The RHC showed mPAP = 42 mmHg, Right Atrial Pressure (RAP) = 2 mmHg, SvO_2 = 68%, PVR = 7.7 Wu, CI = 2.5 L/min/m^2. Ambrisentan 10 mg id and diuretics were added, with improvement.

Pregnancy diagnosis was made at 6 weeks gestation and she refused medical interruption. Close monitoring at the PH clinic and a team of rheumatologists, obstetricians, immuno-hemotherapists and anaesthesiologists worked together to provide the optimal care.

Ambrisentan and warfarin were withheld; sildenafil and furosemide were maintained. Anticoagulation with enoxaparin 60 mg bid and folic acid supplementation were started.

At 16 weeks gestation she was admitted to the Intensive Care Unit (ICU) to initiate intravenous epoprostenol with invasive monitoring. Dosage up-titration was done during 10 days to reach 12.5 ng/kg/min. She remained clinically stable in functional class I. Fetal wellbeing was documented twice during in-hospital epoprostenol titration.

Maternal echocardiography was performed at 25 weeks gestation with no signs of RV failure.

A scheduled hospitalization for surveillance at 35 weeks and cesarean delivery at 36 weeks was decided.

At 36 weeks gestation spontaneous rupture of membranes occurred. An urgent C-section was performed under general anesthesia because of lack of security time interval for neuroaxis block since the last enoxaparin administration. No major bleeding or other complications were registered. A female newborn baby was delivered, 2380 g and Apgar score 9/10/10.

After C-section she was transferred to ICU where she remained stable on epoprostenol 12.5 ng/kg/min, sildenafil 25 mg 8/8 h, furosemide, enoxaparin and imunosuppressors; 24 h after delivery she was transferred to Intermediate Care. To allow the possibility of breastfeeding, maternal milk was collected. Hospital discharge was on the 4th postoperative day. Follow-up was maintained weekly at the PH clinic.

She remained in functional class I. There was no dilation of the right chambers or signs of RV failure on echocardiogram performed three months after delivery. At that point, breastfeeding was stopped, macitentan reinitiated at the dose of 10 mg id and RHC was performed: PmAP = 41 mmHg, RAP = 8 mmHg, PVR = 5.19 Wu, CI = 2.64 L/min/m^2. The cardiopulmonary exercise test showed peak VO_2 15.7 mL/kg/min (35–65% predicted) and VE/VCO_2 36–44.9 grades. Considering the low risk prognosis, epoprostenol was tapered at the rate of 1 ng/kg/min per week.

She is currently on sildenafil and ambrisentan, in functional class I, RHC mPAP = 32 mmHg, RAP = 2 mmHg, PVR = 5.27 Wu, CI = 2.64L/min/m^2: REVEAL score = 1. Her daughter is healthy and growing normally.

To supply the growing demands of fetus and mother there is an increase in blood volume, left ventricular mass and CO during pregnancy.[2] Systemic vascular resistance and blood pressure decrease due to the increasing levels of estrogen and progesterone.[1] Red cell mass also increases but only about 25%, which may lead to physiological anemia.[2] Changes in coagulation lead to hypercoagulability and a higher risk of thromboembolic events.[5,6] These changes affect the RV increasing O_2 consumption and might result in RV failure PAH patients.[2]

The peri-partum period is the most difficult to manage, because during labor there is volume overload with 500 mL of blood diverted to maternal circulation in each contraction.[6,7] On the other hand, during delivery there is significant blood loss contributing to hypotension.[7] This duality of hypotension and volume overload occurring acutely in a patient with PAH might induce RV failure.

In our patient, we also had to consider the risks of SLE *per se* with a higher risk of fetal loss, pre-term birth, intra-uterine growth restriction and neonatal lupus syndrome. Concerning the mother there is a risk of disease flare and pre-eclampsia.[8]

A systematic review comparing overall maternal mortality in patients with PAH in the period of 1997–2007 with previously published data showed a reduction from 38% to 25%, still a very high mortality rate.[4,9] There are no guidelines regarding the management of pregnant women with PAH and published data refers

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mostly to case series. Close follow up by a multidisciplinary team including clinical and echocardiographic monitoring were put in place, according to literature recommendations.[7]

Despite good control with sildenafil and ambrisentan before pregnancy, our patient presented worrisome risk factors, such as high mPAP and PVR and primiparity.[4,10] Considering that ambrisentan had to be interrupted due to potential teratogenic effect, epoprostenol was started after the first trimester, as in other successful cases.[11,12]

Timing and mode of delivery is another matter of debate in PAH. Some authors recommend delivery around 34 weeks gestation because towards the term of pregnancy the physiological changes reach a peak with increased difficulty of cardiovascular system to cope. Delivery between 34 and 37 weeks gestation can be accomplished in stable patients with mild PAH without deterioration during pregnancy.[13,14]

Recents series4 report preference for C-section over vaginal delivery as the latter is associated with increase in CO of 34% at full cervical dilation, increase in venous return during prolonged labor and deleterious hemodynamic effects associated with pushing which may induce acidosis, hypercapnia or hypoxia.[1,13,15]

As in the first month after delivery is when maternal mortality is higher,[5,9,15] weekly follow-up visits and specific therapy with epoprostenol and sildenafil were maintained until reevaluation.

Management of pregnancy in PAH patients is a challenge due to the risks for the mother and fetus. The recommendation is against it and no guidelines exist in how to manage those who refuse therapeutic abortion. The strategy in our case was to guarantee PAH control with the introduction of epoprostenol and ensure the support of a well-articulated multidisciplinary team.

With the improvement of PAH therapy and more patients achieving low risk prognosis, more women will probably want to assume the risk of childbearing.

References

1. Hemnes AR, Kiely DG, Cockrill BA, Safdar Z, Wilson VJ, Hazmi MA, et al. Statement on pregnancy in pulmonary hypertension from the Pulmonary Vascular Research Institute. Pulm Circ. 2015;5:435–65, http://dx.doi.org/10.1086/682230.
2. Olsson KM, Channick R. Pregnancy in pulmonary arterial hypertension. Eur Respir Rev. 2016;25:431–7, http://dx.doi.org/10.1183/16000617.0079-2016.
3. Rashidi F, Sate H. Pregnancy outcome in a pregnant patient with idiopathic Pulmonary Arterial Hypertension: a case report and review of the literature. J Med Case Rep. 2018;12:31, http://dx.doi.org/10.1186/s13256-017-1547-1.
4. Bédard E, Konstantinos Dimopoulos K, Gatzoulis MA. Has there been any progress made on pregnancy outcomes among women with pulmonary arterial hypertension? Eur Heart J. 2009;30:256–65, http://dx.doi.org/10.1093/eurheartj/ehn597.
5. Olsson KM, Jais X. Birth control and pregnancy management in pulmonary hypertension. Semin Respir Crit Care Med. 2013;34:681–8.
6. Regitz-Zagrosek V, Blomstrom Lundqvist C, Borghi C, Cifkova R, Ferreira R, Foidart JM, et al. ESC Guidelines on the management of cardiovascular diseases during pregnancy. Eur Heart J. 2011;32:3147–97.
7. Hsu CH, Gomberg-Maitland M, Glassner C, Chen JH. The management of pregnancy and pregnancy-related medical conditions in pulmonary arterial hypertension patients. Int J Clin Pract Suppl. 2011;175:6–14.
8. Lateef A, Petri M. Managing lupus patients during pregnancy. Best Pract Res Clin Rheumatol. 2013;27, http://dx.doi.org/10.1016/j.berh.2013.07.005.
9. Weiss BM, Zemp L, Seifert B, Hess OM. Outcome of pulmonary vascular disease in pregnancy: a systematic overview from 1978 through 1996. J Am Coll Cardiol. 1998;31:1650–7.
10. Jais X, Olsson KM, Barbera JA, Blanco I, Torbicki A, Peacok A, et al. Pregnancy outcomes in pulmonary arterial hypertension in the modern management era. Eur Respir J. 2012;40:881–5.
11. Bildirici I, Shumway JB. Intravenous and inhaled epoprostenol for primary pulmonary hypertension during pregnancy and delivery. Obstet Gynecol. 2004;103:1102–5.
12. Stewart R, Tuazon D, Olson G, Duarte AG. Pregnancy and primary pulmonary hypertension: successful outcome with epoprostenol therapy. Chest. 2001;119:973–5.
13. Kiely D, Condliffe R, Webster V, Mills G, Wrench I, Gandhi S, et al. Improved survival in pregnancy and pulmonary hypertension using a multiprofessional approach. BJOG. 2010;117:565–74.
14. Ladouceur M. Grossesse et hypertension artérielle pulmonaire. Presse Med. 2019, http://dx.doi.org/10.1016/j.lpm.2019.08.007.
15. Uebing A, Steer PJ, Yentis SM, Gatzoulis MA. Pregnancy and congenital heart disease. BMJ. 2006;332:401–6.

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