Pulmonary hypertension imitating HELLP syndrome

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Abstract

A case of undiagnosed pulmonary hypertension in a woman with mixed connective tissue disease presenting with microangiopathic haemolysis, thrombocytopenia and elevated liver enzymes imitating severe preeclampsia (HELLP syndrome) is described. Connective tissue disorders are associated with an increased prevalence of pulmonary hypertension. Maternal mortality rates with pulmonary hypertension in pregnancy are extremely high. All women with connective tissue disorders should have pulmonary hypertension excluded by echocardiography before attempting conception. End-stage pulmonary hypertension may be associated with haemolysis and thrombocytopenia and thus may imitate severe preeclampsia in pregnant women. There may be a role for extracorporeal membrane oxygenation in the peripartum management of women with severe pulmonary hypertension.

Keywords

HELLP syndrome, mixed connective tissue disease, preeclampsia, pregnancy, pulmonary hypertension

Introduction

Connective tissue disorders are associated with an increased prevalence of pulmonary hypertension (PHT), as well as an increased risk of preeclampsia.^{1–4} Pregnancy with PHT is associated with an extremely high risk of maternal mortality.^{5,6} Microangiopathic haemolysis and thrombocytopenia have rarely been reported with end-stage PHT in non-pregnant subjects.^{7–10} A case of microangiopathic haemolysis, thrombocytopenia and abnormal liver function tests incorrectly attributed to severe preeclampsia in a pregnant woman with undiagnosed PHT complicating mixed connective tissue disease (MCTD) resulting in maternal death is presented.

Case report

A 29-year-old Gravida 2, para 1 at 33 weeks gestation presented to an Emergency Department complaining of three days of dyspnoea and peripheral oedema. MCTD had been diagnosed at age 21 years, manifesting as arthralgia, Raynaud phenomenon, thrombocytopenia and sclerodactyly. Her first pregnancy at age 26 years had been complicated by preeclampsia necessitating delivery at 36 weeks gestation. Previously anticardiolipin antibody was negative and urine micro albumin was normal. Prior to the current pregnancy, the subject had not required medication for two years. At 14 weeks gestation, prednisone 25 mg mane was commenced because of a fall in platelet count to $41 \times 10^9/L$ (normal 150–450). There was a satisfactory response and the subject was subsequently maintained on 15 mg of prednisone a day until presentation.

On examination in the emergency room, oxygen saturations were 96% while breathing room air, respiratory rate was 20 breaths per minute, pulse was regular at 100 beats per minute and blood pressure was 130/90 mm Hg. Jugular venous pressure was elevated 5 cm above the sternal angle, heart sounds were dual with a normal pulmonary component of the second sound, chest auscultation was normal, there was no liver tenderness and ward test of urine revealed ++ protein. Laboratory investigations revealed haemolysis, elevated liver enzymes, coagulopathy and a fall in platelet count compared with a week earlier (Table 1). Computerised axial tomography pulmonary angiography was negative for pulmonary embolism. The provisional diagnosis was preeclampsia complicated by haemolysis, elevated liver enzymes and low platelets (HELLP syndrome). The mother was given intravenous hydrocortisone and proceeded to emergency caesarean section with general anaesthesia. Immediately following delivery of a healthy boy, the mother suffered a cardiac arrest and was unable to be resuscitated.

The autopsy findings were of severe PHT and extensive centrilobular congestion of the liver (Figures 1 and 2). Lung histology demonstrated intimal thickening of large pulmonary arteries, severe extensive cellular intimal proliferation in small arteries and arterioles, numerous plexiform lesions and occasional fibrin deposition, without amniotic fluid embolism or interstitial lung disease. There were no features of HELLP syndrome on liver or placental histology. Centrilobular hepatic congestion is the typical histology seen in subjects with liver disease due to right heart failure.¹¹

Discussion

The prevalence of PHT (based on echocardiographic criteria and symptomatic complications) and preeclampsia in connective tissue disorders is summarised in Table 2.^{1–4} One previous case of PHT presenting with features consistent with HELLP syndrome has been reported in abstract, the woman suffering cardiac arrest after emergency surgical termination of pregnancy at 22 weeks gestation.¹² The subject was successfully resuscitated and following two weeks of bridging extracorporeal membrane oxygenation (ECMO) underwent heart-lung transplantation.

Seven non-pregnant subjects with PHT have been reported as manifesting microangiopathic haemolytic anaemia and thrombocytopenia.^{7–10} All seven patients died within 10 days of presentation.

PHT in pregnancy is associated with a 25–56% maternal mortality.^{5,6} Haemodynamic decompensation may occur in second trimester due to the normal maternal physiologic changes of increase in plasma volume, rise in red cell mass and increase in cardiac output. Subjects with PHT and increased pulmonary vascular resistance may be unable to accommodate these changes resulting in progressive right ventricular failure, reduced left ventricular preload and symptoms of progressive dyspnoea, chest pain, presyncope and syncope.¹³ Risk of maternal death is greatest at time of delivery and in the first fortnight postpartum. Autotransfusion of 500 mL blood from the placenta, sudden increase in pulmonary vascular resistance and reduced ventricular

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Table 1. Laboratory investigations at presentation and one week earlier.

	1 Week earlier	On presentation	Normal range
Cr ($\mu\text{mol/L}$)	60	78	30–70
Urate (mmol/L)	0.38	0.54	0.14–0.35
AST (U/L)	31	215	0–41
ALT (U/L)	30	196	0–45
LDH (U/L)	274	377	80–250
Bilirubin ($\mu\text{mol/L}$)	15	26	<20
Haptoglobin (g/L)	–	<0.06	
Haemoglobin ($\times 10^9/\text{L}$)	143	157	115–165
Platelets ($\times 10^9/\text{L}$)	76	51	150–400
Reticulocytes ($\times 10^9/\text{L}$)	–	161	27–135
PT (s)	–	18.7	11–16
APTT (s)	–	45.1	25–42
Fibrinogen (g/L)	–	3.3	1.5–4.0
D-dimer (mg/L)	–	>4.0	<0.5

Cr: Serum creatinine; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; LDH: Lactate dehydrogenase; PT: Prothrombin time; APTT: Activated partial thromboplastin time.

Figure 1. H&E preparation ($\times 200$ magnification) of lung histology revealing remodelled pulmonary artery.

contractility immediately after delivery are factors in acute right ventricular failure, loss of preload to the left ventricle and cardiovascular collapse.

There are no factors predictive of maternal mortality. Foetal and neonatal complications include stillbirth and neonatal death (13%), foetal growth restriction (in up to 33%) and preterm delivery (up to 100%). There are no controlled trials or consensus recommendations regarding treatment of PHT in pregnancy. Calcium channel blockers, intravenous prostacyclin, inhaled nitric oxide, nebulised iloprost and oral sildenafil have been used. One study of 16 non-pregnant subjects with mild-moderate PHT due to MCTD and SLE found that 50% of patients demonstrated a significant fall in mean pulmonary artery pressure and improvement in New York Heart Association functional class following six months treatment with monthly intravenous cyclophosphamide and oral prednisone 0.5–1 mg/kg/day.¹⁴ The dose of prednisone used to treat thrombocytopenia in the subject presented would

Figure 2. Liver histology demonstrating severe centrilobular congestion.**Table 2.** Prevalence of PHT and preeclampsia in connective tissue disorders.

Connective tissue disease	PHT on echo	Symptomatic PHT	Preeclampsia
MCTD	16%	5%	Up to 15%
SLE	9.3%	0.9%	13–66%
Systemic sclerosis	11.4%	2.6%	10–23%
Polymyositis/dermatomyositis	0.6%	–	Unknown
Primary antiphospholipid Syndrome	23.5%	3.5%	10–25%
SLE and antiphospholipid syndrome	43%	1.8%	50%
Sjogrens syndrome	Unknown	Rare	Unknown

MCTD: mixed connective tissue disease; SLE: systemic lupus erythematosus; PHT: pulmonary hypertension.

have been unlikely to be of any benefit regarding the severity of her PHT. Anticoagulation with low molecular weight or unfractionated heparin should be considered, and oxygen administered if the mother is hypoxic. Endothelin-1 receptor antagonists are teratogenic in animals and therefore contraindicated in pregnancy. There is no consensus regarding the relative safety of vaginal delivery versus caesarean section in mothers with PHT.¹² While all forms of regional anaesthesia have been employed successfully in mothers with PHT, advantages of general anaesthesia include ease of use of trans oesophageal echocardiography to monitor cardiac output during delivery, ease of delivery of direct vasodilators and rapid initiation of cardiac bypass in the event of maternal complications. A case report described the successful use of vasopressin (bolus 0.5 units intravenously followed by infusion at 0.06–0.08 units/min) in improving maternal hemodynamics in two subjects with PHT who developed profound hypotension after caesarean section.¹⁵

ECMO has been successfully used as a bridging treatment to lung transplantation, while awaiting adequate pharmacotherapy, and prior to pulmonary endarterectomy in non-pregnant subjects with pulmonary arterial hypertensive crisis.^{16–18} ECMO has also been used as a support to general anaesthesia in delivery by caesarean section, as well as the termination of pregnancy in women with severe primary PHT.^{19,20}

Conclusion

In conclusion, a case of maternal death due to undiagnosed PHT presenting with features of HELLP syndrome in a woman with MCTD is presented.

The lessons from this case are:

1. The extreme risk of maternal death with PHT in pregnancy mandates that PHT is excluded in women with connective tissue disorders by echocardiography prior to attempting conception. Expert guidelines recommend annual screening for PHT by echocardiography in subjects with the scleroderma spectrum of diseases.²¹ Contraception advice is both critical and complex in women with PHT. Oestrogen-containing oral contraceptive pills must be avoided because of thromboembolic risk, implanted progestagens may have reduced efficacy in the setting of bosentan therapy, sterilisation in young women is associated in a significant failure rate and risk of ectopic pregnancy, and insertion of the levonorgestrel-releasing intrauterine device may be associated with a vagal reaction and cardiovascular collapse.^{22,23} Hysteroscopic insertion of a micro-insert system (Essure) may be the preferred method of sterilisation for women with PAH.²⁴
2. Antepartum care of women with PHT should be by multidisciplinary teams with expertise in this area. The availability of ECMO should be a consideration regarding the location of delivery and postpartum care of women with moderate-severe PHT.
3. Obstetricians, physicians, anaesthetists and intensive care specialists involved in the care of high-risk pregnancies should be aware that severe PHT may manifest as microangiopathic haemolysis and thrombocytopenia and thus imitate HELLP syndrome.

Ethical approval

The subject's partner gave verbal permission for the case to be published at the time of counselling. It was not possible to obtain written approval as he returned to his native country with his two children a short time later.

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