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Case Report

Acute Pulmonary Edema and Pulmonary Hypertension in a Pre-Eclamptic Pre-Term Woman

Robert Ricketts*, Henry Huang and Ashutosh Wali

Department of Anesthesiology, Baylor College of Medicine, USA

***Corresponding Author:** Robert Ricketts MD, Department of Anesthesiology, Baylor College of Medicine, USA.

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Abstract

Although uncommon, acute pulmonary edema is a significant cause of morbidity and mortality in the peripartum woman. Many factors intrinsic to pregnancy and the patient herself contribute to the development of pulmonary edema in the peripartum woman. We present a unique pre-term patient who was identified as having acute onset pulmonary edema and pulmonary hypertension concurrently with having pre-eclampsia and pre-existing chronic hypertension. The combined pulmonary edema and pulmonary hypertension of this patient posed unique challenges in her initial assessment and management, which we review. We further review the literature on the causes of acute pulmonary edema in the peripartum woman in addition to discussing diagnostic and management considerations of these patients.

Keywords: Pulmonary Edema; Pulmonary Hypertension; Pre-Eclampsia; Pregnancy

Introduction

Acute pulmonary edema is a rare event in pregnancy with estimated rates ranging from 0.08% to 0.5% of pregnancies being affected [1-3]. Despite its infrequent occurrence, acute pulmonary edema accounts for nearly one in four of maternal deaths in the peripartum period in resource rich countries [4,5]. This figure is likely even higher in developing countries with some countries reporting upwards of 30% maternal mortality associated with pulmonary edema [6]

There are many reasons pregnant woman are at increased risk for acute pulmonary edema. Given the variety of potential causes of pulmonary edema in the peripartum woman, its work up and management can often be complex and usually necessitates a multidisciplinary approach [5].

We present a case of acute pulmonary edema in a peripartum woman. She had preexisting and developing comorbidities that likely contributed to her pulmonary edema. In this article, we will discuss the causes of acute pulmonary edema in the peripartum woman. We also present a discussion on the therapeutic and diagnostic approach to such patients.

Clinical Case

A 40-year-old woman, Gravida 5, para 3 at 29 weeks 5 days gestation with known chronic hypertension and type 2 diabetes mellitus presented with elevated blood pressure. She was known to be non-compliant with her home anti-hypertensive medicines of nifedipine and labetalol. She had no other significant medical issues.

At presentation, the patient had blood pressures measured to be in the 250s systolic and 120s diastolic. She denied headaches, chest pain, shortness of breath, or nosebleeds and otherwise appeared well. The patient reported being off her medications for three days. Her fetus was breech presentation on ultrasound, but otherwise had reassuring fetal heart tones. Given the patient's pregnancy, she was admitted for further management and to investigate possible pre-eclampsia.

The patient was administered 6 grams of magnesium sulfate as a loading dose and then placed on a magnesium drip at a rate intravenently of 2 grams per hour for seizure prophylaxis. She was given betamethasone for fetal lung maturity. Her blood pressure was initially managed with intravenous labetalol and nifedipine, but she eventually needed a nicaridpine infusion. By HD#2, her blood pressure was in the 150s/90s on nifedipine and labetalol. The patient's urine protein to creatinine ratio was 0.33 which qualified her as having pre-eclampsia

On HD#3 the patient became tachypneic and had oxygen desaturations to the 80's. Bibasilar inspiratory pulmonary crackles were noted on examination and chest radiograph revealed new onset mild pulmonary edema and an enlarged cardiac silhouette (Figure 1). Given these new findings, the patient was diagnosed as having pre-eclampsia with severe features. The decision was made to deliver the patient's baby via cesarean section given the patient's fetus was breech presentation.

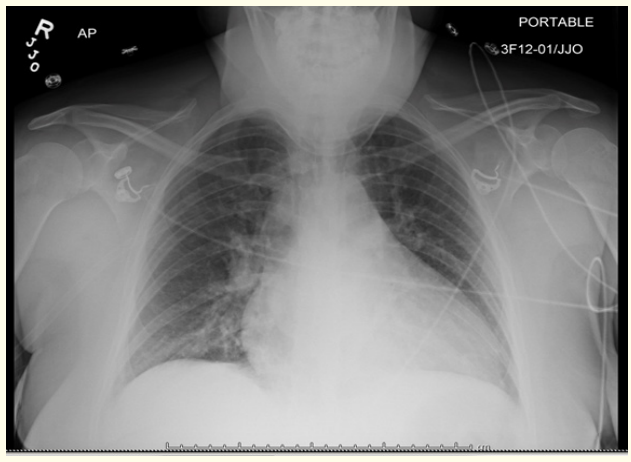

Figure 1: AP view chest radiograph view of our patient prior to delivery via cesarean section.

As the patient had normal platelet and coagulation studies, anesthesia was obtained via epidurally administered 2% lidocaine with bicarbonate. A total of 20 ml of local anesthetic was given to the patient and a T4 level was obtained. As we established a surgical block for the procedure, the patient had marked decrease in blood pressure from an initial reading of 167/73 mm of Hg to 100/40 mm Hg as we bloused her epidural. Given this precipitous fall in the setting of acute pulmonary edema, the patient was placed on a norepinephrine drip to support her blood pressures (2 - 4 mcg/min). We further attempted to diurese her with 10 mg of IV furosemide which produced modest urine output of 150 ml over the course of the two-hour procedure. The Anesthesia team elected for a conservative approach to intraoperative fluids. The patient received only 800 ml of intravenous lactated ringer's solution during the procedure. The procedure proceeded without incident and the baby was successfully delivered.

The patient had an echocardiogram performed after her procedure, which showed normal left ventricular size, mild concentric left ventricular hypertrophy and a left ventricular ejection fraction of 55-59%. There was impaired LV relaxation with elevated filling pressures. Her pulmonary artery systolic pressures were 45-50 mm Hg. Subsequent consultation with cardiology concluded that the patient's pulmonary hypertension and pulmonary edema were likely secondary to diastolic dysfunction from elevated filling pressures. At this point in the patient's hospitalization, the patient had a net positive fluid intake of approximately 2700 ml. The patient's beta natriuretic peptide was 373 pg/mL, further reflecting a volume overload status. Cardiology recommended diuresis with continued blood pressure control.

The patient was kept on labetalol and nifedipine in addition to being diuresed over the next two days using intravenous furosemide. She was kept on magnesium sulfate for another 24 hours for seizure prophylaxis. POD#1, her blood pressure was in the 170 s/90s with worsening pulmonary crackles and continued oxygen desaturations. Her oxytocin drip and her IV magnesium infusions were discontinued to further restrict fluids. On POD#2, the patient had amlodipine and lisinopril added with the goal to decrease labetalol and establish a blood pressure regimen that could be administered as an outpatient. During this time, the patient's volume status and pulmonary edema improved, with improving crackles and less frequent oxygen desaturations. By POD#3, her pulmonary crackles had resolved, and she was off oxygen. On POD#5, the patient had blood pressures consistently in the 180's/100's which was felt stable for discharge. Her home blood pressure regimen at discharge was nifedipine XL 60 mg BID, lisinopril 40mg, HCTZ 25mg BID, and a Clonidine patch 0.1 mg weekly.

Discussion

Acute pulmonary edema in any patient results from a disturbance of cardiovascular function and/or lung permeability [7]. This is best captured by Ernest Starling's equation describing the factors contributing to filtration of a liquid across a semi permeable membrane:

$$\text{Rate of Filtration of Fluid} = K_f([P_{cap} - P_{is}] - \sigma[\Pi_{cap} - \Pi_{is}])$$

Where K_f represents membrane permeability, P_{cap} and P_{is} represent lung capillary and interstitial pressures respectively, and Π_{cap} and Π_{is} represent the oncotic pressures of the capillary and interstitial spaces. The σ factor represents endothelial permeability to protein.

Many factors can contribute to the development of pulmonary edema. Indeed, numerous causes and contributing factors have been confirmed or suspected in the literature, a summary of which is listed in table 1.

Factors related to patient prior to pregnancy
Hypertension, ischemic heart disease, congenital heart disease, valvular heart disease, arrhythmias, cardiomyopathy, heart failure (systolic or diastolic), high BMI, advanced maternal age, endocrine disorders (pheochromocytoma, hyperthyroidism), use of illicit drugs (cocaine)
Factors related to pregnancy
Multiple gestations, Pre-Eclampsia (with or without severe features), cardiomyopathy due to pregnancy, sepsis, pre-term labor, amniotic fluid embolism, pulmonary embolism, HELLP syndrome, delivery via cesarean-section.
Factors related to management of pregnancy
Use of nifedipine or labetalol, use of steroids, use of oxytocin, non-restrictive fluid management and positive fluid balance (>2000), colloid fluid administration, magnesium sulphate administration

Table 1: Factors confirmed or suspected to contribute to the development of acute pulmonary edema in the peripartum woman [3,5,8-13].

With our patient, there were many potential causes and contributing factors to her acute onset of pulmonary edema. Chief among them was the patient being pre-eclamptic. Pre-eclampsia is a multi-system cardiovascular disease with its main manifestations being hypertension and proteinuria [14]. It affects 3-5% of all pregnancies and is a leading cause of maternal mortality [15]. The presence of concurrent pulmonary edema is an infrequent occurrence in pre-eclampsia. It has been estimated that approximately 3% of peripartum women suffering from pre-eclampsia will develop pulmonary edema, with most cases occurring postpartum [5]. As pre-eclampsia can be classified based on its severity, the finding of pulmonary edema in the pre-eclamptic woman qualifies her as having severe pre-eclampsia and often indicates the delivery of the fetus [16] The exact pathophysiology behind pre-eclampsia is the subject of ongoing research, but is believed to be related to mal-implantation of the placenta leading to release of soluble factors into the maternal bloodstream that cause endothelial cell dysfunction and intravascular inflammation [15,17,18]. It would be presumed that pre-eclampsia generates pulmonary edema by increasing lung capillary pressure and permeability as described by the Starling equation. The definitive treatment of pre-eclampsia is delivering the fetus [16]. However, this was not ideal given our patient being at only 29 weeks gestation. It was for this reason we elected a supportive approach.

As the patient underwent work up by our cardiology service, yet another contributing factor for her pulmonary edema was identified. The patient was noted on echocardiogram to have concentric hypertrophy of the left ventricle, elevated end diastolic pressures, and elevated pulmonary arterial pressures. The consulting service felt these findings were due to a combination of hypervolemia and acute exacerbation of hypertension in the setting of long standing chronic hypertension.

Acute cardiac failure, either diastolic or systolic, is another cause of pulmonary edema [19]. Specifically, diastolic heart failure is often due to a failure of LV relaxation due to hypertrophy from long standing hypertension which leads to elevated left ventricular end diastolic pressures [20]. Interestingly, patients with diastolic heart failure can have a normal ejection fraction and ejection frac-

tion should not be used as proxy for cardiac output in such patinets [21] It is believed that the increased end diastolic pressures seen in such heart failure leads to a 'backward failure' that increases both left atrial pressure and pulmonary venous pressure [22]. The associated increase in pulmonary vasculature pressures seen in diastolic heart failure would lead to pulmonary edema by an increase in the P_{cap} as described in the Starling equation, further contributing to pulmonary edema. It was for concern of heart failure that the anesthesiology team elected to use a norepinephrine drip for pressure support during the patient's neuraxial anesthesia for her cesearean section. Norepinephrine has both alpha and beta agonist properties which increase chronotropy, inotropy, and act as a peripheral vasoconstrictor [23]. All these properties made it an ideal selection for intraoperative blood pressure support in our patient.

Another factor that likely contributed to our patient's pulmonary edema was a volume overload. At the time our patient developed pulmonary edema, she had a net fluid status of positive 2700 ml. Net fluid intake of > 2000 ml has been highlighted as a major risk factor for developing pulmonary edema in the peripartum woman [5]. Unrestricted fluid administration to the peripartum woman is considered to be dangerous and a significant contributor to the development of pulmonary edema [24]. Iatrogenic fluid administration is likely a preventable factor in many similar cases of acute pulmonary edema [8]. A significant source of our patient's fluid intake was in the form of magnesium sulfate for seizure prophylaxis. It has long been suspected that magnesium sulfate may contribute to the development of pulmonary edema as the literature has shown the two are linked [9]. However, there is some debate whether magnesium sulfate itself contributes to pulmonary edema or if increased rates of pulmonary edema in these patients simply reflect the fact that they are receiving higher amounts of IV fluids as a delivery vehicle for magnesium sulfate [25].

Our patient was also on oxytocin post cesarean section for control of post-partum hemorrhage. A bolus of 40 units was given post-delivery in the OR to help with uterine tone and constriction. Oxytocin has been shown to be a potential contributor to or a cause of pulmonary edema [26,27]. The mechanism for this is presumed to be secondary to oxytocin's anti-diuretic effect [28]. If given in conjunction with free water, oxytocin can cause acute hyponatremia, pulmonary edema, and conceivably coma and death [26]. Once it was established that our patient was not having significant postpartum bleeding, the oxytocin infusion causes discontinued so as not to add to or exacerbate the patient's pulmonary edema.

Work Up and Management of Acute Pulmonary Edema in the Peripartum Woman

As acute pulmonary edema in the peripartum woman can have many contributing causes, the work up and management of these patients can be daunting and necessitate a multidisciplinary approach [5]. In a comprehensive review of the subject, Dennis and Solenoidal proposed conceptualizing the work up and management of acute pulmonary edema in the peripartum woman by distinguishing those patients who are normotensive from those patients who are hypertensive [5]. Their management algorithm is reproduced with modification in figure 1. Ultimately, the goal must be to identify causes and contributing factors listed in table 1 and eliminate modify them, if possible.

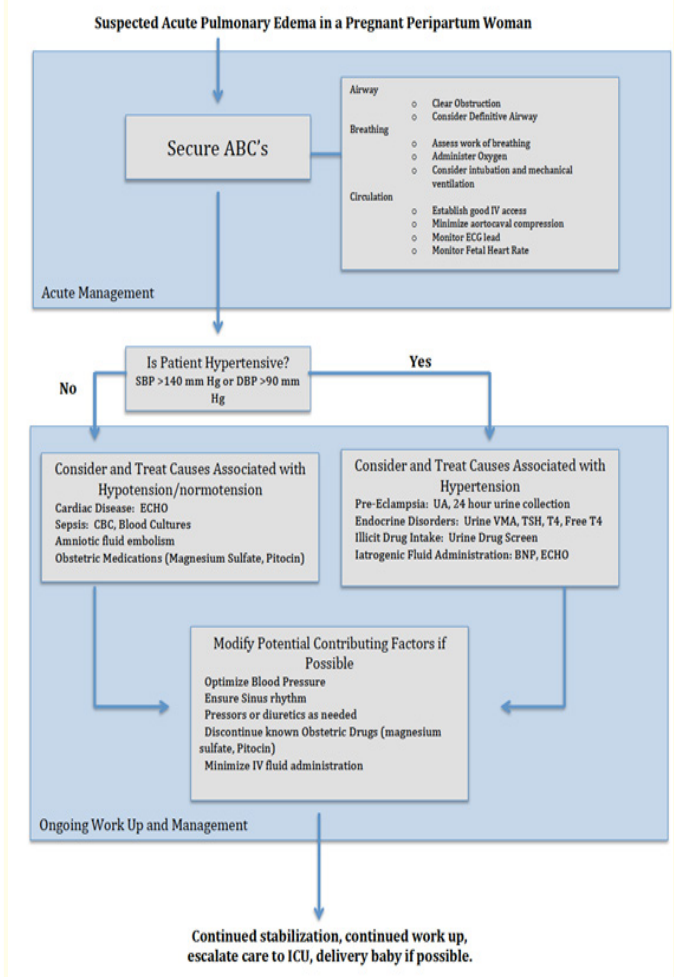

Figure 2: Modified management algorithm for acute pulmonary edema in the peripartum woman as proposed by Dennis and Solnordal [5].

Conclusion

Our patient was in some ways unique for a peripartum woman that developed acute pulmonary edema in the peripartum period. Her pre-existing hypertension, concentric LV hypertrophy, and acute development of pulmonary hypertension with diastolic heart failure is an infrequent cause of acute pulmonary edema in the peripartum period. However, our case is also typical in that there were likely many simultaneous contributory causes to the patient's pulmonary edema while she was on our service. As is often the case, management of the patient taking a multidisciplinary approach is crucial to success .

Conflicts of Interest

The authors declare no conflicts of interest.

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Bibliography

1. Dunne C and Meriano A. "Acute postpartum pulmonary edema in a 23-year-old woman 5 day after cesarean delivery". *Canadian Journal of Emergency Medicine* 11.2 (2009): 178-181.

2. Vigil-De Gracia P. "Pregnancy and severe chronic hypertension: maternal outcome". *Hypertension in Pregnancy* 23.3 (2004): 285-293.

3. Sciscione AC., *et al*. "Acute pulmonary edema in pregnancy". *Obstetrics and Gynecology* 101.3 (2003): 511-515.

4. Grobman WA., *et al*. "Frequency of and factors associated with severe maternal morbidity". *Obstetrics and Gynecology* 123.4 (2014): 804-810.

5. Dennis AT and Solnordal CB. "Acute pulmonary oedema in pregnant women". *Anaesthesia* 67.6 (2012): 646-659.

6. Gebhardt GS., *et al*. "National Committee for Confidential Enquiries into Maternal Deaths in South A. Maternal death and caesarean section in South Africa: Results from the 2011-2013 Saving Mothers Report of the National Committee for Confidential Enquiries into Maternal Deaths". *South African medical journal = Suid-Afrikaanse tydskrif vir geneeskunde*. 105.4 (2015): 287-291.

7. Murray JF. "Pulmonary edema: pathophysiology and diagnosis". The International Journal of Tuberculosis And Lung Disease15.2 (2011):155-160.

8. Thornton CE., *et al*. "Acute pulmonary oedema as a complication of hypertension during pregnancy". *Hypertension in Pregnancy* 30.2 (2011): 169-179.

9. Yeast JD., *et al*. "The risk of pulmonary edema and colloid osmotic pressure changes during magnesium sulfate infusion". *American Journal of Obstetrics and Gynecology* 169.6 (1993): 1566-1571.

10. Tuffnell DJ., *et al*. "Outcomes of severe pre-eclampsia/eclampsia in Yorkshire 1999/2003". *BJOG : An International Journal of Obstetrics and Gynaecology* 112.7 (2005): 875-880.

11. Vaast P., *et al*. "Acute pulmonary oedema during nicardipine therapy for premature labour; Report of five cases". *European Journal of Obstetrics, Gynecology, and Reproductive Biology* 113.1 (2004): 98-99.

12. Le Bret F., *et al*. "Transesophageal echocardiographic assessment of left ventricular function in response to labetalol for control of postoperative hypertension". *Journal of Cardiothoracic and Vascular Anesthesia* 6.4 (1992): 433-437.

13. Gul A., *et al*. "Maternal and fetal outcomes in HELLP syndrome complicated with acute renal failure". *Renal Failure* 26.5 (2004): 557-562.

14. Tomimatsu T., *et al*. "Pathophysiology of preeclampsia: an angiogenic imbalance and long-lasting systemic vascular dysfunction". *Hypertension research: official journal of the Japanese Society of Hypertension* 40.4 (2017): 305-310.

15. Chaiworapongsa T., *et al*. "Pre-eclampsia part 1: current understanding of its pathophysiology. Nature reviews". *Nephrology* 10.8 (2014): 466-480.

16. Publications Committee SfM-FM and Sibai BM. "Evaluation and management of severe preeclampsia before 34 weeks' gestation". *American Journal of Obstetrics and Gynecology* 205.3 (2011): 191-198.

17. Roberts JM., *et al*. "Sera from preeclamptic women specifically activate human umbilical vein endothelial cells in vitro: morphological and biochemical evidence". *American Journal of Reproductive Immunology* 27.3-4 (1992): 101-108.

18. Redman CW., *et al*. "Preeclampsia: an excessive maternal inflammatory response to pregnancy". *American Journal of Obstetrics and Gynaecology* 180 (1999): 499-506.

19. Ware LB and Matthay MA. "Clinical practice. Acute pulmonary edema". *The New England Journal of Medicine*. 353.26 (2005): 2788-2796.

20. Kindermann M., *et al*. "Heart failure with normal left ventricular ejection fraction: what is the evidence?". *Trends in cardiovascular medicine* 18.8 (2008): 280-292.

21. Andrew P. "Diastolic heart failure demystified". *Chest* 124.2 (2003): 744-753.

22. MacIver and Clark AL. "The vital role of the right ventricle in the pathogenesis of acute pulmonary edema". *The American Journal of Cardiology* 115.7 (2015): 992-1000.

23. Tariq S and Aronow WS. "Use of Inotropic Agents in Treatment of Systolic Heart Failure". *International Journal of Molecular Sciences* 16.12 (2015): 29060-29068.

24. Christiansen LR and Collins KA. "Pregnancy-associated deaths: a 15-year retrospective study and overall review of maternal pathophysiology". *The American Journal of Forensic Medicine and Pathology* 27.1 (2006): 11-19.

25. Samol JM and Lambers DS. "Magnesium sulfate tocolysis and pulmonary edema: the drug or the vehicle?". *American journal of obstetrics and gynecology* 192.5 (2005): 1430-1432.

26. Dogdu O., *et al*. "Fatal pulmonary oedema following oxytocin administration in a pregnant woman with acute myocardial infarction". *Cardiovascular Toxicology* 11.1 (2011): 74-77.

27. Ghai B., *et al*. "Acute pulmonary oedema following oxytocin administration: a life threatening complication". *Journal of the Indian Medical Association* 104.5 (2006): 261-262.

28. Li C., *et al*. "Molecular mechanisms of antidiuretic effect of oxytocin". *Journal of the American Society of Nephrology: JASN* 19.2 (2008): 225-232.

Volume 2 Issue 3 June 2018