Pregnancy in a Patient with Idiopathic Pulmonary Fibrosis: A Case Report

Rebecca Horgan, MD[1] Zeinab Kassem, MD[1] Gloria Too, MD[1] Alfred Abuhamad, MD[1] Steven Warsof, MD[1]

[1] Department of Obstetrics and Gynecology, Division of Maternal-Fetal Medicine, Eastern Virginia Medical School, Norfolk, Virginia

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Address for correspondence Rebecca Horgan, MD, Department of Obstetrics and Gynecology, Division of Maternal-Fetal Medicine, Eastern Virginia Medical School, Norfolk, VA 23507 (e-mail: horganr@evms.edu).

Abstract

Idiopathic pulmonary fibrosis (IPF) is a progressive restrictive lung disease. Data on the impact of pregnancy on IPF and maternal outcome is extremely limited. We present the case of a 35-year-old woman, gravida 1 para 0 with familial IPF with no oxygen requirement prior to pregnancy. The patient demonstrated significant deterioration in her lung function beginning at 22 weeks' gestation and underwent hospitalization at $27^{2/7}$ weeks gestation due to acute on chronic hypoxic respiratory failure, ultimately requiring delivery at 28 weeks' gestation. The patient has not regained her baseline pulmonary function and remains oxygen dependent at 5 months postpartum. Based on limited available data, significant maternal morbidity and mortality is reported for women with IPF who become pregnant.

Keywords

- idiopathic pulmonary fibrosis
- pregnancy
- respiratory failure

Key Points

- Pregnancy outcomes in IPF are more severe than chronic interstitial lung disease due to connective tissue disorders.
- Deterioration in lung function amongst pregnant women with IPF occurs predominantly in the late second trimester, and lung function does not appear to recover postpartum.
- Significant maternal morbidity and mortality (40% at 1 year postpartum) is reported for women with IPF who become pregnant.

Idiopathic pulmonary fibrosis (IPF) is a progressive restrictive lung disease that results from an abnormal proliferation of mesenchymal cells, varying degrees of fibrosis, deposition of collagen and extracellular matrix, and distortion of both pulmonary architecture and subpleural cystic airspaces.[1] Familial IPF is a rare form of chronic interstitial lung disease that is believed to be autosomal dominant with variable penetrance.[2] The worldwide incidence of IPF is estimated to be 0.33 to 4.51 per 10,000 persons.[3]

In normal pregnancy, several changes in respiratory function occur. Functional residual capacity decreases by approximately 20% toward the latter half of pregnancy due to a decrease in both residual volume and expiratory reserve volume.[4] Minute ventilation at rest rises nearly 50% at term primarily due to increased tidal volume.[5] Progesterone-induced increase in ventilation results in the "air hunger of pregnancy" with arterial PCO_2 decreasing to 27 to 32 mm Hg during pregnancy and an increase in maternal arterial oxygen tension (PaO2) to 106 to 108 mm Hg in the first trimester and to 101 to 104 mm Hg in the third trimester.[6,7] As IPF typically presents in the fourth to sixth decade of life, data on the impact of pregnancy on IPF and maternal outcome is extremely limited.

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Case

We present the case of a 35-year-old woman, gravida 1 para 0, who was referred to the maternal fetal medicine service at our institution for management of pregnancy with IPF. The patient's mother had previously undergone lung transplantation at the age of 60 for IPF, thus the patient's condition was believed to be familial but without a specific genetic etiology identified. Echocardiogram immediately prior to pregnancy demonstrated an ejection fraction of 61% and no evidence of pulmonary hypertension. The patient did not have an oxygen requirement and exercised 5 days per week. She reported some shortness of breath with exertion but immediate recovery with rest. The patient had undergone a preconception consult and was extensively counseled on the uncertain impact of pregnancy on her pulmonary function. Her history was significant for multiple pneumothoraces with a total of five pleurodesis procedures, a history of a prior loop electrosurgical excision procedure of her cervix and recently diagnosed chronic hypertension not requiring medications. Her medical and surgical history was otherwise non-contributory. The patient's vaccination status was up to date including three doses of the Pfizer COVID-19 vaccine.

The patient established prenatal care at 5 weeks' gestation. At that time, she had noted the recent onset of occasional episodic desaturations but did not require oxygen supplementation. The patient subsequently underwent a sleep study at 16 weeks' gestation which demonstrated no requirement for supplemental oxygen. By 22 weeks' gestation, she was taken out of work as she was requiring intermittent supplemental oxygen due to desaturation with activity. She was placed on modified bed rest at home having declined hospital admission at that time. Chest CT demonstrated progressive worsening of an upper lung zone predominant parenchymal disease process with traction bronchiectasis and fibrosis. At 26 weeks' gestation, the patient required 4 to 5 liters of oxygen with activity but reported her oxygen requirement had been stable over several weeks. The patient was hospitalized with acute hypoxic respiratory failure at $27^{2/7}$ weeks gestation when she had an acute change in her status as evidenced by increasing shortness of breath and episodes of oxygen desaturation as low as 80% occurring with minimal activity.

Upon admission, the patient had a negative COVID-19 polymerase chain reaction and viral respiratory panel. CT angiogram demonstrated a new nonspecific ground glass lung process throughout the left and right lower lobes but no pulmonary embolism. Betamethasone was administered for fetal lung maturity and a 2-week course of IV methylprednisolone 40 mg daily was initiated. Following multidisciplinary team review, a decision was made to proceed with primary cesarean section at 28 weeks' gestation due to the patient's worsening respiratory status as she then was requiring 5 L/min of oxygen at rest. Daily fetal non-stress tests remained reassuring and the fetus was appropriately grown with an estimated fetal weight of 1,251 g at 27 weeks + 6 days gestation, at the 66th percentile. Magnesium sulfate was administered for fetal neuroprotection with the approval of the patient's pulmonologist. The patient underwent an uncomplicated primary low transverse cesarean section, and bilateral tubal ligation under epidural anesthesia. She delivered a live born male infant weighing 1,304 g with APGARs of 4 and 8 at 1 and 5 minutes, respectively. The infant went to the NICU and had an uneventful course. The child was discharged to home at day of life 63, intact with good prognosis. The patient's oxygen requirement remained at 4 to 5 L/min postpartum. She received several doses of IV furosemide postoperatively per pulmonology. The patient was discharged home on postoperative day 6 with an oral prednisone taper. At 5 months postpartum, she continues to be oxygen dependent with a requirement of 3 to 5 L/min despite multiple courses of high dose prednisone. The patient's pulmonologist and lung transplant team intend to proceed with lung transplantation if she does not demonstrate significant improvement in the coming months.

Comment

This case report describes pregnancy in a patient with IPF, which resulted in progression of disease and ultimate premature delivery at 28 weeks' gestation due to worsening hypoxic respiratory failure. Delivery did not result in return of the patient's respiratory status to baseline at 5 months postpartum and she remains oxygen dependent postpartum. The aim of this case report is to review the outcomes of pregnancies with IPF to guide patient counseling.

A review of the literature found few reported cases of pregnancy amongst women with IPF, whether familial in nature or not. The first reported case of a pregnant woman with familial IPF was in 1984.[8] The patient's pulmonary function remained unchanged until 26 weeks' gestation when she developed progressively increasing shortness of breath ultimately requiring delivery at 38 weeks' gestation. Similar to our case, pulmonary function did not return to baseline and the patient remained "incapacitated by breathlessness" at 3 months postpartum.[8] Another reported case in 1985 of pregnancy in a patient with IPF diagnosed at the age of 17 reported the patient became oxygen dependent at 15 weeks' gestation, delivered at 37 weeks and a maternal death occurred 3 weeks postpartum following acute onset of shortness of breath and chest pain.[9] A final cause of death was not established as the patient's family declined autopsy. Zanutto et al also reported a maternal death in 2002 1-year postpartum following progression of a patient's familial IPF during pregnancy.[10]

In 2020, a case was reported by Sekine et al of a pregnant woman with IPF who presented with rapid decline in respiratory function and hypoxemia at 25 weeks' gestation.[11] Similar to our case, delivery was required at 28 weeks' gestation due to further deterioration in the patient's pulmonary status requiring 4 L/min of oxygen not responsive to high dose steroid therapy. The woman required lung transplantation at 26 days postpartum due to worsening hypoxemic respiratory failure unresponsive to steroid therapy.[11] Sholapurkar et al reported a case in 1990 of pregnancy in a woman with IPF who experienced an acute deterioration in

Table 1 Summary of reported cases of Idiopathic pulmonary fibrosis in pregnancy

Author Year	Maternal age	Diagnosis	Gestational age at delivery	Outcome
Prichard and Musk 1984	25	Familial IPF	Increasing dyspnea noted from 26 wk, vaginal delivery at 38 wk following induction of labor	The patient dialed to respond to high dose prednisolone and azathioprine postpartum and the patient "remained incapacitated by breathlessness 3 mo later".
Smythe et al 1985	31	IPF	34 wk following admission with PPROM	Discharged on postpartum day 6 requiring oxygen with prophylactic heparin. Maternal death occurred at 3 wk postpartum following sudden onset of shortness of breath and chest pain. Autopsy was declined.
Sholapurkar et al 1991	35	IPF	Termination of pregnancy at 24 wk gestation due to severe hypoxic respiratory failure	Return to near normal lung function following treatment with high dose corticosteroids. The patient remained well with grade 1 dyspnea noted at 2.5 y postpartum.
Zanutto et al 2003	26	Familial IPF	Not reported[a]	Severe respiratory failure complicated by pulmonary arterial hypertension leading to death 1 y postpartum.
Sekine et al 2020	29	IPF	Cesarean section at 28 wk following admission for worsening respiratory failure at 25 wk gestation.	Lung transplantation required at 26 d postpartum due to failure to respond to high dose corticosteroids and cyclosporine with oxygen requirement of 5 L/min.

Abbreviations: IPF, idiopathic pulmonary fibrosis; PPROM, preterm premature rupture of membranes.
[a]Unable to obtain full text for Zanutto et al.

respiratory status at 19 weeks' gestation, which also failed to respond to steroid therapy.[12] Therefore, the decision was made to proceed with termination of pregnancy at 24 weeks due to severe maternal hypoxemia. The authors reported a marked improvement in the patient's hypoxemic respiratory failure immediately postoperative. The patient was treated with a prolonged 6-month course of oral steroids and she remained well at follow-up 2.5 years later. ►**Table 1** summarizes the literature with regards to reported cases of IPF in pregnancy.

While pregnancy does not appear to result in a rapid decline in pulmonary function amongst patients with interstitial lung disease secondary to connective tissue disease, our case and the few reported cases in the literature of pregnancies have demonstrated an acute decline in respiratory status in the late second trimester of pregnancy amongst patients with IPF.[2,8,9,13] Worsening hypoxemic respiratory failure amongst pregnant patients with IPF does not appear to respond to steroid therapy based on the limited available data.[11,12] Unfortunately, delivery does not appear to result in return of the patient's respiratory status to pre-pregnancy baseline.[8–11] The limited cases reported in the literature demonstrate a significant mortality rate (40%) by 1 year postpartum. However, as there is only five previously published individual case reports, we acknowledge this may be an overestimation due to publication bias. The significant maternal morbidity and potential mortality as well as the risk to the fetus of inheriting this condition is important information to consider when counseling patients with IPF who are considering pregnancy. Definitive treatment of IPF involves lung transplantation. Successful pregnancy outcome has been reported following lung transplantation in a patient with pulmonary fibrosis.[14] However, data on pregnancy following lung transplantation is extremely limited.

To conclude, it is important for providers to be aware that data regarding pregnancy outcomes in women with chronic interstitial lung disease due to connective tissue disorders is not applicable to patients with IPF and that based on limited available data, significant maternal morbidity and mortality has been reported for women with IPF who become pregnant.

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Conflict of Interest
None declared.

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