A rare cause of respiratory failure in pregnancy - acute exacerbation of undiagnosed Hypersensitivity Pneumonitis mimicking complication of severe preeclampsia

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Abstract

Respiratory failure occurs in 0.1-0.2% of pregnancy patients. This can be due to pre-eclampsia, venous thromboembolism, asthma, gastric aspiration, and viral pneumonitis. Rarely exacerbation of underlying diseases (like asthma, Interstitial Lung Disease, ILD, *etc*.) can cause respiratory failure. The underlying disease can be recognized previously or presented as exacerbation in pregnancy for the first time. Respiratory failure leads to harm to both mother and fetus; hence, the cause should be evaluated as soon as possible. Here, we are describing the case of acute exacerbation of Hypersensitivity Pneumonitis (HP) in a pre-eclampsia patient.

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Introduction

The symptom of acute onset breathlessness associated with falling saturation in a pregnant woman with pre-eclampsia often raises the suspicion of pulmonary edema. In the COVID-19 pandemic background, the dilemma increases as respiratory complaints and pre-eclampsia are known to occur in COVID-19 illness. Hence, it is essential to recognize the flare-up of undiagnosed Interstitial Lung Disease (ILD) in such a situation as the management is different. Here, we present one such case where a pregnant woman presented with severe pre-eclampsia and respiratory symptoms and was found to have undiagnosed ILD.

Case Report

A 33-year-old primigravida at 31 weeks of gestation was presented to our tertiary care center in 2021, with complaints of breathlessness on exertion, on and off for two months, with acute exacerbation for one day requiring oxygen support. She had conceived on the first cycle of IUI after11 years of unexplained infertility. She was diagnosed with gestational hypertension and gestational diabetes mellitus at 30 weeks of gestation. She received T. labetalol 200 mg 8th hourly, T. nifedipine 10 mg 12th hourly for Blood Pressure (BP) control, and T. Metformin 500 mg twice a day for sugar controlat the time of referral. She was also diagnosed with hypothyroidism during the routine antenatal workup, and took T. thyroxine 50 µg OD. There was no history of fever, recent travel, contact with COVID-19-positive patients, chest pain, hemoptysis, syncope, nocturnal cough, seasonal allergies, or asthma. She had been exposed to pigeon pets in her childhood, since the age of 10 years. She had a history of occasional intermittent breathlessness of mMRC grade 1-2 for 4 years. No specific treatment or workup has been done for these respiratory symptoms till now. On physical examination, she was dyspneic at rest, conscious, oriented to time, place, and person. There was grade 3 clubbing noted in all four limbs, grade 2 pedal edema but no pallor, cyanosis, lymphadenopathy, or skin lesions, and Jugular Venous Pressure (JVP) was not raised. She was afebrile, with a pulse rate of 90/min regular, BP 150/90 mmHg, respiratory rate 24/min, SpO_2 88% in room air, which improved to 97%-99% with 4 L oxygen via face mask. Arterial Blood Gas (ABG) at room air revealed PO_2 56 mmHg, PCO_2 31 mmHg, HCo-22, Ph-7.46, and lactate 0.6 mmol/L. Her PaO_2/FiO_2 ratio was 266**.** Chest ausculta-

tion revealed bilateral basal fine end-inspiratory crept. Cardiovascular examination revealed normal first and second heart sounds without any murmur. In per abdomen examination, uterus size corresponded to 28 weeks gestation with good fetal heartrate. There were no impending symptoms of eclampsia like headache, epigastric pain, and visual disturbances). Spot urine protein was 2+, and knee jerk was normal. Given clinical suspicion of pre-eclampsia with pulmonary edema, antidiuretic (Inj. frusemide 40 mg IV) and Inj. morphine 4 mg IV were given, following which there was no resolution of the crepitations or clinical improvement in oxygen saturation. Hence, a working diagnosis of chronic lung disease with acute worsening was made. A chest X-ray with the abdominal shield revealed bilateral reticulations with nodules suggestive of interstitial infiltrates (Figure 1). Her Reverse Transcriptase-Polymerase chain Reaction (RT-PCR) for COViD-19 was negative. Ultrasound of the thorax showed minimal pleural space fluid collection and mild blunting of the costophrenic angle. A two-dimensional (2D) echocardiography showed preserved cardiac function with an ejection fraction of 60%. High Resolution Computed Tomography (HRCT) thorax revealed multiple variable-sized predominantly subpleural cystic changes with honeycombing, traction bronchiectasis, mosaic attenuation, and interlobular septal thickening, noted in bilateral lungs with ground-glass opacity (Figure 2a). Fibrotic hypersensitivity pneumonitis with acute flare causing acute hypoxemic respiratory failure diagnosis was provisionally made during the present admission in view of clinical and HRCT findings, along with a background history of pigeon birds since 10 years of age.

A lung biopsy was deferred owing to her antenatal status and respiratory failure. With the diagnosis of ILD, a multidisciplinary team approach involving an obstetrician, pulmonary physician, rheumatologist, intensivist, and neonatologist was initiated. A provisional diagnosis of acute worsening of ILD was made. We explained to the patient the necessity for immediate initiation of steroid therapy. We also explained that it might be difficult to tolerate labor if her respiratory condition worsened and she had pregnancy complications, including intrauterine growth restriction due to the mother's hypoxia or immunosuppressive therapy and preterm birth; however, she and her family hoped to continue the pregnancy. She was started on T. prednisolone 75 mg OD in consultation with the pulmonary medicine team. She also received an empirical antibiotic, Inj. ceftriaxone 1g IV BD for seven days duration. The fetal wellbeing was assessed, and ultrasound showed a fetus with EFW-1.5 kg, oligohydramnios, and normal Doppler study. Antenatal corticosteroids for fetal lung maturity were covered. Her peripheral blood count and liver and renal function tests were normal, and her spot urine protein creatinine ratio was 0.4. Her sputum for Acid-Fast Bacteria (AFB), gene expert, and bacterial culture werenegative. Serum Antinuclear Antibody (ANA) was 1+, the Extractable Nuclear Antigen Antibody (ENA) blot was non-significant, Lupus Anticoagulant (LAC) and Antiphospholipid Antibody (APLA) were reported negative. C reactive protein was 29 mg/L.

Broncho alveolar lavage suggestive of lymphocytic effusion (lymphocytes-40%) and pyogenic culture were negative. There is not much literature on pregnancy management in ILD, and with the gradual reduction inthe oxygen requirement, conservative management with oral prednisolone was continued. Serial fetal monitoring was done with a Non-Stress Test (NST) and ultrasound. After a multidisciplinary team consultation, labor induction was planned at 33 weeks of gestation, given increasing maternal blood pressure, abnormal fetal Doppler study (reversal of cerebroplacental ratio), and reduced perception of fetal movements. Emergency cesarean section was done under combined spinal-epidural anesthesia due to intrapartum pathological Cardiotocograph (CTG). The intraoperative period was uneventful, and blood loss was 500 mL. She delivered a preterm male baby, 1.48 kg, with APGAR 8 & 9 at 1 & 5 minutes. Given prematurity and low birth weight, the baby was shifted to the Neonatal Intensive Care Unit (NICU). During the postoperative period, the maternal resolution of symptoms was noticed with a gradual reduction in the oxygen requirement. She maintained 95-97% oxygen saturation in room air without oxygen support within one week postpartum. She was continued on T. prednisolone 75 mg once a day and T. amlodipine 5 mg once a day dosing for BP control during the postpartum period. The HRCT was performed postnatally after three weeks of systemic steroids, which showed a significant reduction in ground-glass opacity (Figure 2b). Post-treatment arterial blood gas at room air revealed: PO_2:75 mmHg, PCO_2: 35 mmHg, HCO_3- 24, Ph-7.43. Prednisolone dose was tapered over the next 3 months.6-minute walk test distance walked 400 meters without desaturation.

Discussion

Diffuse Parenchymal Lung Disease (DPLD), or Interstitial Lung Disease (ILD), as it is commonly known, is an inflammatory and fibrotic infiltrative process of the lung that is often associated

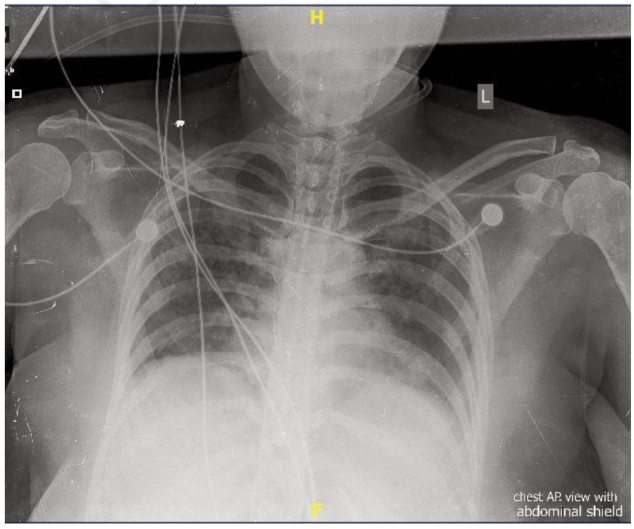

Figure 1. Chest X-ray AP view showing reticulations and nodules in all areas.

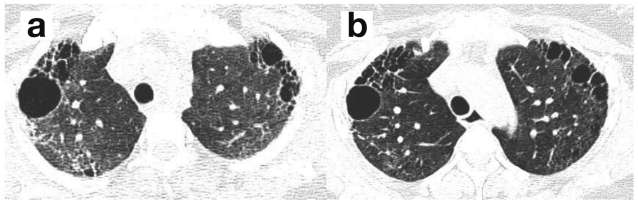

Figure 2. a) High-Resolution Computed Tomography (HRCT) chest done antenatal at admission showing sub pleural honeycombing and ground- glass opacity in both upper lobes. **b**) Repeat HRCT chest done post-natal after three weeks of systemic steroids, showing improvement in ground-glass opacity.

with collagen vascular disease in women. Most ILDs are not commonly associated with pregnancy because only a minority of them occur in women of childbearing age. However, ILDs may arise de novo in pregnancy, or a previously known ILD may be exacerbated. Pregnancy may affect the diagnosis, management, and outcome of ILD.[1] It includes a spectrum of conditions varying from self-limiting inflammatory processes to severe debilitating fibrosis of the lungs. In our case, given the clinical, radiological picture and rapid improvement with steroids, acute exacerbation of ILD diagnosis was made. Considering her age and history of exposure to pigeons in her childhood, a provisional diagnosis of acute worsening ofchronic hypersensitivity pneumonitis was made. We decided to allow the pregnancy to continue because i) the patient strongly desired to continue the pregnancy; ii) she did not have pulmonary hypertension, and her cardiac function was normal; iii) her worsening lung condition showed a response to steroids within 48 hours; iv) the primary treatment for any acute ILD (systemic steroids) is safe during pregnancy. Our patient presented with symptoms/ signs mimicking pulmonary edema and severe pre-eclampsia, such as breathlessness, falling saturation, and high BP recordings. Preeclampsia is known to complicate around 15% of cases with ILD.[2] In our patient, as there was no response to pulmonary edema measures and grade 3 clubbing in all four limbs, a high suspicion of underlying chronic lung disease was made, supported by the radiological findings in chest X-ray and HRCT thorax. HP, also called extrinsic allergic alveolitis, is a complex syndrome of varying intensity, clinical presentation, and natural history rather than a single, uniform disease Itrepresents an immunologic reaction to an inhaled agent, particularly an organic antigen, occurring within the pulmonary parenchyma.[3]

HP due to pigeons is known as bird fancier's lung and is caused by bird serum proteins, droppings, or feathers. Diagnosis of HP can be confidently made without tissue diagnosis whenthere is a clear history of antigen exposure (pigeons) and compatible HRCT findings.[4]

Literature has reported that HRCT can often confirm the diagnosis of fibrotic HP, and tissuediagnosis may not be necessary in cases where lung biopsy is contraindicated due to severe cardiopulmonary compromise/ complications, as in advanced disease.

Labor was induced at a preterm gestational age for obstetrical indication in our patient, and shewas delivered by cesarean section under combined spinal-epidural anesthesia for fetal indication. Various case reports have shown that patients diagnosed with ILD during pregnancy have been found to have higher rates of pneumothorax and obstetric complications like preterm delivery and miscarriage. Elective instrumental delivery is suggested to avoid increasing intrathoracic pressure during normal labor. Epidural anesthesia is preferred in such cases as itreduces hyperventilation and decreases the chance of pneumothorax.[5]

Pregnancy is often avoided or even terminated in such patients because of limited published data on the complications and pregnancy outcomes. But in our case, the diagnosis was made when the patient presented to us for the first time during her third trimester of pregnancy. However, pregnancy complicated with ILD requires close monitoring before, during, and after pregnancy with a multidisciplinary team of physicians.

Conclusions

Hence, an undiagnosed ILD can present for the first time during pregnancy with acute exacerbation mimicking pre-eclampsia with severe features or COVID illness during this pandemic. One needs to be vigilant in differentiating these medical conditions during pregnancy as the management is discrete in each scenario.

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