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Case report

Thoracic ultrasound improves outcome in pregnant woman with severe asthma and respiratory failure

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Abstract. Severe asthma during pregnancy presents significant management challenges, particularly when complicated by respiratory failure. We report the case of a 26-year-old pregnant woman with a history of severe allergic asthma who experienced a severe asthma exacerbation during her third trimester after discontinuing Benralizumab therapy. The patient, who had also recently contracted a SARS-CoV-2 infection, presented with worsening dyspnea and hypoxemia. Despite high-flow oxygen therapy and bronchodilators, her condition deteriorated, necessitating transfer to intensive care. Thoracic ultrasound, a non-invasive and radiation-free diagnostic tool, played a pivotal role in monitoring lung condition and guiding treatment, revealing pleural effusions and subpleural consolidations. Antibiotic therapy and the resumption of Benralizumab led to gradual clinical improvement. The patient delivered a healthy baby, and thoracic ultrasound confirmed full recovery. This case highlights the utility of thoracic ultrasound in managing severe respiratory failure in pregnant women, minimizing fetal risk while providing critical diagnostic information. The case also raises important considerations regarding the influence of viral infections such as SARS-CoV-2 and Zika virus on asthma exacerbations and lung function. (www.actabiomedica.it)

Key words: thoracic ultrasound, severe asthma, pregnancy and respiratory failure, biologics

Introduction

Severe asthma during pregnancy poses significant challenges for both maternal and fetal health. The physiological changes of pregnancy, including increased oxygen demand and altered immune responses, can exacerbate respiratory conditions, increasing the risk of severe complications such as respiratory failure. Management of severe asthma in pregnant women is further complicated by concerns about the safety of pharmacological therapies and the need to minimize fetal risks. Recent studies have suggested that respiratory viral infections, including SARS-CoV-2 and Zika virus, may have a profound impact on asthma control and lung function (1,2). In particular, SARS-CoV-2 infection has been associated with increased airway inflammation, persistent lung dysfunction, and prolonged recovery in asthmatic individuals, particularly in pregnant women whose immune responses are altered due to pregnancy (1). Understanding the interplay between viral infections and asthma is crucial for optimizing therapeutic strategies and preventing severe exacerbations in pregnancy. Thoracic ultrasound has emerged as a valuable, non-invasive diagnostic tool for evaluating and managing acute respiratory conditions. Unlike traditional imaging methods such as chest X-rays or computed tomography (CT), ultrasound avoids ionizing radiation, making it particularly suitable for pregnant patients. Recent advancements in ultrasound technology have enabled its use at the bedside, offering immediate insights into lung pathology and guiding clinical decisions. Additionally,

betaine and inositol supplementation have been proposed as potential therapeutic interventions in pregnancy due to their roles in modulating metabolic and inflammatory pathways (3,4). Betaine has been shown to influence lung maturation, while inositol plays a crucial role in fetal development, including breast density and pulmonary surfactant production, which may be beneficial in maternal respiratory health (3,4). In this report, we present the case of a 26-year-old pregnant woman with severe allergic asthma and respiratory failure exacerbated by discontinuation of biologic therapy and a recent SARS-CoV-2 infection. This case underscores the utility of thoracic ultrasound in managing complex respiratory conditions during pregnancy, highlighting its role in ensuring both maternal and fetal safety.

Case report

A 26-year-old non-smoker woman with allergies to NSAIDs, grass pollen, and Aspergillus, suffering from severe allergic asthma (T2 endotype, early onset), had been on biological therapy with Benralizumab for about a year (5). Three months before hospitalization, she contracted a SARS-CoV-2 infection. She also suffered from allergic rhinitis and conjunctivitis, for which she underwent occasional check-ups. She voluntarily discontinued Benralizumab therapy at 29th week of pregnancy, resorting instead to fluticasone (250 μg) + formoterol fumarate dihydrate (10 μg) as needed (6,7). Due to a worsening of her dyspnea with mild exertion and sometimes even at rest, she presented to the emergency room, where room air arterial blood gas (ABG) analysis revealed moderate hypoxemia (PaO2 64 mmHg, PaCO2 36 mmHg, pH 7.46, HCO3- 18.5 mmol/l). She was transferred to the gynecology department (8,9). Despite treatment with bronchodilators via aerosol and oxygen, her ABG values further deteriorated. On 60% Venturi oxygen, she had a saturation of 88%, which worsened to 82% even with minimal exertion. Her respiratory rate was 26/min, with a BORG score of 6. She was immediately treated with High flow Nasal Cannula high-flow oxygen with FiO2 of 100%, but her oxygen saturation remained low at around 92% (10). She exhibited prolonged expiration, more evident during forced maneuvers, with a productive cough and basal wheezing. Her heart sounds were rhythmic but slightly reduced in intensity, with no lower limb edema. Due to difficulties in moving her, an integrated ultrasound (chest, heart, vessels, and lower limbs) was performed immediately using an older device with a 3.5 MHz convex probe for general thoracic imaging, which is often used in emergency or ICU settings (GE Logiq-e, GE Healthcare, Chicago, IL, USA) (11,12). Lung sliding was noted, without bilateral basal pleural effusion. A small subpleural consolidation was noted in the posterior middle field on the left side (Figure 1). The cardiac chambers were of normal size with preserved global kinetics, and no valvular defects were observed. The femoral and popliteal veins were compressible, with no evidence of thrombosis. The ultrasound suggested a superimposed infectious disease alongside severe bronchial obstruction. Empirical therapy with Ceftriaxone and Clarithromycin was initiated. A bedside chest X-ray later confirmed retrocardiac lung consolidation on the left side, with clear costophrenic angles, along with evidence of mild scoliosis, which was noted and considered in the interpretation of thoracic imaging findings (13) (Figure 1). Due to persistent severe respiratory failure, she was transferred to the intensive care unit, although the patient explicitly refused non-invasive ventilation (NIV), opting instead for high-flow oxygen therapy (14). Subsequent lab tests showed negative D-dimer results, with increased CRP, white blood cells, and neutrophils. A repeat echocardiogram and venous Doppler ultrasound of the lower limbs confirmed the previous findings. However, during the echocardiogram, a pleural effusion was detected at the base of the left lung, which had not been present earlier (Figure 1). A second chest X-ray confirmed the pleural effusion on the left side, and a follow-up X-ray after 4 days showed pleural effusion Cand consolidation also on the right side (Figure 1). A weak positivity was found in the urine for pneumococcal antigen, In the sputum for *Streptococcus pneumoniae* and rhinovirus, and in tracheal aspirate for *Staphylococcus aureus*. Ceftriaxone was replaced with piperacillin + tazobactam and vancomycin, and bronchodilator therapy was increased. Low-dose anticoagulant prophylaxis (enoxaparin 1 mg/kg/day) was administered. Despite everything,

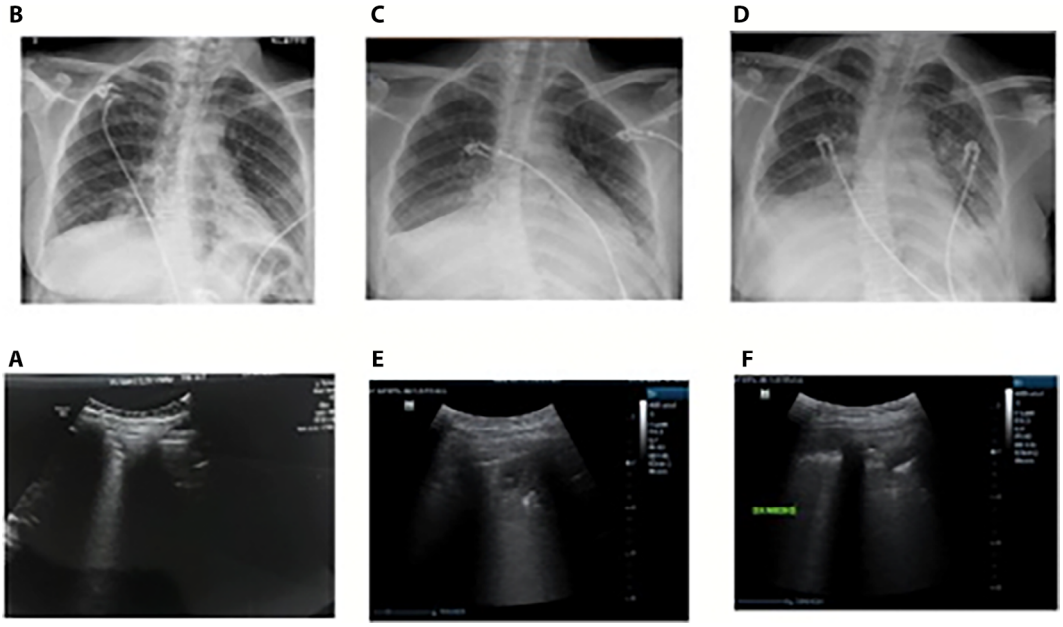

Figure 1. A) Chest ultrasound at admission showing a small left subpleural consolidation (lower left). B) Chest X-ray at admission revealing left-sided subpleural consolidation and scoliosis (upper left). C) CXR taken 24 hours after admission, showing increased opacities in the left lower lung region (upper middle). D) CXR obtained 7 days post-admission, demonstrating bilateral consolidations and pleural effusions (upper right). E) Chest ultrasound 20 days after admission, displaying a consolidation on the left and interstitial involvement on the right (lower middle). F) Follow-up chest ultrasound after 20 days, showing further resolution of left pleural effusion with minimal residual consolidations (lower right).

severe respiratory failure persisted, with a P/F ratio sometimes below 100. After several days of therapy with high doses of bronchodilators and corticosteroids, Benralizumab therapy was resumed. After a few days, the patient showed progressive improvement in gas exchange. Obstetric follow-up at 29 weeks showed normal amniotic fluid, a normal fetal heart rate, and active fetal movements. Twenty days after admission, a thoracic ultrasound showed regression of pleural effusion bilaterally, with small subpleural consolidations in the left interscapular, infrascapular and axillary areas and a small consolidation on the right side, with subpleural interstitial thickening in the infrascapular area (Figure 1). A follow-up ultrasound 5 days later showed a reduction of the consolidations on the left side and almost complete disappearance of the consolidation on the right side. The ultrasound improvement was associated with progressive clinical improvement. At a 60-day outpatient follow-up, the patient had made a complete clinical recovery, and thoracic ultrasound showed total regression of the pulmonary consolidations. The pregnancy ended without complications, resulting in the birth of a healthy baby girl with no subsequent complications at follow-up. To recap for timeline clarity, our patient was admitted to the ICU immediately following her transfer due to persistent hypoxemia. She was started on high-dose steroids and bronchodilators upon admission to the ICU. Benralizumab therapy was reintroduced on the third day of ICU admission after the patient demonstrated no improvement with conventional treatments. Clinical improvement in her respiratory parameters was noted within 48 hours of Benralizumab reintroduction, with progressive stabilization over the next few days. After a total of 7 days in the ICU, she was weaned off the High-Flow Nasal Cannula (HFNC) and subsequently transferred to a general medical ward. She remained in the hospital for another week to ensure continued

respiratory stability and was discharged from medical care approximately 14 days after ICU admission.

Discussion

This case highlights the complexity of managing severe asthma during pregnancy, particularly in the context of respiratory failure and the potential complications associated with a concurrent SARS-CoV-2 infection. Severe asthma in pregnancy is a significant challenge due to the physiological changes that occur in the respiratory system during gestation, including increased oxygen demand, reduced functional residual capacity, and altered immune responses (5,7) These factors make pregnant women more vulnerable to exacerbations, which can pose risks not only to the mother but also to fetal health (5,7). Asthma is one of the most common respiratory conditions encountered during pregnancy, affecting up to 8% of pregnant women (5,7). In this case, the patient was diagnosed with severe allergic asthma (T2 early onset) and had been on biologic therapy with Benralizumab. The decision to discontinue biologic therapy during pregnancy without medical consultation was likely driven by concerns regarding potential risks to the fetus, which, while understandable, may have led to the exacerbation of her asthma symptoms. Current evidence suggests that biologics, including Benralizumab, may be safe during pregnancy, though data is still limited (15). A key aspect of this case is the role of thoracic ultrasound in managing the patient's severe respiratory condition. Traditionally, chest X-rays and computed tomography (CT) scans are used to assess lung pathology. However, in pregnant patients, there is a strong preference to minimize radiation exposure to the fetus, making ultrasound a valuable alternative. Lung ultrasound has gained prominence in recent years as a non-invasive, radiation-free diagnostic tool that can provide immediate bedside information about lung and pleural conditions (11,12). Studies have shown that ultrasound can reliably detect pleural effusions, lung consolidations, and interstitial syndromes, all of which are relevant to the management of asthma exacerbations and respiratory infections (11,12). In this case, thoracic ultrasound provided critical insights into the patient's lung condition, revealing the presence of small subpleural consolidations and, later, pleural effusion, which helped guide treatment decisions. Ultrasound allowed continuous monitoring of the patient's response to therapy and the progression of her pulmonary condition, reducing the need for repeated radiographic imaging. This approach is consistent with recent literature advocating for the use of lung ultrasound in the management of acute respiratory conditions in pregnant women (16). The presence of respiratory infections, including *Streptococcus pneumoniae* and *Staphylococcus aureus*, further complicated the clinical picture. These pathogens are known to cause pneumonia and other respiratory complications, which can be particularly severe in pregnant women due to the altered immune responses during pregnancy (10). The initiation of broad-spectrum antibiotics was crucial in controlling the infection and preventing further deterioration of the patient's condition. Given the patient's immunological vulnerability, timely antibiotic therapy likely played a significant role in her recovery. A relevant consideration in this case is the potential influence of recent viral infections, particularly SARS-CoV-2, on asthma exacerbation. SARS-CoV-2 has been associated with increased airway hyperresponsiveness, prolonged inflammation, and altered immune responses that may contribute to worsening asthma symptoms (1). Interestingly, post-COVID airway dysfunction may persist for weeks or months, necessitating close monitoring in asthmatic patients (1). Awareness of these viral interactions is critical in assessing risk and optimizing management strategies for pregnant asthmatic women. Moreover, this case underlines the importance of multidisciplinary management involving pulmonologists, obstetricians, and intensivists. The combination of high-flow oxygen therapy, bronchodilators, corticosteroids, and eventually the resumption of biologic therapy contributed to the gradual improvement in the patient's respiratory status. Studies have shown that the use of high-dose bronchodilators and corticosteroids is generally safe and effective in pregnant women with severe asthma (5) Despite the severity of the respiratory failure, the patient's pregnancy continued without complications, resulting in the delivery of a healthy baby. This outcome emphasizes the importance of careful monitoring and appropriate therapeutic interventions in managing asthma exacerbations during pregnancy. Notably, the use of Benralizumab towards the later stage of the patient's treatment was well-tolerated and likely contributed to stabilizing her condition (7,15). To conclude, ultrasound proved to be a powerful diagnostic tool, allowing immediate and effective treatment

in a pregnant woman with severe asthma and respiratory distress. It helped reduce radiation exposure and was very useful in accurately monitoring clinical progress. Despite the use of older equipment and general-purpose probes, the operators clinical expertise and skill in ultrasound interpretation enabled timely and accurate management, contributing to the patient's positive outcome. Finally, given the potential for asthma exacerbations to compromise fetal lung function, the consideration of betaine and inositol supplementation as supportive interventions warrants further exploration in clinical practice.

Conflict of Interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

Ethics Approval: All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. This is an observational study. For this type of study, formal consent is not required because no personal data was contained, and there is no concern about identifying information.

Authors' Contribution: MAP and SD contributed to the conception, design, and manuscript drafting; SP and PC were involved in data collection and interpretation. GEC was involved in supervision. All authors reviewed and approved the final version of the manuscript.

Declaration on the Use of AI: None.

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