Life Threatening Pulmonary Renal Syndrome in Pregnancy When Diagnostic Uncertainty Meets Clinical Emergency

ABSTRACT

Background: Diffuse alveolar hemorrhage (DAH) is an exceptionally rare and life-threatening manifestation of systemic lupus erythematosus (SLE), particularly during pregnancy. Non-specific myeloperoxidase (MPO) antibody positivity without clinical vasculitis features creates diagnostic complexity, as these antibodies can occur in various inflammatory conditions beyond ANCA-associated vasculitis.

Case Presentation: A 35-year-old pregnant woman (G2P1) with established SLE since 2012 developed catastrophic pulmonary-renal syndrome at 27 weeks gestation, following methotrexate discontinuation 3 months prior preconceptionally. Despite an uneventful first pregnancy, she presented with a triad of diffuse alveolar hemorrhage, crescentic glomerulonephritis, and hypoxemic respiratory failure. She had a history of proteinuria and hematuria with positive MPO-ANCA dating back to 2015, though previous Nephrology assessment had not warranted renal biopsy.

Initial presentation showed normal anti-dsDNA (7 IU/mL), normal C3, chronically low C4, and creatinine 48 µmol/L rising to 199 µmol/L.Renal biopsy revealed focal necrotizing crescentic glomerulonephritis with pathognomonic full-house immunofluorescence pattern characteristic of lupus nephritis, contrasting with the pauci-immune pattern typical of ANCA vasculitis. The biopsy favored lupus nephritis with possible early superimposed ANCA features based on unusual necrotizing lesions. Despite two courses of pulse steroids, rituximab was initially considered but deemed slow-acting given the patient's rapid deterioration. Plasmapheresis was urgently initiated as a life-saving temporizing measure while infectious causes were excluded. Cyclophosphamide was administered as an emergency last resort measure when maternal survival became paramount. Tragically, fetal demise occurred at 29+2 weeks, but the patient survived with significant morbidity.

Conclusion: This case demonstrates that pregnancy-associated immune shifts can unmask severe SLE manifestations, even in patients with previously stable disease. DAH in SLE represents a true rheumatologic emergency requiring immediate aggressive intervention, regardless of diagnostic uncertainty surrounding non-specific antibody findings.

Keywords: Diffuse alveolar hemorrhage, systemic lupus erythematosus, pregnancy, crescentic glomerulonephritis, MPO antibodies, plasmapheresis, methotrexate withdrawal.

Authors: Dr. Arzoo Shahid PGY-5 GIM, Dr. Mena Bishay Rheumatology

No conflicts of intertest to declare.

UNIVERSITY OF ALBERTA

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When Diagnostic Uncertainty Meets Clinical Emergency

Case Presentation

Patient Demographics & History

Age
35-year-old G2P1 woman

SLE since 2012
Photosensitive rash, Raynaud's, positive ANA

Previous pregnancy (2018)
Completely uneventful

Medications
Hydroxychloroquine 300mg daily

MTX stopped
3 months preconceptionally

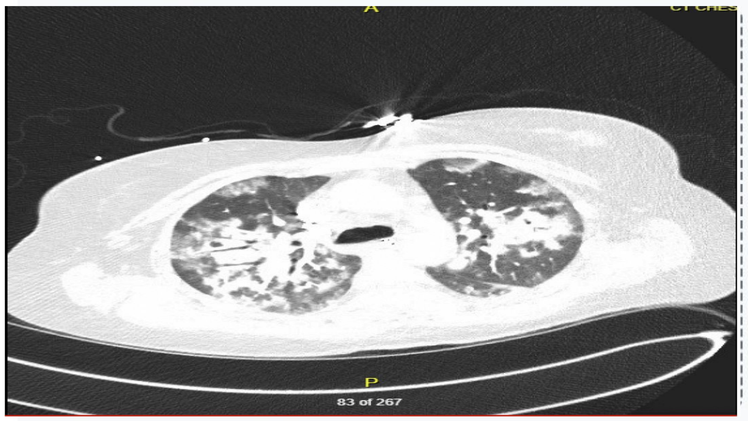
Presentation at 27 weeks:

- Hemoptysis
- Epistaxis
- Rapidly progressive dyspnea

Timeline

- **Week 25:** Arthritis flare → steroids
- **Week 26:** Steroid completion
- **Week 27:** Respiratory symptoms onset

Imaging



CT chest Feb 12: Progressive ground glass infiltrates consistent with pulmonary hemorrhage

Investigations

Parameter	Initial	Peak
Creatinine	**48 µmol/L**	**199 µmol/L**
CRP	**22 mg/L**	**308 mg/L**
Anti-dsDNA	7 IU/mL	Normal
C3	1.46 g/L	Normal
C4	**0.05 g/L**	**Low**
Protein/Cr	**389**	**2863 mg/mmol**
MPO-ANCA	**8.0 AI**	**Positive**

Key Finding: Normal anti-dsDNA despite severe nephritis challenges typical SLE flare pattern

Bronchoscopy (Feb 6): Sequential lavage confirmed diffuse alveolar hemorrhage

Renal Biopsy - Diagnostic Gold Standard:

- **Light Microscopy:** Focal necrotizing crescentic glomerulonephritis
- **Immunofluorescence:** "Full-house" pattern (IgG, IgA, IgM, C3, C1q)
- **Diagnosis:** Lupus nephritis with possible ANCA overlap

Background

Diffuse alveolar hemorrhage (DAH) is an exceptionally rare and life-threatening manifestation of systemic lupus erythematosus (SLE), particularly during pregnancy. Non-specific myeloperoxidase (MPO) antibody positivity without clinical vasculitis features creates diagnostic complexity.

Conclusion

Key Takeaways

This case demonstrates that pregnancy-associated immune shifts can unmask severe SLE manifestations. DAH in SLE represents a true rheumatologic emergency requiring immediate aggressive intervention.

Future Research Directions:

- Biomarkers for predicting severe pregnancy-associated SLE flares
- Optimizing treatment protocols for DAH in pregnancy
- Understanding pregnancy-specific immune mechanisms

Clinical Imperatives:

- Rapid recognition of DAH emergency
- Aggressive management despite diagnostic uncertainty
- Multidisciplinary care approach
- Enhanced monitoring protocols

Treatment Timeline

Critical Interventions

February 8-9, 2025
Pulse methylprednisolone (1st course)
Insufficient response

February 10-14, 2025
Plasmapheresis initiated
Life-saving temporizing measure

February 12, 2025
Mechanical ventilation required
Cyclophosphamide administered

February 14-18, 2025
Pulse steroids (2nd course)
During intubation

TRAGIC OUTCOME

Fetal demise: February 14 (29+2 weeks)
Maternal survival with morbidity
Successfully extubated: February 18

Dr. Arzoo Shahid PGY-5 GIM
Dr. Mena Bishay Rheumatology

Discussion

Pathophysiology & Diagnostic Challenge

Contributing Factors:

- **Methotrexate Discontinuation:** Withdrawal associated with lupus flares
- **Pregnancy Immune Shifts:** Paradoxical worsening despite uneventful first pregnancy
- **Post-Steroid Rebound:** Onset one week after completion

MPO Antibodies - Non-Specific:

- Present since 2015 (344 MFU → 8.0 AI)
- No clinical vasculitis features
- Can occur in infections, malignancies, autoimmune diseases
- Do NOT definitively indicate ANCA vasculitis

Emergency Recognition - DAH Warning Signs:

- Hemoptysis with dyspnea
- Rapid respiratory deterioration
- Bilateral pulmonary infiltrates
- High mortality if delayed treatment

References: 1. Zamora MR, et al. Diffuse alveolar hemorrhage and systemic lupus erythematosus. Medicine (Baltimore). 1997;76(3):192-202. 2. Walsh M, et al. Plasma exchange and glucocorticoids in severe ANCA-associated vasculitis. N Engl J Med. 2020;382(7):622-631. 3. Sun Y, et al. Systemic lupus erythematosus-associated diffuse alveolar hemorrhage: a single-center study. Lupus. 2020;29(8):870-876. 4. Yousif PA, et al. Lupus-induced vasculitis and multiple organ dysfunction syndrome as the first presentation of SLE in pregnancy. Am J Case Rep. 2020;21:e921299. 5. Lim S, et al. The outcome of pulmonary-renal syndromes in pregnancy: a systematic review. Obstet Med. 2018;11(1):17-23.

Learning Points

1. DAH is an exceptionally rare but life-threatening SLE manifestation requiring immediate aggressive treatment

2. MPO antibodies are non-specific markers that can occur in various conditions beyond ANCA vasculitis

3. Renal biopsy with immunofluorescence remains the gold standard for distinguishing lupus nephritis from ANCA vasculitis

4. Pregnancy-associated immune shifts can vary between pregnancies in the same individual

5. Plasmapheresis may serve as a life-saving temporizing measure in critically ill patients with diagnostic uncertainty

.6. Methotrexate discontinuation, while appropriate for pregnancy planning, may trigger severe flares in some patients

Disclosure: No conflicts of intertest to declare.

Patient Consent: Written informed consent was obtained from the patient for publication of this case report.