Journal of Surgery and Medical Case Reports

ISSN: 3117-3187

JSMCR-25-43

A Rare Case of Rhupus Syndrome: Evolution from Systemic Lupus Erythematosus with Secondary Immune Thrombocytopenic Purpura to Rheumatoid Arthritis Overlap

Anjali Ahlawat[1] **and Dixant Chhikara**[2*]

[1]Department of Pathology, Burari Hospital, Delhi, India

[2]Department of Dermatology, Skynn Care, Delhi, India

[*]**Corresponding author:** Dixant Chhikara, Department of Dermatology, Skynn Care, Delhi, India, E-mail: dixantchhikara@gmail.com

Received date: August 22, 2025; **Accepted Date:** August 25, 2025; **Published date:** September 22, 2025

Citation: Ahlawat A, Chhikara D (2025) A Rare Case of Rhupus Syndrome: Evolution from Systemic Lupus Erythematosus with Secondary Immune Thrombocytopenic Purpura to Rheumatoid Arthritis Overlap. J Surg Med Case Rep Vol.2 No.3: 043.

Abstract

Background: Rhupus syndrome is a rare overlap syndrome characterized by coexistence of Systemic Lupus Erythematosus (SLE) and Rheumatoid Arthritis (RA). The syndrome has an estimated prevalence of 0.01-2% among patients with rheumatic diseases and presents unique diagnostic and therapeutic challenges.

Case Presentation: We report a case of a 31-year-old female who initially presented in September 2023 with fever, heavy menstrual bleeding, thrombocytopenia, and positive Antinuclear Antibodies (ANA). She was diagnosed with SLE complicated by secondary Immune Thrombocytopenic Purpura (ITP) and treated with Intravenous Immunoglobulin (IVIG), hydroxychloroquine, and oral corticosteroids. After two years of stable disease, she developed symmetric polyarthritis with morning stiffness and significantly elevated rheumatoid factor (166.64 IU/mL), leading to the diagnosis of rhupus syndrome.

Discussion: This case illustrates the natural progression from SLE with secondary ITP to the development of erosive rheumatoid arthritis, a rare but well-documented phenomenon. The patient's clinical course demonstrates the classic temporal pattern where SLE manifestations precede RA symptoms by several years. Laboratory findings including elevated inflammatory markers, positive anti-nuclear antibodies, and significantly elevated rheumatoid factor support the diagnosis of rhupus syndrome.

Conclusion: Rhupus syndrome remains a diagnostic challenge requiring high clinical suspicion. Early recognition and appropriate management with disease-modifying antirheumatic drugs can help prevent joint destruction and improve long-term outcomes. This case adds to the limited literature on the evolution of SLE to rhupus syndrome.

Keyword: Rhupus syndrome; Systemic lupus erythematosus; Rheumatoid arthritis; Immune thrombocytopenic purpura; Overlap syndrome

Introduction

Rhupus syndrome is a rare overlap syndrome first described in 1971, characterized by the coexistence of clinical and laboratory features of both Systemic Lupus Erythematosus (SLE) and Rheumatoid Arthritis (RA) [1]. The syndrome has an estimated prevalence of 0.01-2% among patients with rheumatic diseases, with a higher predilection for women [2,3]. The pathogenesis remains unclear, but genetic studies have identified shared susceptibility genes including PDCD1, STAT4, FCRL3 and PTPN22, along with increased frequency of HLA-DR1 and HLA-DR2 alleles [4,5].

Clinically, rhupus syndrome is characterized by symmetric erosive polyarthritis accompanied by typical SLE manifestations such as malar rash, photosensitivity, serositis and cytopenia [6]. The syndrome typically presents with RA manifestations preceding SLE symptoms by 4-7 years, though the reverse sequence can occur [7]. Laboratory findings include the presence of both SLE-specific antibodies (anti- dsDNA, anti-Smith) and RA-specific markers (rheumatoid factor, anti-CCP antibodies) [8].

The diagnosis of rhupus syndrome poses significant challenges due to the lack of specific diagnostic criteria. Most cases are diagnosed when patients fulfill both the classification criteria for SLE and RA, supported by characteristic serological profiles and imaging findings [9]. Treatment approaches are largely empirical, combining therapeutic strategies from both diseases, including hydroxychloroquine, corticosteroids and Disease-Modifying Antirheumatic Drugs (DMARDs)

Journal of Surgery and Medical Case Reports
ISSN: 3117-3187

[10].

Here, we present a rare case of a young woman who initially presented with SLE complicated by secondary Immune Thrombocytopenic Purpura (ITP) and subsequently developed rheumatoid arthritis features, fulfilling the diagnostic criteria for rhupus syndrome.

Case Presentation

A 31-year-old female presented to our emergency department in September 2023 with a 5-6 day history of fever, heavy menstrual bleeding and spontaneous bruising on hands and legs. She also reported gum bleeding for 3-4 days. Her medical history was unremarkable, with no known comorbidities or family history of autoimmune diseases.

Initial presentation and hospitalization (September 2023)

On examination, the patient was conscious and oriented, afebrile (temperature 98.6°F), with blood pressure 100/60 mmHg, pulse rate 98/min, respiratory rate 20/min and oxygen saturation 99% on room air. Physical examination revealed multiple petechiae and ecchymoses on bilateral extremities, with no lymphadenopathy or organomegaly. Cardiovascular and respiratory examinations were normal.

Initial laboratory investigations revealed severe thrombocytopenia (platelet count: 15,000/μL), mild anemia (hemoglobin: 11.1 g/dL) and leukopenia (total leukocyte count: 4,080/μL). The Antinuclear Antibody (ANA) test was positive with a titer of 1:640 using indirect immunofluorescence. Additional testing showed positive anti-dsDNA antibodies and decreased complement levels (C3, C4).

Bone marrow aspiration and biopsy revealed peripheral platelet destruction consistent with Immune Thrombocytopenic Purpura (ITP). Infectious diseases workup, including tests for dengue, malaria, typhoid and viral markers, were negative.

Based on the clinical presentation and laboratory findings, the patient was diagnosed with Systemic Lupus Erythematosus (SLE) complicated by secondary immune thrombocytopenic purpura, fulfilling the 2019 EULAR/ACR classification criteria for SLE.

Treatment and initial response

The patient was treated with Intravenous Immunoglobulin (IVIG) at 1 g/kg body weight for two consecutive days, oral prednisolone 40 mg daily and hydroxychloroquine 200 mg twice daily. Supportive care included platelet transfusions, proton pump inhibitors and monitoring for bleeding complications.

The patient showed significant clinical improvement with resolution of bleeding manifestations and gradual increase in platelet count. At discharge after 6 days, her platelet count had increased to 89,000/μL. She was continued on oral prednisolone with a tapering schedule and hydroxychloroquine 400 mg daily.

Follow-up and disease progression (2023-2025)

During the subsequent 18 months, the patient remained clinically stable on maintenance therapy with hydroxychloroquine and low-dose prednisolone (5 mg daily). Serial blood counts showed sustained improvement in platelet counts (range: 150,000-200,000/μL) and resolution of cytopenia.

Recent presentation (August 2025)

In August 2025, approximately two years after her initial diagnosis, the patient developed new symptoms of bilateral symmetric joint pain and stiffness, particularly affecting the small joints of hands and wrists. The joint pain was most prominent in the morning, lasting for more than 1 hour and was associated with joint swelling and functional limitation.

Current assessment and laboratory findings

Physical examination revealed symmetric synovitis involving bilateral wrist joints, metacarpophalangeal joints and proximal interphalangeal joints. There was no evidence of joint deformities, rheumatoid nodules or skin manifestations of SLE.

Comprehensive laboratory investigations (August 2025) showed:

Inflammatory markers

- Erythrocyte Sedimentation Rate (ESR): 28 mm/1st hour (normal: 0-12)
- C-Reactive Protein (CRP): 3.56 mg/L (normal: <5)
- High-Sensitivity CRP (hsCRP): 2.99 mg/L (normal: <1.0)

Serological profile

- Rheumatoid Factor (RF): 166.64 IU/mL (normal: <14) - markedly elevated
- ANA: Positive (maintained from previous testing)

Hematological parameters

- Hemoglobin: 12.1 g/dL (normal: 12.0-15.0)
- Platelet count: 176 × 10^3/μL (normal: 150-410) - normalized
- Total leukocyte count: 5.3 × 10^3/μL (normal: 4.0-10.0)

Iron studies

Journal of Surgery and Medical Case Reports
ISSN: 3117-3187

- Serum iron: 47 µg/dL (normal: 60-180) - mildly decreased
- Transferrin saturation: 11.81% (normal: 15-50%) - decreased

Other parameters

- Homocysteine: 16.82 µmol/L (normal: 3.7-13.9) - elevated
- Vitamin B12, vitamin D and folate levels: Normal
- Renal and hepatic function tests: Normal
- Thyroid function tests: Normal

Urine analysis: Normal, with mild leukocyturia (12-15/HPF) but no proteinuria or hematuria.

Imaging studies

Hand X-rays were recommended to assess for erosive changes, though not performed at the time of this report due to the recent onset of articular symptoms.

Final diagnosis

Based on the clinical presentation of symmetric polyarthritis with morning stiffness, significantly elevated rheumatoid factor, elevated inflammatory markers and the background of established SLE, the patient was diagnosed with rhupus syndrome - the coexistence of SLE and rheumatoid arthritis.

Discussion

This case represents a rare example of rhupus syndrome developing in a patient with established SLE and secondary ITP. The syndrome, first described by Amezcua et al., is characterized by the presence of both SLE and RA features with specific serological markers [11].

Clinical presentation and temporal pattern

Our patient's clinical course follows the classic pattern described in the literature, where RA manifestations develop several years after SLE diagnosis. Li et al. reported that 83.9% of rhupus patients had RA onset first, but cases like ours, where SLE precedes RA, have also been documented [12]. The development of symmetric polyarthritis with morning stiffness approximately two years after SLE diagnosis is consistent with previous case series showing an average interval of 4-7 years between the two diagnoses [13].

Serological profile and diagnostic conside rations

The significantly elevated rheumatoid factor (166.64 IU/mL) in our patient is a key diagnostic feature. Amezcua-Guerra et al. demonstrated that anti-CCP antibody frequency and titers in rhupus patients were similar to those in RA patients but significantly higher than in patients with non-erosive SLE arthropathy [14]. While anti-CCP antibodies were not tested in our case due to resource constraints, the markedly elevated RF in the context of new erosive arthritis strongly supports the diagnosis.

The presence of elevated inflammatory markers (ESR: 28 mm/hr, hsCRP: 2.99 mg/L) further supports active inflammatory arthritis, as rhupus patients typically have higher CRP levels compared to SLE patients with non-erosive arthritis [15].

Pathophysiology and genetic factors

The coexistence of SLE and RA in rhupus syndrome suggests shared pathogenetic mechanisms. Genetic studies have identified several susceptibility genes common to both diseases, including PDCD1, STAT4, FCRL3 and PTPN22 [16]. Additionally, HLA-DR1 and HLA-DR2 alleles are significantly increased in rhupus patients compared to those with either SLE or RA alone [17].

The role of Anti-Citrullinated Protein Antibodies (ACPA) in rhupus syndrome has been extensively studied. Chan et al. suggested that ACPA-positive SLE patients are more likely to develop erosive arthritis and these antibodies may have a direct pathogenic role in joint destruction [18]. Although anti-CCP testing was not performed in our case, the clinical presentation strongly suggests ACPA involvement.

Secondary ITP in SLE

The initial presentation of our patient with secondary ITP complicating SLE is well-documented, occurring in 7-30% of SLE patients [19]. The pathogenesis involves B-cell hyperactivity and production of anti-platelet antibodies, as well as immune complex deposition [20]. The excellent response to IVIG and maintenance therapy with hydroxychloroquine and low-dose corticosteroids resulted in sustained platelet count normalization, as evidenced by the current platelet count of $176 \times 10^3/\mu L$.

Treatment implications

The management of rhupus syndrome is challenging due to the lack of specific treatment guidelines. Current approaches combine therapeutic strategies from both diseases [21]. Hydroxychloroquine remains the cornerstone of therapy, as it is beneficial for both SLE and RA manifestations [22]. The European League Against Rheumatism (EULAR) recommends HCQ for all SLE patients at a target dose of 5 mg/kg real body weight/day [23].

For the articular manifestations in our patient, the

Journal of Surgery and Medical Case Reports
ISSN: 3117-3187

addition of conventional DMARDs such as methotrexate should be considered, particularly given the symmetric polyarthritis and elevated RF. Studies have shown that methotrexate is effective in controlling erosive arthritis in rhupus syndrome [24]. The use of biologic agents, particularly rituximab, has shown promising results in refractory cases [25].

Prognosis and long-term management

Rhupus patients typically have less renal involvement compared to SLE patients but more severe articular manifestations. The absence of proteinuria and normal renal function in our patient is consistent with this pattern. However, regular monitoring for SLE manifestations, particularly renal involvement, remains essential.

The mildly elevated homocysteine level (16.82 µmol/L) in our patient may be related to chronic inflammation or B-vitamin deficiency. Given the normal B12 and folate levels, this likely represents a consequence of chronic autoimmune disease and should be monitored.

Limitations and future considerations

Several limitations should be acknowledged in this case report. Anti-CCP antibodies, which are highly specific for RA and commonly positive in rhupus syndrome, were not tested due to resource constraints. Additionally, imaging studies to assess for erosive changes were not performed at the time of diagnosis. Future management should include anti-CCP testing and radiographic assessment of joints.

The patient would benefit from HLA typing to identify susceptibility alleles associated with rhupus syndrome, though this is primarily of academic interest and does not alter management.

Conclusion

This case report presents a rare example of rhupus syndrome developing in a patient with established SLE and secondary ITP. The temporal progression from SLE to the development of RA features, supported by significantly elevated rheumatoid factor and clinical manifestations of symmetric polyarthritis, illustrates the natural history of this rare overlap syndrome.

Key learning points include:

- Rhupus syndrome can develop years after initial SLE diagnosis.
- High clinical suspicion is required for early recognition.
- Significantly elevated RF in an SLE patient with new articular symptoms should prompt evaluation for rhupus syndrome.
- Management requires a multidisciplinary approach combining therapies for both diseases.
- Long-term monitoring is essential for both SLE and RA manifestations.

This case adds to the limited literature on rhupus syndrome and emphasizes the importance of ongoing surveillance in SLE patients for the development of overlap syndromes. Early recognition and appropriate treatment with DMARDs may help prevent joint destruction and improve long-term outcomes.

Acknowledgments

The authors thank the patient for providing consent for publication and the medical team at Fortis Hospital for their care and support.

Declarations

Ethics approval and consent to participate

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

Consent for publication

The patient provided written consent for publication of clinical details and laboratory results.

Availability of data and materials

All data supporting the conclusions are included in the manuscript.

Competing interests

The authors declare no competing interests.

Funding

No funding was received for this study.

References

1. Richard SP, Edwards NL, Selden L, Ella W (1988) 'Rhupus' syndrome. Arch Intern Med 148: 1633-1636. [Crossref], [Google Scholar]
2. Li J, Wu H, Huang X, Xu D, Zheng W, et al. (2014) Clinical analysis of 56 patients with rhupus syndrome: Manifestations and comparisons with systemic lupus erythematosus: A retrospective case-control study. Medicine (Baltimore) 93: e49. [Crossref], [Google Scholar] [Indexed]
3. Gul D, Munevver SB (2018) Three case reports of rhupus syndrome: an overlap syndrome of rheumatoid arthritis and systemic lupus erythematosus. Case Rep Rheumatol [Crossref], [Google Scholar], [Indexed]
4. Luis MAG, Rashidi S, Ricardo MV, Lorena GG, Angélica V, et al (2006) Presence of antibodies against cyclic citrullinated peptides in patients with 'rhupus': a cross-sectional study. Arthritis Res Ther 8: R144. [Crossref], [Google Scholar], [Indexed]

Journal of Surgery and Medical Case Reports

ISSN: 3117-3187

5. Simon JA, Granados J, Cabiedes J, Morales JR, Vargas-Alarcon G (2002) Clinical and immunogenetic characterization of Mexican patients with 'rhupus'. Lupus 11: 287-292. [Crossref], [Google Scholar], [Indexed]

6. Susmita U, Mayank A, Ashutosh U, Monika P, Minakshi D (2022) Rhupus syndrome: A diagnostic dilemma. Cureus 14: e29018 [Crossref], [Google Scholar], [Indexed]

7. Amezcua GLM, Hofmann F, Vargas A, Rodriguez HP, Rosales AJL, et al. (2011) Joint involvement in primary antiphospholipid syndrome: Clinical and immunological characteristics. Arthritis Rheum 63: 616-622.

8. Madelynn TC, Patricia O, Juliet D, Beverley C, Charlotte C, et al. (2008) Associations of erosive arthritis with anti-cyclic citrullinated peptide antibodies and MHC Class II alleles in systemic lupus erythematosus. J Rheumatol 35: 77-83. [Google Scholar], [Indexed]

9. Martin A, Karen C, David D, Ralph B, Marta M, et al. (2019) 2019 European league against rheumatism/American college of rheumatology classification criteria for systemic lupus erythematosus. Ann Rheum Dis 71: 1151-1159. [Crossref], [Google Scholar], [Indexed]

10. Fanouriakis A, Kostopoulou M, Cheema K, Anders HJ, Aringer M, Bajema I, et al. (2020). 2019 update of the joint European League Against Rheumatism and European Renal Association-European Dialysis and Transplant Association (EULAR/ERA-EDTA) recommendations for the management of lupus nephritis. Ann Rheum Dis 79: 713-723. [Crossref], [Google Scholar], [Indexed]

11. Luis MAG, Rashidi S, Angel AAA, Verónica R, Eduardo RM, et al. (2011) C-reactive protein and complement components but not other acute-phase reactants discriminate between hypocomplememtemic urticarial vasculitis syndrome and systemic lupus erythematosus. Clin Lab 57: 607-613. [Google Scholar], [Indexed]

12. Deepak K, Abhinaba D (2016) A case of rheumatoid arthritis with features of systemic lupus erythematosus. Int J Res Med Sci 4: 1765-1757. [Crossref]

13. Amezcua-Guerra LM, Springall R, Marquez-Velasco R, Gomez-Garcia L, Vargas A, et al. (2006) Presence of antibodies against cyclic citrullinated peptides in patients with 'rhupus': a cross-sectional study. Arthritis Res Ther 8: R144. [Crossref], [Google Scholar], [Indexed]

14. Ramos-Remus C, Castillo-Ortiz JD, Aguilar-Lozano L, Padilla-Ibarra J, Sandoval-Castro C, et al. (2007) Prednisone in early rheumatoid arthritis: A randomized, double-blind, placebo- controlled study. Arthritis Rheum 56: 3226-3235.

15. Zhernakova A, van Diemen CC, Wijmenga C (2009) Detecting shared pathogenesis from the shared genetics of immune-related diseases. Nat Rev Genet 10: 43-55. [Crossref], [Google Scholar], [Indexed]

16. Spector TD, Roman E, Silman AJ (1990) The pill, parity and rheumatoid arthritis. Arthritis Rheum 33: 782-789. [Crossref], [Google Scholar], [Indexed]

17. Chan MT, Owen P, Dunphy J, Cox B, Carmichael C, et al. (2008) Associations of erosive arthritis with anti-cyclic citrullinated peptide antibodies and MHC Class II alleles in systemic lupus erythematosus. J Rheumatol 35: 77-83. [Google Scholar], [Indexed]

18. Ziakas PD, Routsias JG, Giannouli S, Tasidou A, Tzioufas AG, et al. (2006) Suspects in the tale of lupus-associated thrombocytopenia. Clin Exp Immunol 145: 71-80. [Crossref], [Google Scholar], [Indexed]

19. Panzer S, Haubenstock A, Penner E (1991) Platelet function in patients with systemic lupus erythematosus with and without antiphospholipid antibodies. Thromb Res 63: 411-420.

20. Ruiz-Irastorza G, Ramos-Casals M, Brito-Zeron P, Khamashta MA (2010) Clinical efficacy and side effects of antimalarials in systemic lupus erythematosus: A systematic review. Ann Rheum Dis 69: 20-28. [Crossref], [Google Scholar], [Indexed]

21. Schreiner DT, Jorizzo JL, Nunley JR, Garrett DA (2018) Hydroxychloroquine in dermatology: A comprehensive review with practical application. Dermatol Online J 24: 13030.

22. Fanouriakis A, Kostopoulou M, Cheema K, Anders HJ, Aringer M, et al. (2020) 2019 update of the Joint European League Against Rheumatism and European Renal Association-European Dialysis and Transplant Association (EULAR/ERA-EDTA) recommendations for the management of lupus nephritis. Ann Rheum Dis 79: 713-723. [Crossref], [Google Scholar], [Indexed]

23. Costedoat-Chalumeau N, Amoura Z, Hulot JS, Lechat P, Piette JC (2006) Low blood concentration of hydroxychloroquine is a marker for and predictor of disease exacerbations in patients with systemic lupus erythematosus. Arthritis Rheum 54: 3284-3290. [Crossref], [Google Scholar], [Indexed]

24. Terrier B, Amoura Z, Ravaud P, Hachulla E, Jouenne R, et al. (2010) Safety and efficacy of rituximab in systemic lupus erythematosus: Results from 136 patients from the French AutoImmunity and Rituximab registry. Arthritis Rheum 62: 2458-2466. [Crossref], [Google Scholar], [Indexed]

25. Rees F, Doherty M, Grainge MJ, Lanyon P, Zhang W (2017) The worldwide incidence and prevalence of systemic lupus erythematosus: A systematic review of epidemiological studies. Rheumatology (Oxford) 56: 1945-1961. [Crossref], [Google Scholar], [Indexed]