CASE REPORT / REPORTE DE CASO

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Severe Thrombocytopenia and Subdural Hematoma in Rhupus Syndrome: A Case Report

Trombocitopenia severa y hematoma subdural en síndrome de Rhupus: reporte de caso

Nathalie Victoria Zacarías-Mendoza [1,a], *Grethel Zarimah Díaz-Vargas* [1;2,b], *Daniel Andrés Cáceres-Alpaca* [1,c;3,d]

[1] Universidad Peruana Cayetano Heredia, Facultad de Medicina Alberto Hurtado. Lima, Perú.
[2] Department of Cardiology, Hospital Nacional Arzobispo Loayza. Lima, Perú.
[3] Department of Internal Medicine, Hospital Nacional Arzobispo Loayza. Lima, Perú.
[a] Medical student.
[b] Cardiology resident.
[c] Assistant Professor.
[d] Internal Medicine Physician.

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Correspondence:
Nathalie Victoria Zacarías Mendoza
✉ nathalie.zacarias@upch.pe

SUMMARY

Rhupus is a rare overlap syndrome of rheumatoid arthritis and systemic lupus erythematosus. Severe hematological and neurological manifestations are unusual and pose a diagnostic challenge. We present the case of a 58-year-old woman with long-standing joint deformities who developed ecchymosis, epistaxis, and progressive neurological impairment. Imaging studies revealed a subdural hematoma, and laboratory tests showed severe thrombocytopenia, elevated titers of rheumatoid factor and anti-CCP antibodies, as well as positive antinuclear antibodies. The patient met diagnostic criteria for both diseases. Following corticosteroid therapy and surgical evacuation of the hematoma, she progressed favorably and was discharged on immunosuppressive therapy. This case highlights the importance of timely recognition of Rhupus syndrome and the risk of life-threatening complications, underscoring the need for early multidisciplinary management.

KEYWORDS: rheumatoid arthritis; systemic lupus erythematosus; thrombocytopenia; autoimmune diseases.

RESUMEN

Rhupus es una rara superposición de artritis reumatoide y lupus eritematoso sistémico. Las manifestaciones hematológicas y neurológicas graves son inusuales y representan un reto diagnóstico. Se presenta el caso de una mujer de 58 años con deformidades articulares de larga evolución, que desarrolló equimosis, epistaxis y deterioro neurológico progresivo. Los estudios de imagen evidenciaron un hematoma subdural; los exámenes de laboratorio mostraron trombocitopenia severa, títulos elevados de factor reumatoide y anticuerpos anti-CCP, así como anticuerpos antinucleares positivos. La paciente cumplió criterios diagnósticos para ambas enfermedades. Tras el tratamiento con corticosteroides y la evacuación

quirúrgica del hematoma, evolucionó favorablemente y fue dada de alta con tratamiento inmunosupresor. Este caso resalta la importancia de reconocer oportunamente el síndrome de Rhupus y el riesgo de complicaciones mortales, destacando la necesidad de un manejo multidisciplinario precoz.

PALABRAS CLAVE: artritis reumatoide; lupus eritematoso sistémico; trombocitopenia; enfermedades autoinmunes.

INTRODUCTION

Rhupus syndrome is a recognized overlap syndrome characterized by the coexistence of rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) [1]. It is a rare entity, with a reported prevalence ranging from 0.01 to 2% among patients with SLE or RA [2] and presents with clinical features of both diseases [2,3]. It often follows sequential conditions, with RA preceding SLE in about 69-84% of cases [2]. The syndrome is marked by erosive polyarthritis typical of RA, alongside symptoms and signs of SLE, such as hematological abnormalities, skin involvement, and occasionally renal involvement. Diagnosis remains challenging due to the lack of standardized criteria and relies on the combination of clinical findings and serological markers of both RA and SLE [3–5].

Given the rarity and clinical relevance of severe hematologic complications, this report describes a patient who initially presented RA-related joint deformities and later developed SLE complicated by severe thrombocytopenia and subdural hematoma.

CASE PRESENTATION

A 58-year-old Peruvian woman with no known comorbidities aside from a long-standing history of progressive hand joint deformities and functional limitation without prior medical evaluation, presented to the emergency department with a two-month history of progressive bruising, headaches, and epistaxis. She had previously worked in agriculture but discontinued this activity years earlier due to joint pain and hand deformities affecting manual function.

Symptoms began two months earlier with spontaneous hematomas involving the right upper limb, followed within one week by the left upper and left lower limbs. She also experienced intermittent holocraneal headache of moderate intensity and two episodes of self-limited epistaxis. Three days before admission, she developed recurrent epistaxis associated with hematemesis and syncope. Initial evaluation revealed severe thrombocytopenia ($26{,}000/mm^3$). Due to progressive somnolence and hyporexia, she was referred to our hospital.

On admission, she was somnolent but arousable, with transient left eyelid ptosis. Vital signs showed a blood pressure of 91/53 mm Hg, a heart rate of 63 bpm, a respiratory rate of 18 breaths per minute, and an oxygen saturation of 93%. Physical examination revealed multiple ecchymoses on the upper extremities, bilateral ulnar deviation of the fingers, and swollen, tender metacarpophalangeal joints, wrists, and knees (Figure 1). Neurological examination demonstrated right-sided hemiparesis (muscle strength 3/5) and hyporeflexia, without meningeal signs.

Laboratory tests showed hemoglobin of 9.9 g/dL, leukocyte count of $6{,}320/mm^3$, and platelet count of $26{,}000/mm^3$; the direct Coombs test was negative. Peripheral blood smear demonstrated marked thrombocytopenia with preserved platelet morphology and anisocytosis (1–2+) and hypochromia (1–2+) of red blood cells. Reticulocyte count ranged from 1.68 to 2.78%, indicating mild reticulocytosis. Lactate dehydrogenase levels remained within normal limits (115 U/L). Coagulation studies showed preserved hemostasis, with prothrombin time ranging from 13.6 to 14.4 seconds, INR ranging from 1.01 to 1.07, and activated partial thromboplastin time of 38.8 seconds. D-dimer levels were elevated, reaching up to 3.54 mg/L FEU. Renal function was preserved, with creatinine levels ranging from 0.38 to 0.46 mg/dL and urea levels between 28 and 62 mg/dL. Electrolyte analysis showed mild hypokalemia, with potassium levels ranging from 2.85 to 3.36 mEq/L. Iron studies revealed low serum iron levels (27–28 μg/dL) and reduced transferrin saturation (16%), consistent with iron deficiency anemia. Vitamin B12 (442 pg/mL) and folate levels (11.3 ng/mL) were within normal limits. Brain computed tomography performed on the second day after admission revealed a left front parietotemporal subdural hematoma with midline shift (Figure 2A). Follow-up imaging on day ten showed hematoma progression, with an increase in thickness from 19 mm to 22 mm and a midline shift increasing to 15 mm (Figure 2B).

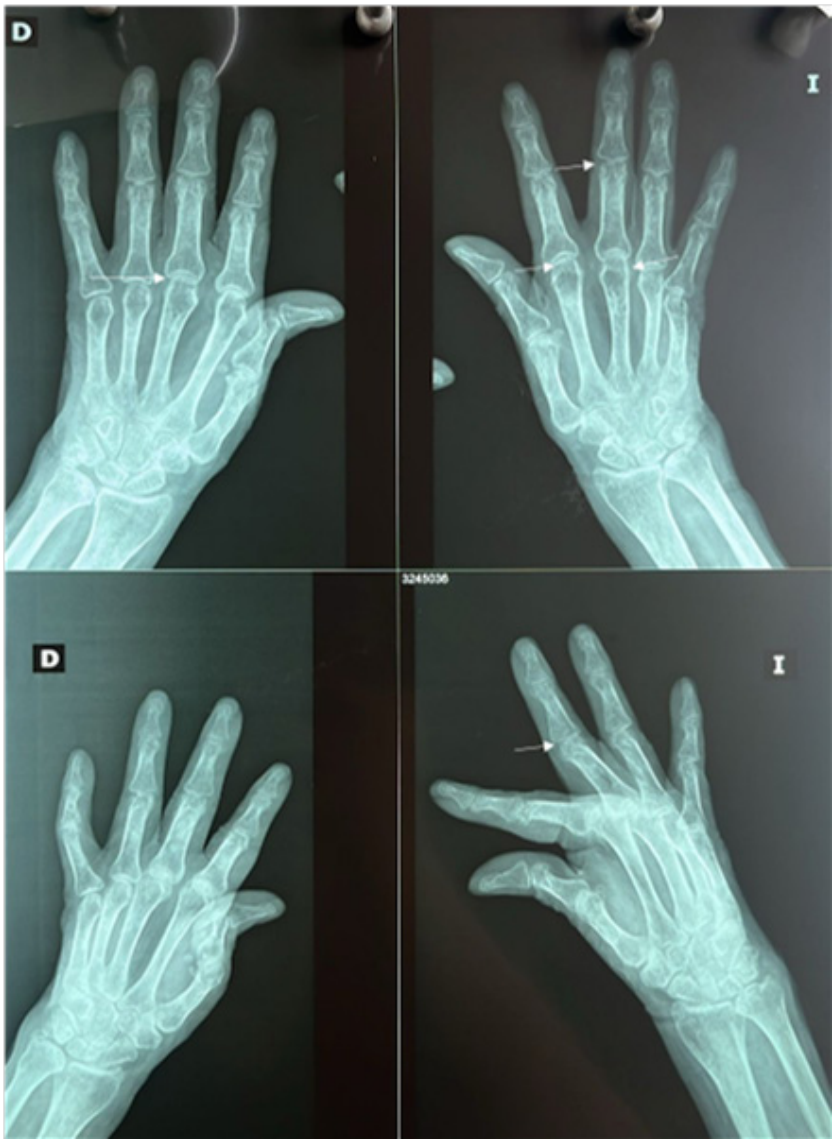

Figure 1. Radiographs of both hands showing erosive changes (arrows), joint space narrowing, and ulnar deviation, consistent with rheumatoid arthritis in the setting of Rhupus syndrome. Erosions are identified at the head of the third metacarpal in the right hand, and at the head of the proximal phalanx of the third digit as well as the second and third metacarpal heads in the left hand.

On day ten, the patient experienced acute neurological deterioration with flaccid quadriparesis, hypotension, fever, and unresponsiveness, accompanied by miotic nonreactive pupils and generalized areflexia. Emergency resuscitation measures were initiated, and a neurosurgical consult was requested. Laboratory evaluation revealed worsening thrombocytopenia (21,000/mm^3) and a hemoglobin level of 8.4 g/dL.

Autoimmune and hematologic testing revealed elevated rheumatoid factor (RF) (96.82 IU/mL), C-reactive protein (2.1 mg/dL), and erythrocyte sedimentation rate (140 mm/h), with anti-cyclic citrullinated peptide (anti-CCP) >1000 U/mL; cANCA and pANCA tests were negative. Complement levels were slightly reduced (C3: 103.16 mg/dL; C4: 16.7 mg/dL), and lupus anticoagulant testing was negative. Bone marrow aspiration showed mild hyperplasia of megakaryocytes, focal dysplastic changes in the erythroid lineage, and no evidence of malignancy.

After initiating high-dose corticosteroids, platelet counts improved to 110,000/mm^3. Antinuclear antibodies (ANA) were positive (1:1000, homogeneous

pattern), and the ENA panel revealed nucleosome antibody positivity (342.64 U/mL). Anti-dsDNA, anti-Sm, Ro52, PCNA, RNP, and histone antibodies were negative, as confirmed by the Microbiolot-Array ANA Plus IgG (44 Antigens) panel.

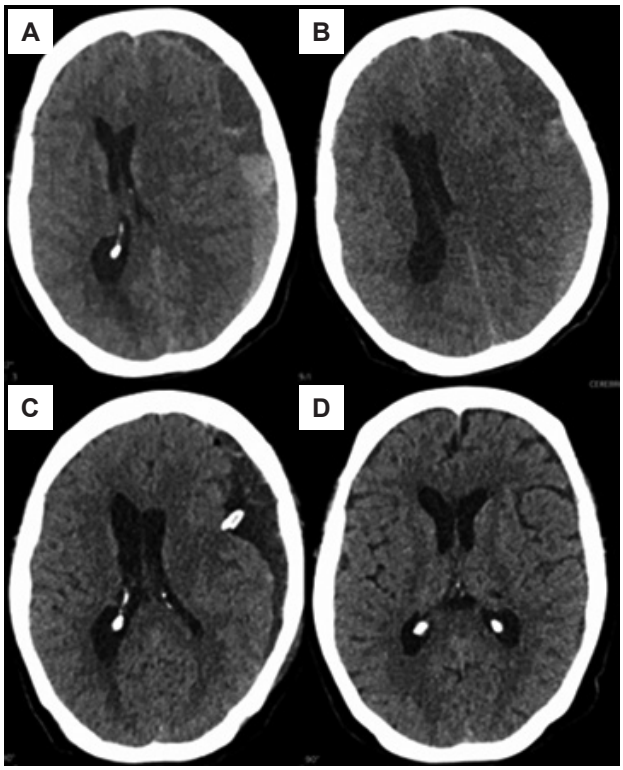

Figure 2. A: Non-contrast axial brain CT performed on the second day after admission showing a left frontoparietotemporal subacute subdural hematoma with rebleeding, measuring approximately 19 mm in thickness and causing significant mass effect with a midline shift of up to 15 mm. **B:** Follow-up non-contrast brain CT obtained on the tenth day after admission showing progression of the left frontoparietotemporal subdural hematoma, with increased thickness to approximately 22 mm and persistent midline shift, consistent with worsening intracranial mass effect. **C:** Immediate postoperative non-contrast brain CT performed after trepanopuncture with evacuation of the subdural hematoma and placement of a left frontoparietal subdural drain, demonstrating marked reduction of the hematoma and improvement of mass effect compared with preoperative imaging. **D:** Follow-up non-contrast brain CT obtained approximately 8 weeks after surgery, demonstrating near-complete resolution of the left frontoparietotemporal subdural hematoma, with restoration of midline structures and no residual mass effect.

The patient received four pulses of IV dexamethasone followed by oral prednisone, with progressive neurological improvement. After platelet transfusion, she underwent trepan puncture with evacuation of the subdural hematoma on day twenty-eight (Figure 2C). Postoperative recovery was uneventful, and she was discharged on prednisone and hydroxychloroquine (Figure 2D).

DISCUSSION

Hematological involvement is the most frequent systemic feature in Rhupus syndrome, occurring in 70% of cases. Although extra-articular manifestations are generally milder compared to classic SLE, serious complications such as lupus-related thrombocytopenia and secondary intracranial hemorrhage may still occur. Other systemic features, such as renal involvement (35%), cutaneous manifestations (41%), serositis (26%), and neurological involvement (5%) have also been documented, though they tend to present with less frequency and severity. [3,5,6]

In this case, longstanding joint pain and progressive hand deformities preceded systemic manifestations by several years, suggesting an initial RA–predominant presentation. This pattern is consistent with published data indicating that RA precedes SLE in approximately 84% of patients with Rhupus syndrome, with a mean delay of 9.2 years before SLE onset. [2]

Unlike the nonerosive deformities seen in Jaccoud's arthropathy, Rhupus arthritis is characterized by erosive, RA-like joint involvement [5,7]. Patients typically present with joint swelling, elevated inflammatory markers such as C-reactive protein, and radiological features including joint space narrowing and erosions [4,8]. Rhupus arthropathy has a typical clinical and radiological distribution like AR, with no significant differences in the frequencies of morning stiffness, joint pain, tenderness, and symmetrical polyarthritis when compared to RA [3]. The most frequently affected joints are the radiocarpal and intercarpal joints in the wrist, and the proximal interphalangeal or metacarpophalangeal joints—particularly the second and fifth fingers—in the hand [4,5]. These features were observed, which exhibited progressive hand deformities, joint swelling, elevated CRP (2.1 mg/dL), and ultrasound evidence of chronic synovitis and bilateral flexor tenosynovitis.

Diagnosis of Rhupus syndrome remains challenging due to the absence of standardized criteria. Imaging modalities such as ultrasound or magnetic resonance

imaging may improve the detection of erosive changes in patients with SLE and facilitate early diagnosis [3,5]. Serologically, Rhupus syndrome is commonly associated with RF and anti-CCP antibodies, in addition to lupus-related autoantibodies [7]. Anti-CCP antibodies are detected in 57-100% of cases and are strongly associated with erosive arthritis (OR 28.5, $p < 0.001$), whereas RF positivity ranges from 42–100% [4,5]. In this case, the patient had markedly elevated RF and anti-CCP. The ANA test was positive with a homogeneous pattern at a titer of 1:1000, and the ENA panel revealed positivity for nucleosome antibodies. Other SLE-associated antibodies, including anti-dsDNA, anti-Sm, Ro52, PCNA, RNP, and histone, were negative.

Anti-nucleosome antibodies (ANuA) are directed against DNA–histone complexes released during apoptosis, reflecting defective clearance of nuclear debris in SLE. They are considered sensitive markers of SLE and have been associated with disease activity, particularly renal involvement, and overall organ damage. Importantly, ANuA may be detected in patients who are negative for anti-dsDNA antibodies, thereby increasing diagnostic sensitivity in serologically incomplete presentations [9,10]. In this context, the presence of our patient is clinically relevant, as it supports the diagnosis of SLE despite the absence of anti-dsDNA and anti-Sm antibodies.

The patient fulfilled the 2019 EULAR/ACR classification criteria for SLE with a total score of 12 points (2 points for fever, 4 points for thrombocytopenia, and 6 points for joint involvement) [11]. Additionally, the patient also fulfilled the 2010 ACR/EULAR classification criteria for RA, with a total score of 10 points, based on extensive joint involvement, high-positive serology (RF and anti-CCP), symptom duration longer than 6 weeks, and elevated acute-phase reactants [12]. The concurrent fulfillment of SLE and RA classification criteria supports the diagnosis of Rhupus syndrome in this patient.

This case underscores the importance of early recognition of Rhupus syndrome, particularly when RA -like features dominate the initial clinical picture. The subsequent emergence of SLE manifestations, including severe thrombocytopenia complicated by subdural hematoma, highlights the potential for serious and life-threatening extra-articular involvement in Rhupus syndrome. Timely diagnosis and a coordinated multidisciplinary approach addressing both RA and SLE were crucial to achieving neurological recovery and clinical stability.

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