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Case Report

A Case Report of a Male with Systemic Lupus Erythematous with First Presentation of Annular Macular Itchy Rashes on his Extremities

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Abstract

Background: Systemic lupus erythematosus (SLE) is an idiopathic autoimmune disease which impacts multiple organs and has various clinical presentations. Among all the organs, the skin is the most frequently affected.

Case Presentation: This case report presents a 34-year-old male who presented with severe, itchy, and painful rashes over his right arm and both legs, along with a history of pigmented skin lesions. Initially, the patient was given corticosteroid creams by a dermatologist, but the condition progressed, requiring further investigation. The patient's medical history revealed hypertension and, on review, signs of rashes, fatigue, and arthralgias were noted.

Physical examination indicated mild swelling and tenderness in both knees. Additionally, an examination revealed his skin was warm, he had fast capillary refill (<2 seconds), and he had an erythematic rash on the right arm and both legs. A nodular erythema rash was seen on the left leg, along with pigmented skin lesions on the right leg, including a bigger lesion measuring approximately 2.5 cm. Laboratory results indicated increased creatinine, low white blood cell count, anemia, and abnormal protein levels, raising doubts about SLE. Further tests confirmed a raised level of autoantibodies, low complement levels, and positive lupus-related antibodies.

Later, the patient was referred to a rheumatologist and an SLE diagnosis was confirmed based on laboratory results and hematological manifestations, mucocutaneous involvement, and lupus nephritis. Treatment initially started with hydroxychloroquine and prednisolone, then tests were repeated and the patient underwent a renal biopsy that revealed focal segmental glomerulosclerosis. He was again prescribed methylprednisolone and prednisolone for three days. The patient's condition resolved and he made a successful recovery.

Conclusion: This case demonstrates the multiple clinical manifestations of SLE, the necessity of in-depth investigations, and the requirement for multidisciplinary care to address the intricacies of organ involvement in the disease.

Keywords: SLE, Systemic Lupus Erythematous, Cutaneous, Antinuclear, Antibodies

Introduction

Systemic lupus erythematosus (SLE) is an idiopathic connective tissue disease. It is most prevalent in women of reproductive age [1]. The female-to-male ratio as reported is 8–15:1, whereas the ratios prior to puberty and post menopause are significantly lower at 2–6:1 and 3–8:1, respectively [2]. In fact, in the United States in 2021, the annual prevalence of SLE was reported to be approximately 72.8 cases per 100,000 people [3]. Among various ethnic groups, the prevalence for Indians, Malaysia, and ethnic Chinese were 12, 26, and 46 per 100,000 individuals, respectively, with an overall male-to-female ratio of 1:12[4]. Although hormonal factors are connected to the pathogenesis of the disease, there is not yet an accurate explanation for the decreased occurrence in men[5]. Symptoms such as joint pain, extreme fatigue, and skin rashes are more common in both males and females, but males tend to experience a more severe clinical course[1].

The cutaneous manifestations of LE are diagnosed using skin lesion immunohistochemistry, clinical examination, and histopathology[6]. Furthermore, serum autoantibodies are regarded as immunological markers that correspond to specific clinical subtypes of the disease[6]. As a clinical tool, the Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) provides guidelines for identifying clinical changes and standardizes the description of disease activity[6]. This clinical technique is used to quantify damage and disease activity in cutaneous lupus erythematosus patients[6]. The activity score is calculated based on the erythema, scale, mucous membrane lesions, and nonscarring alopecia[6]. Research has recently proposed a solid basis for using the CLASI in clinical trials to assess the severity of the condition and how responsive it is to treatment[7].

The approach to managing systemic lupus erythematosus (SLE) frequently relies on the specific disease severity and the manifestations of individual patients[8]. However,

hydroxychloroquine remains the primary long-term treatment component for all SLE patients[8]. Medications including corticosteroids (e.g. prednisone, methylprednisolone) are prescribed for a short duration[9]. Other medications include non-biological disease-modifying antirheumatic drugs (DMARDS) such as mycophenolate, azathioprine cyclosporine, cyclophosphamide and methotrexate, and non-steroidal anti-inflammatory agents[10].

Case Presentation

A 34-year-old male presented to the primary care clinic with complaints of severely itchy and painful rashes over his right arm and both his legs which had persisted for three weeks. The rash initially developed on his legs, then spread to the right arm and was associated with a history of multiple pigmented skin lesions on his right leg. The presence of associated symptoms such as fever or joint pain led to an initial visit to a dermatologist one week after the onset of symptoms. The dermatologist diagnosed the patient with a urticarial rash and started treatment with corticosteroid creams. However, the rash proceeded to the right arm, and the intensity of itching and pain increased, leading the patient to seek further clinical evaluation.

The patient's medical history indicated a known case of hypertension, managed with 10mg daily Valsartan 320/Amlodipine. No important surgical history was reported and family history included hypertension in the mother, with no indication of autoimmune diseases.

Review of Systems

The patient was found to be positive for fatigue but negative for chills, diaphoresis, and fever. There were no signs of congestion or sore throat in the head, eyes, ears, nose, and throat (HENT) examination. There was no presentation of cough and cardiovascular findings were unremarkable. The patient denied abdominal pain, anorexia, changes in bowel habits, nausea, and vomiting. While the musculoskeletal examination was positive for arthralgias, there were no signs of back pain, gait problems, joint swelling, myalgias, or neck pain. A skin examination confirmed the presence of a rash. A neurological examination indicated no signs of vertigo, weakness, numbness, or headaches. All other systems were reviewed and found to be unremarkable.

System	Positive	Negative
Constitutional	Fatigue	Chills, diaphoresis, fever
HENT		Congestion, sore throat
Respiratory		cough
Cardiovascular		Unremarkable findings
Gastrointestinal		Abdominal pain, anorexia, changes in bowel habits, nausea, vomiting
Musculoskeletal	Arthralgias	Back pain, gait problems, joint swelling, myalgias, neck pain
Skin	Rash	
Neurological		Vertigo, weakness, numbness, headaches

Physical Examination

The patient's vital signs were observed during the examination, revealing a blood pressure of 139/87 mmHg, a pulse rate of 78 beats per minute, a tympanic temperature of 36°C (96.8°F), and a respiratory rate of 18 breaths per minute. Anthropometric measurements encompassed a height of 176 cm (69.29 inches) and a weight of 108 kg, resulting in a calculated body mass index (BMI) of 34.87 kg/m^2. The patient's oxygen saturation (SpO2) level was recorded at 99%.

The patient's overall constitutional examination appeared normal. In the head, eyes, ears, nose, and throat (HENT) examination, the patient presented with normocephalic and atraumatic features, with tympanic membranes intact in both the right and left ears. The nose revealed no abnormalities and the mucous membranes in the mouth were moist. Cardiovascular and pulmonary valuations indicated a normal pulse and pulmonary effort. A musculoskeletal examination showed tenderness and mild swelling in both knees, while the cervical and back regions had a normal range of motion. The systemic examination was considered unremarkable. The skin examination identified several notable findings, including a generally warm condition, capillary refill taking less than two seconds, and the presence of an erythematous skin rash on the right arm and both legs. A nodular erythema rash was noted over the left leg and multiple pigmented skin lesions were noted on the right leg, with one larger lesion measuring around 2.5 cm. Neurologically, the patient displayed no focal deficits and his mental status was reported as alert and oriented to person, place, and time. A psychiatric evaluation revealed a normal mood, affect, and behavior.

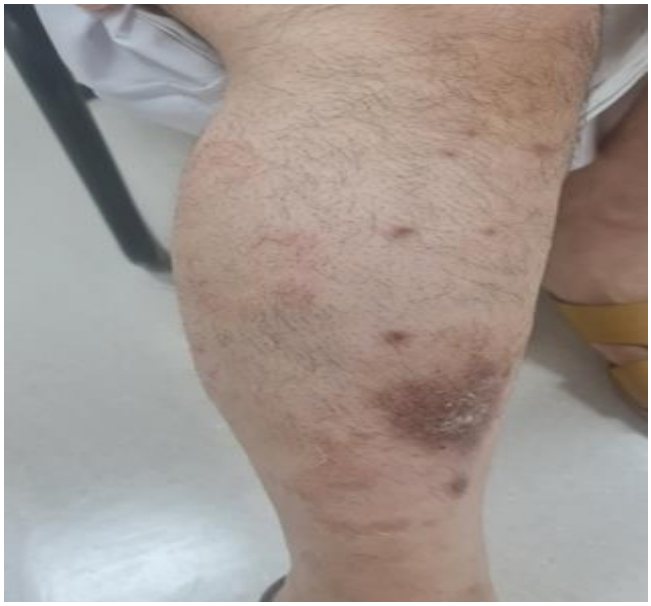

Figure 1: Multiple pigmented skin lesions

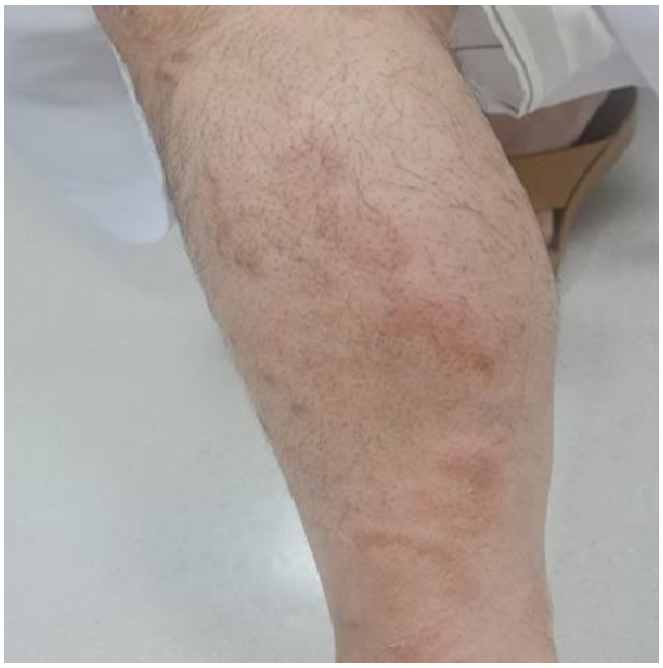

Figure 2: Nodular erythema rash

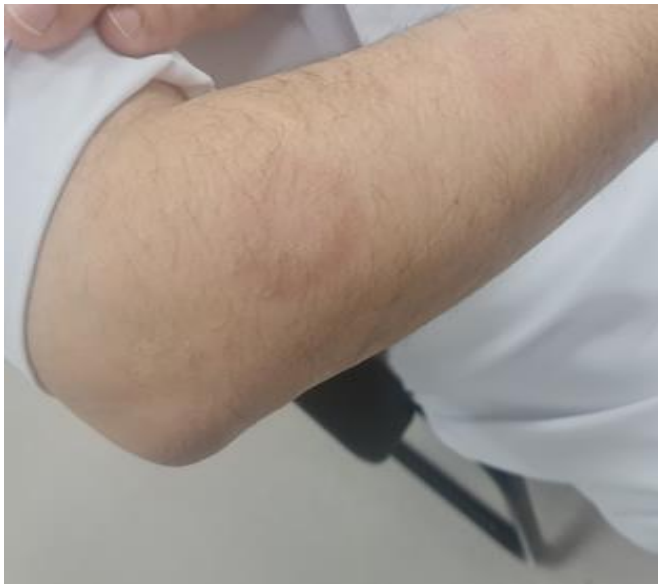

Figure 3: Erythematous skin rash on his right arm

Laboratory Examination

The patient's lab results showed elevated creatinine levels were elevated at 1.51 mg/dL, a high Erythrocyte Sedimentation Rate (ESR) at 51 mm/1hr, a low white blood cell count (WBC) at 2.9 10^3/uL, his neutrophil absolute count was low at 1.40 10^3/uL, his hemoglobin was low at 11.2 g/dL, his globulin was high at 4.9 g/dL, and albumin was low at 3.3 g/dL.

Component	Result	Reference Range
WBC Count	2.9 (L)	3.6 - 11.0 10^3/uL
Hematocrit	35.7 (L)	40.0 - 50.0 %
Blood Hemoglobin	11.2 (L)	13.0 - 17.0 g/dL
RBC Count	5.10	4.50 - 5.50 10^6/uL
MCHC	31.4 (L)	31.5 - 34.5 g/dL
MCV	70.0 (L)	77.0 - 95.0 fL
RDW	15.7 (H)	11.5 - 14.0 %
MCH	21.9 (L)	27.0 - 32.0 pg
MPV	10.9 (H)	7.4 - 10.4 fL
Platelets Count	193	150 - 410 10^3/uL
Neutrophil Absolute	1.40 (L)	2.00 - 7.00 10^3/uL
Eosinophils Absolute	0.10	0.00 - 0.50 10^3/uL
Lymphocytes Absolute	1.00	1.00 - 3.00 10^3/uL
Basophils Absolute	0.00	0.00 - 0.10 10^3/uL
Monocytes Absolute	0.40	0.20 - 1.00 10^3/uL
Lymphocyte %	33.6	20% to 40%
Neutrophil %	48.6	40% to 60%
Monocyte %	13.4	2% to 10%
Eosinophil %	3.5	1% to 6%
Differential Type	AUTO DIFF	-
Basophil %	0.9	0.1% to 1%
Nucleated RBC'S	0	0 Per 100WBC
Alkaline Phosphatase	89	40 - 129 U/L
Bilirubin, Total	0.21	0 - 1.2 mg/dL
Total Protein	8.2	6.6 - 8.7 g/dL
SGPT(ALT)	18	0 - 41 U/L
Albumin	3.3 (L)	3.4 - 4.8 g/dL
eGFR (CKD-EPI)	61.8	>60 mL/min/1.73m^2
TSH	1.260	0.27 - 4.2 uIU/mL
Creatinine	1.51 (H)	0.70 - 1.20 mg/dL
Free T4	15.1	12.0 - 22.0 pmol/L
Globulin	4.9 (H)	2.8 - 3.4 g/dL
ESR	51 (H)	2 - 28 mm/1hr
C-Reactive Protein	1.1	<5.0 mg/L
Ferritin	174.7	30 - 400 ng/mL
Vitamin B-12	386	197 - 771 pg/mL
HbA1C	5.3	<5.7 %

The rest of the tested components were found to be in normal ranges. On the basis of the abnormal findings in the laboratory tests, systemic lupus erythematosus was suspected so the patient was called back to repeat some tests and for more investigation into R/U systemic lupus erythematous.

The repeated laboratory results also indicated elevated creatinine (1.39 mg/dL) and urea (49 mg/dL). Neutropenia was observed with a low neutrophil absolute count (1.50 10:3/uL), indicative of a compromised immune response. Anemia was noted with low hemoglobin levels (10.9 g/dL). A high Erythrocyte Sedimentation Rate (ESR) at 50 mm was also found. Furthermore, proteinuria was evident with a 2+ result and the Anti-Nuclear Antibody (ANA) test was positive at a dilution of 1/320.

Component	Result	Reference Range
RBC Count	4.95	4.50 - 5.50 10^6/uL
MCV	70.7 (L)	77.0 - 95.0 fL
Blood Hemoglobin	10.9 (L)	13.0 - 17.0 g/dL
MCH	21.9 (L)	27.0 - 32.0 pg
RDW	15.7 (H)	11.5 - 14.0 %
Platelets Count	187	150 - 410 10^3/uL
MCHC	31.0 (L)	31.5 - 34.5 g/dL
Neutrophil Absolute	1.50 (L)	2.00 - 7.00 10^3/uL
Monocytes Absolute	0.40	0.20 - 1.00 10^3/uL
Lymphocytes Absolute	1.30	1.00 - 3.00 10^3/uL
Eosinophils Absolute	0.10	0.00 - 0.50 10^3/uL
Hematocrit	35.0 (L)	40.0 - 50.0 %
WBC Count	3.3 (L)	3.6 - 11.0 10^3/uL
MPV	10.4	7.4 - 10.4 fL
Neutrophil %	45.6	40% to 60%
Lymphocyte %	38.2	20% to 40%
Monocyte %	12.1	2% to 10%
Eosinophil %	2.5	1% to 6%
Basophil %	1.6	0.1% to 1%
Basophils Absolute	0.10	0.00 - 0.10 10^3/uL
Nucleated RBC's	0	0 Per100WBC
Differential Type	AUTO DIFF	-
Chloride	108	98 - 108 mmol/L
Potassium	4.1	3.3 - 4.8 mmol/L
Anion Gap	9	6 - 14 mmol/L
Bicarbonate (HCO3)	20.6	20 - 28 mmol/L
Sodium	138	136 - 145 mmol/L
Creatinine	1.39 (H)	0.70 - 1.20 mg/dL
Urea	49 (H)	12 - 40 mg/dL
Anti-Nuclear Antibody (ANA) by IFA	POSITIVE 1/320 COARSE SPECKLED	
ESR	50 (H)	2 - 28 mm/hr
eGFR (CKD-EPI)	68.2	>60 mL/min/1.73m(2)

Urine Routine Exam					
Collection Time:					
Result			**Result**		**Ref Range**
Urine Clarity			SLIGHTLY TURBID (A)		CLEAR
Urine Color			YELLOW		YELLOW
Urine Protein			**2+ (A)**		NEGATIVE
Urine pH			6.0		5.0 - 7.5
Urine Bilirubin			NEGATIVE		NEGATIVE
Urine Glucose			NEGATIVE		NEGATIVE
Nitrite			NEGATIVE		NEGATIVE
Urobilinogen mg/dl			NORMAL		NORMAL
Ketone			NEGATIVE		NEGATIVE
Leukocyte Esterase			NEGATIVE		NEGATIVE
WBC/HPF	0-5	0 - 5	0-5	0 - 5	0 – 5
RBC/HPF	0-2	0 - 2	0-2	0 - 2	0 – 2
Epithelial Cells/HPF	OCCASIONAL (A)	NOT SEEN	OCCASIONAL (A)	NOT SEEN	NOT SEEN

First Rheumatology Visit

Following multiple laboratory results indicative of systemic lupus, the patient was promptly referred to a rheumatologist for further evaluation and confirmation of the diagnosis. In the initial visit with the rheumatologist, the patient complained of an unspecific rash which had persisted for three weeks, accompanied by neutropenia, elevated ESR, and increased creatinine levels, prompting the need for urgent medical attention. Clinical examination revealed an annular macular rash and erythema nodosum on the left leg. Additionally, laboratory findings indicated bicytopenia and positive proteinuria of +2. On the basis of these findings and the laboratory results, a diagnosis of systematic lupus erythematosus was confirmed.

The management plan included additional laboratory investigations and the initiation of medication, specifically oral hydroxychloroquine at a daily dose of 400 mg, along with oral prednisolone at 7.5 mg daily. The patient was advised to continue using topical steroids as part of the treatment regimen. A follow-up appointment was scheduled in two weeks to assess the patient's progress and make any necessary adjustments to the treatment plan.

Second Rheumatology Visit

The laboratory results from the second rheumatology visit indicated abnormalities in specific autoimmune markers. Cyclic citrullinated peptide antibodies were below 8.00 U/ml, utilizing a new methodology (ECLIA). The Rheumatoid Factor was less than 10 IU/mL, employing a new methodology (Immunoturbidimetric assay).

In terms of the ENA-Profile, several ratios deviated from the normal range. The ENA RNP-SM ratio was 1.111, ENA SM ratio was 0.806, the ENA SS-A (RO) ratio was 5.234, the ENA SS-B (LA) ratio was 6.066, the ENA Scleroderma SCL-70 ratio was 0.125, the ENA JO-1 ratio was 0.134, and the ENA Centromeres ratio was 0.214. These ratios are used to assess autoimmune activity, with values exceeding the reference ranges indicating abnormalities.

In the assessment of specific antibodies, Double-Stranded DNA antibodies were notably elevated at 190.15 IU/ml, surpassing the threshold for positivity (>100 IU/ml). Anti Cardiolipin IgG, Anti Cardiolipin IgM, Anti ß2-Glycoprotein 1 IgG, and Anti ß2-Glycoprotein 1 IgM were all within normal limits and did not show any abnormalities. The complement levels revealed low C3 (0.85 g/L) and elevated C4 (0.18 g/L) concentrations, indicating abnormalities. The Lupus Anticoagulant test had a negative result.

The Direct Coombs test exhibited a positive result, with a 3+ score for the broad-spectrum Coombs test. The blood bank comment returned a positive Direct Antiglobulin Test (3+), and the Monospecific Direct Antiglobulin test was positive for IgG (2+) and negative for complement.

Cyclic citrullinated peptide antibodies	<8.00	<17 U/ml
Comment:	New methodology (ECLIA) with amended unit and reference range in use from 17/08/2020	
Rheumatoid Factor	<10	<14 IU/mL
Comment:	New methodology (Immunoturbidimetric assay.) in use with amended reference range from 01/04/2020	

The Indirect Coombs test results for the antibody screen were negative. In terms of urine analysis, the Protein Creatinine Ratio (UPCR) was significantly elevated at 735 (H), surpassing the normal range of <50 mg Prot/g Creat. This indicates severely high proteinuria, as per KDIGO guidelines for CKD 2012. The 24-hour urine protein measurement was notably high at 1,450.4 mg/24hrs, confirming the presence of substantial protein excretion.

Test	Result	Reference Range	Interpretation
ENA Profile			
- ENA RNP-SM	1.111 Ratio	<1.0 Ratio	Borderline
- ENA SM	0.806 Ratio	<1.0 Ratio	Negative
- ENA SS-A (RO)	5.234 Ratio	<1.0 Ratio	High Positive
- ENA SS-B (LA)	6.066 Ratio	<1.0 Ratio	High Positive
- ENA Scleroderma SCL-70	0.125 Ratio	<1.0 Ratio	Negative
- ENA JO-1	0.134 Ratio	<1.0 Ratio	Negative
- ENA Centromeres	0.214 Ratio	<1.0 Ratio	Negative
Anti Double-Stranded DNA	190.15 IU/ml	<100 IU/ml	Positive
Anti Cardiolipin			
- IgG	<2.6 CU	Negative	Negative
- IgM	1.2 CU	Negative	Negative

Anti Beta-2 Glycoprotein			
- IgG	<6.4 CU	Negative	Negative
- IgM	<1.1 CU	Negative	Negative
Complements			
- C3	0.85 g/L (L)	0.90 - 1.80 g/L	Low
- C4	0.18 g/L	0.10 - 0.40 g/L	Low
Lupus Anticoagulant	NEGATIVE	Negative	Negative
Direct Coombs Test	Positive (3+)	Negative	Positive
Monospecific	IgG (2+), Complement (Negative)	N/A	Suggests autoantibodies bound to red blood cells (IgG positive)
Indirect Coombs Test			
Antibody Screen	Negative	N/A	No antibodies detectable in serum
Protein, Random Urine	179.3 mg/dL (H)	<15.0 mg/dL	High
Urine Creatinine	244.1 mg/dL	N/A	N/A
Protein Creatinine Ratio	735 mg Prot/g Creat (H)	<50 mg Prot/g Creat	Severely high
24 hrs. Urine Protein	1,450.4 mg/24hrs (H)	<140 mg/24hrs	High
Protein 24 hr Urine Volume	1,650 mL	N/A	N/A
Protein, Random Urine	87.9 mg/dL (H)	<15.0 mg/dL	High
Urine Protein Creatinine Ratio	-	-	-
Protein,24Hours Urine	-	-	-

Based on the latest results of the second visit, the patient received a diagnosis of systemic lupus with hematological manifestations, including hemolytic anemia (Coombs positive), microcytosis, and leucopenia. Additionally, the patient exhibited features of mucocutaneous involvement, specifically subacute cutaneous lupus annular type and Erythema nodosum. Notably, there was evidence of lupus nephritis, marked by significant proteinuria at 1,450.4 mg/24hrs. The serological profile indicated positivity for various antibodies, including ANA, anti-ds DNA, anti-Ro, and Anti La, with a borderline result for RNP-SM. Furthermore, complement C3 levels were found to be low and the patient tested negative for APS. In light of these findings, the patient underwent hospital admission for a U/S-guided renal biopsy to further assess the renal involvement.

A renal biopsy showed focal segmental glomerulosclerosis with tubular atrophy and interstitial fibrosis. The patient was administered intravenous pulse methylprednisolone at a dosage of 500 mg daily for three days, followed by an oral prednisolone regimen of 50 mg once daily. A post-renal biopsy showed parenchymal attenuation and cortical medullary differentiation of the left kidney grossly preserved.

Discussion

Systemic lupus erythematosus (SLE) is an idiopathic autoimmune disease, exhibiting clinical heterogeneity[5]. Serologically, it is caused by the presence of autoantibodies targeting self-proteins, leading to tissue damage facilitated by immune complexes[5]. While the exact cause of SLE remains unclear, environmental factors, hormonal influences, and genetic predisposition are recognized as significant contributors to its pathogenesis[2].

SLE most frequently affects females, and hormonal factors, particularly the estrogen effect, have been implicated in this gender disparity[11]. The incidence of SLE is elevated in women who are exposed to oral contraceptives or hormone replacements containing estrogen. It has been observed that females of various mammalian species exhibit greater antibody responses in comparison to males[11].

Hughes et al.[12] found SLE to have sex-specific genetic variations, with significant gene-sex interactions identified in the region containing the human leukocyte antigen gene and the IRF5 gene. This investigation identified a female-specific genetic effect in the KIAA1542 gene. Unexpectedly, males with SLE had greater cumulative genetic risks than females, necessitating a greater quantity of risk alleles for the onset of SLE. SLE sex disparities may be influenced by factors other than X-chromosome and hormonal variations, according to these results[12]. However, in our case, a 34-year-old male was diagnosed with SLE and showed several complications.

Diagnosing systemic lupus erythematosus (SLE) relies on clinical and laboratory assessments, yet there persists a notable delay between symptom onset and diagnosis[13]. On average, it takes around two years to diagnose SLE, despite increased awareness. This delay is particularly pronounced in children, males, and late-onset cases, where suspicion may be lower, contributing to an extended diagnostic timeline[14].

Likewise, in our case diagnostic challenges were encountered during the initial presentation, as our patient presented to the primary care facility with his symptoms on numerous occasions prior to receiving a diagnosis of systemic lupus erythematosus (SLE). SLE patients may exhibit a wide range of clinical symptoms and mimic lupus symptoms. Neoplasms, infections, and medications comprise the group of conditions known as "lupus mimickers" which share laboratory and clinical

characteristics with SLE. Multiple overlapping syndromes, including rheumatoid arthritis (also known as "rhupus"), Sjogren's syndrome, systemic sclerosis, polymyositis/dermatomyositis, and, combine SLE characteristics with those of other diseases[14].

Additionally, it is important to note that symptoms of systemic lupus erythematosus (SLE) are similar between women and men, encompassing joint and skin rashes, and extreme fatigue. Nevertheless, research indicates that the clinical course of the disease tends to be more intricate in men. Some studies have highlighted a higher prevalence of central nervous system and renal involvement, and cardiovascular disease in men compared to women[1]. Our patient faced fatigue, skin rashes, and arthralgias with no heart and central nervous system involvement. However, the renal biopsy showed focal segmental glomerulosclerosis with tubular atrophy and interstitial fibrosis, indicating a renal involvement.

Conclusion

This case emphasizes the importance of considering SLE in a patient presenting with seemingly non-specific symptoms like rashes, fatigue, and arthralgias. Primary recognition and quick diagnosis are vital for the timely initiation of treatment, potentially decreasing the severity of future complications. The findings highlight the complicated nature of SLE, in that it affects various organ systems, necessitating the individualization of treatment based on specific manifestations. The presence of focal segmental glomerulosclerosis adds a layer of complexity and underscores the need for comprehensive management strategies to address both the autoimmune and renal components of the disease.

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