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Silent Storm: The Unfolding of Lupus Nephritis in a Young Female Patient

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Abstract:-

➢ ***Background***

Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disorder with multi-organ involvement, particularly affecting the kidneys in the form of lupus nephritis. Lupus nephritis is a severe complication of SLE and is a leading cause of morbidity and mortality in these patients. The disease primarily affects young adults and is characterized by proteinuria, hematuria, and kidney dysfunction. Early diagnosis and timely treatment are crucial in preventing progression to end-stage renal disease.

➢ ***Case Report***

A 32-year-old female presented with a three-month history of skin rashes, hair loss, oral ulcers, and joint pain, followed by the development of edema, generalized weakness, and frothy urine. Physical examination revealed significant pitting edema, ascites, and pleural effusion. Laboratory investigations showed anemia, hypoalbuminemia, hypercholesterolemia, elevated inflammatory markers, and proteinuria in the nephrotic range. Autoimmune markers were positive for ANA, dsDNA, and other lupus-associated antibodies. Renal ultrasound revealed increased cortical echogenicity, and a kidney biopsy confirmed membranous lupus nephritis (ISN/RPS Class V). The patient was started on high-dose corticosteroids and cyclophosphamide for induction therapy, followed by a maintenance regimen. Her condition improved significantly, with proteinuria reduced to less than 0.5 grams/24 hours, and her edema resolved.

➢ ***Conclusion***

This case emphasizes the importance of early recognition and treatment of lupus nephritis in patients with SLE to prevent irreversible kidney damage. The patient's favorable response to timely immunosuppressive therapy highlights the critical role of aggressive treatment in controlling disease activity and improving outcomes. Regular follow-up and monitoring are essential to ensure long-term disease control and prevent relapses.

Keywords:- *Systemic Lupus Erythematosus (SLE) , Lupus nephritis, Membranous nephropathy, Renal biopsy, Nephrotic syndrome, ANA positivity, dsDNA antibodies, ISN/RPS classification*

I. INTRODUCTION

Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disorder characterized by multisystem involvement. Lupus nephritis is one of the most serious complications of SLE, involving inflammation of the kidneys. It is associated with increased morbidity and mortality, especially if left untreated. The incidence of lupus nephritis varies, but it occurs in approximately 40-70% of patients with SLE, particularly in younger individuals. This report presents the case of a 32-year-old female who was diagnosed with lupus nephritis, providing insight into her clinical presentation, diagnostic investigations, management, and outcome.

II. PATIENT HISTORY AND INITIAL PRESENTATION

A 32-year-old female presented to a tertiary care hospital with a variety of complaints, most of which had been ongoing for the past three months but were not addressed initially. She had no known history of significant illness, although she had experienced the following symptoms:

The patient reported recurrent skin rashes, hair loss, and oral ulcers that had developed three months ago. She dismissed these symptoms as trivial and did not seek medical attention.

Approximately two months after the onset of skin and mucosal symptoms, the patient began to experience multiple joint pains, which were associated with redness and swelling of the joints. The pain was predominantly in the smaller joints, such as the fingers, and was symmetrical on both sides of the body. The pain was notably worse upon waking in the morning and improved gradually throughout the day with physical activity. This pattern is consistent with the inflammatory arthritis seen in autoimmune diseases like SLE.

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Fifteen days before admission, the patient developed periorbital edema (swelling around the eyes) and bipedal edema (swelling in both feet). This edema was painless, insidious in onset, and gradually progressed over the following two weeks.

The patient had an episode of high-grade fever four days prior to admission, which resolved within two days after taking antipyretics. There was no significant history of cough, night sweats, or weight loss during this period.

The patient reported generalized weakness and felt increasingly fatigued over the past two weeks. The edema worsened progressively, eventually leading to anasarca (generalized body swelling). This prompted her to seek medical attention.

On further inquiry, the patient revealed that she had noticed her urine had become frothy over the past two weeks, which is often indicative of proteinuria, a hallmark of lupus nephritis.

III. EXAMINATION FINDINGS

Upon presentation to the hospital, the patient underwent a thorough clinical evaluation.

➢ *General Examination*

The patient was conscious, cooperative, and well-oriented to time, place, and person. She appeared edematous with notable generalized swelling. There was significant pitting edema, particularly in the lower extremities. The patient exhibited pallor, indicating a possible underlying anemia. No evidence of clubbing or cyanosis was observed. Vital signs were as follows: pulse 102 beats per minute (tachycardia), blood pressure 140/100 mmHg (hypertensive), respiratory rate 22 breaths per minute (slightly elevated), and oxygen saturation 97% on room air.

➢ *Respiratory System Examination*

There was decreased air entry bilaterally in the lower lung zones. No adventitious sounds such as crepitations (crackling) or wheezes were heard on auscultation. Despite the reduced air entry, the patient's oxygen saturation remained within the normal range.

➢ *Cardiovascular System Examination*

Cardiovascular examination was largely unremarkable, with no significant findings on auscultation.

➢ *Abdominal Examination*

The patient's abdomen was distended. On percussion, shifting dullness was noted, suggestive of free fluid in the peritoneal cavity (ascites). No hepatosplenomegaly (enlarged liver or spleen) was observed, although a full abdominal examination was limited due to the presence of ascites.

IV. INVESTIGATIONS

Several diagnostic tests were performed to evaluate the patient's condition.

➢ *Imaging Studies*

Ultrasound of the abdomen and pelvis revealed moderate free fluid in the peritoneal cavity. Both kidneys were of normal size but exhibited increased cortical echogenicity with preserved corticomedullary differentiation, suggestive of renal involvement. A chest X-ray demonstrated bilateral pleural effusions but a normal cardiothoracic ratio. A 2D echocardiography revealed concentric left ventricular hypertrophy (LVH), likely a consequence of hypertension secondary to lupus nephritis.

➢ *Laboratory Results*

- Complete Blood Count (CBC): Hemoglobin (Hb) 7.8 g/dL (indicative of anemia), white blood cell count 6000 cells/mm³ (normal), platelet count 300,000 cells/mm³ (normal), mean corpuscular volume (MCV) 70.3 fL, suggesting microcytic anemia. Peripheral smear showed normocytic, normochromic red blood cells, ruling out hemolytic anemia.
- Renal Function and Biochemistry: Serum urea 51 mg/dL (mildly elevated), serum creatinine 0.73 mg/dL (normal), serum albumin 2.58 g/dL (hypoalbuminemia), serum globulin 3.87 g/dL (normal), serum cholesterol 216 mg/dL (elevated), serum triglycerides 190 mg/dL (elevated).
- Inflammatory Markers: Erythrocyte sedimentation rate (ESR) 98 mm/hr (elevated), C-reactive protein (CRP) positive (1.2 mg/dL).
- Autoimmune Markers: Antinuclear antibody (ANA) positive, dsDNA positive, nucleosome positive, histone positive, SmD1 positive, PmScl positive, SSA strongly positive (+++), SSB strongly positive (+++).
- Urine Analysis: Proteinuria ++ by dipstick. No glycosuria, hematuria, or pyuria were noted. A 24-hour urinary protein excretion measured 4.5 grams with a volume of 1.5 liters, indicating nephrotic range proteinuria.

➢ *Diagnosis*

Based on the clinical presentation, laboratory findings, and imaging studies, the patient was diagnosed with lupus nephritis, a complication of Systemic Lupus Erythematosus (SLE). Her ANA positivity, high titers of dsDNA, and significant proteinuria strongly pointed toward active lupus nephritis. A renal biopsy was performed to confirm the diagnosis. Histopathological analysis of the kidney tissue, using indirect immunofluorescence microscopy, revealed findings consistent with membranous lupus nephritis, classified as ISN/RPS Class V.

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➢ *Management:*

Given the patient's diagnosis of active lupus nephritis, she was promptly initiated on treatment to control the autoimmune activity and prevent further kidney damage.

The patient was started on high-dose corticosteroids to suppress the immune-mediated inflammation.In combination with corticosteroids, she was initiated on an induction regimen of cyclophosphamide, which is a standard immunosuppressive agent used in the management of lupus nephritis.After induction therapy, the patient was placed on a maintenance regimen to prevent relapse and manage the chronic nature of SLE.

She was advised to have regular monitoring of ANA and dsDNA titers to assess disease activity and adjust treatment accordingly.

➢ *Outcome and Follow-Up*

Over the course of her treatment, the patient showed a marked improvement in her condition. After one month, her proteinuria reduced to less than 0.5 grams/24 hours, indicating a favorable response to treatment. Edema and anasarca subsided gradually, and her renal function remained stable throughout.

V. DISCUSSION

Lupus nephritis (LN) is a significant and potentially life-threatening manifestation of systemic lupus erythematosus (SLE), affecting approximately 40% of patients with lupus. It is associated with substantial morbidity and a heightened risk of progressing to end-stage kidney disease (ESKD) in up to 10% of patients. The management of lupus nephritis is challenging due to its complex and heterogeneous nature, and despite improvements in therapies, many patients fail to achieve complete remission. This discussion delves into the underlying pathophysiology of LN, its classification, the challenges surrounding diagnosis, treatment strategies, the role of biomarkers, and the need for emerging therapies to address unmet clinical needs.

Lupus nephritis is driven by the deposition of immune complexes, predominantly anti-dsDNA antibodies, within the glomeruli of the kidneys. These immune complexes trigger the activation of the complement system, leading to the recruitment of inflammatory cells and subsequent kidney damage. The activation of inflammatory pathways, including the release of cytokines like TNF-α and IFN-γ, plays a key role in the progression of lupus nephritis. These cytokines not only contribute to glomerular inflammation but also affect other areas of the kidney, such as the tubulointerstitial and vascular compartments, which are increasingly recognized as critical components in determining long-term outcomes.

The classification of lupus nephritis has been refined over the years to better capture its clinical and pathological heterogeneity. The International Society of Nephrology/Renal Pathology Society (ISN/RPS) classification, introduced in 2003 and updated in 2018, remains the cornerstone for categorizing LN based on histological findings. The six classes of lupus nephritis range from class I (minimal mesangial involvement) to class VI (advanced sclerosing lesions). The proliferative forms of lupus nephritis, classes III and IV, are the most aggressive and are associated with a higher risk of renal failure. Class V, or membranous lupus nephritis, typically presents with nephrotic syndrome but tends to have a more indolent course. However, these classifications focus primarily on glomerular involvement, while recent research highlights the importance of incorporating tubulointerstitial and vascular changes, as these can significantly impact patient prognosis. For example, chronicity indices, which measure the extent of fibrosis and irreversible damage, are now considered essential in predicting long-term kidney outcomes.

The diagnosis of lupus nephritis is traditionally based on a combination of clinical features, laboratory findings, and kidney biopsy results. Proteinuria, hematuria, and elevated serum creatinine are the most commonly used markers in clinical practice. However, these markers have limitations, as they often reflect kidney function rather than the underlying inflammatory activity. Additionally, anti-dsDNA antibody titers and complement levels (C3 and C4) are used to monitor disease activity, but they lack the precision needed to correlate directly with histological damage. This gap in diagnostic accuracy has led to an increased focus on identifying novel biomarkers that can provide a more accurate reflection of kidney involvement in lupus patients.

Emerging biomarkers, such as urinary microRNAs, MCP-1, and TWEAK, have shown promise in reflecting real-time kidney injury and inflammation. These biomarkers have the potential to complement traditional markers by offering a more dynamic and specific assessment of lupus nephritis activity. Urinary biomarkers are of particular interest because they provide non-invasive insights into renal pathology, making them ideal for monitoring disease progression and therapeutic response. However, despite their potential, most of these biomarkers are still in the research phase and have not yet been validated in large, multicenter trials, limiting their use in routine clinical practice.

Kidney biopsy remains the gold standard for diagnosing and staging lupus nephritis. Biopsies not only confirm the diagnosis but also provide crucial information about the extent of glomerular, tubulointerstitial, and vascular involvement. The ISN/RPS classification system, based on biopsy findings, guides treatment decisions, particularly in identifying patients who require more aggressive immunosuppressive therapy. In recent years, the role of repeat kidney biopsies has been the

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subject of debate. While repeat biopsies are invasive, they can provide valuable information in patients who are in clinical remission or experiencing a flare. Several studies suggest that histological activity, even in the absence of clinical symptoms, may predict future relapses, and repeat biopsies can help refine treatment decisions, such as when to taper or discontinue immunosuppression.

One of the most critical challenges in lupus nephritis management is determining the optimal duration of immunosuppressive therapy. The standard approach to LN treatment consists of two phases: induction and maintenance. Induction therapy, which lasts 3 to 6 months, aims to achieve remission by using high-dose corticosteroids combined with immunosuppressive agents such as mycophenolate mofetil (MMF) or cyclophosphamide. Maintenance therapy, which typically lasts several years, aims to prevent relapses using lower doses of immunosuppressants. Despite these strategies, achieving complete remission is difficult, and approximately 30-40% of patients experience relapses within five years.

One of the main issues with current treatment regimens is the reliance on high-dose corticosteroids, which are associated with significant side effects, including hypertension, diabetes, osteoporosis, and an increased risk of infections. The development of steroid-sparing regimens is a major area of interest, particularly with the use of biologics and other novel agents that target specific components of the immune system. Rituximab, a monoclonal antibody targeting CD20-positive B cells, has been used in refractory cases of lupus nephritis, with some success in reducing disease activity and allowing for steroid reduction. However, the LUNAR trial, which evaluated rituximab in lupus nephritis, failed to demonstrate significant improvements in kidney outcomes compared to placebo, highlighting the limitations of this approach.

Belimumab, an anti-BAFF monoclonal antibody, has shown more promising results, particularly as an adjunct to standard therapy in maintaining remission. The BLISS-LN study demonstrated that belimumab, when added to conventional therapy, significantly reduced the risk of kidney disease progression and relapse. This has made belimumab a valuable tool in lupus nephritis management, especially for patients with high disease activity who are at risk of relapses. Another biologic, anifrolumab, which targets the interferon receptor, has shown efficacy in systemic lupus erythematosus and is being investigated for its potential role in treating lupus nephritis.

The emergence of **complement inhibitors** has also generated interest, as the complement system plays a crucial role in the pathogenesis of lupus nephritis. Eculizumab, a monoclonal antibody that inhibits the complement protein C5, has been used in patients with lupus nephritis complicated by thrombotic microangiopathy and antiphospholipid syndrome (APS). While this treatment shows promise in specific cases, its use in typical lupus nephritis remains limited, and further studies are needed to determine its efficacy in broader patient populations.

Despite the availability of new biologic agents, there remain significant gaps in lupus nephritis treatment. One such gap is the lack of consensus on the optimal duration of maintenance therapy. While some studies suggest that immunosuppression should be continued for at least three years, others advocate for longer periods, particularly in patients with severe disease. The MAINTAIN Nephritis trial, which compared mycophenolate mofetil and azathioprine as maintenance therapies, found that extending immunosuppression reduced the risk of relapse but also increased the risk of drug toxicity. Balancing the benefits of prolonged immunosuppression with the risks of side effects remains a key challenge in lupus nephritis management.

Another important consideration is the need for more personalized treatment approaches. Currently, most patients are treated using standardized regimens, regardless of their individual disease characteristics or response to therapy. However, advances in the understanding of lupus nephritis pathophysiology and the development of new biomarkers could pave the way for more personalized treatment strategies. For example, patients with high levels of interferon activity may respond better to interferon-targeting therapies like anifrolumab, while those with severe B-cell-driven disease may benefit more from agents like rituximab or belimumab.

Looking to the future, the integration of novel biomarkers, histological findings from kidney biopsies, and genetic risk factors could help clinicians tailor treatment to the individual patient, improving outcomes and reducing the need for long-term immunosuppression. Additionally, the use of combination therapies, such as rituximab with belimumab, may offer a more effective approach to achieving durable remission while minimizing the risks of steroid use and immunosuppressant toxicity.

VI. CONCLUSION

In conclusion, lupus nephritis remains a complex and challenging condition to manage. While advances in biologic therapies, biomarkers, and diagnostic techniques offer hope for more effective treatment strategies, significant gaps remain in our ability to predict which patients will respond to specific treatments and how long immunosuppressive therapy should be continued. The future of lupus nephritis management lies in the development of personalized treatment approaches that incorporate biomarkers, genetic data, and histological findings to guide therapy and improve long-term outcomes. As research into new therapies and diagnostic tools continues, there is optimism that the prognosis for patients with lupus nephritis will improve in the years to come.

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