Section: Nephrology

Case Series

LUPUS NEPHRITIS IN MALES: A CASE SERIES

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ABSTRACT

Background: The prevalence of systemic lupus erythematosus (SLE) in the general population ranges from 8 to 180 cases per 100,000 individuals. The female to male ratio varies from 6 to 13 cases in females for every 1 case in males. Several observations suggest an estrogen effect as a potential explanation for this gender difference. In children, the impact of sex hormones is assumed to be minimal, resulting in a female to male ratio of 3 to 1. We report a case series of five male patients who presented at the Kurnool Medical College, Kurnool in the state of Andhra Pradesh and were diagnosed to have lupus nephritis (LN). Male patients with SLE typically present with renal involvement and seizures rather than photophobia and skin manifestations. The prognosis for male patients also appears to be more severe. Therefore, despite the rarity of male patients with lupus, the symptoms are life-threatening, and early detection of the disease is crucial for improving patient outcomes.

Keywords: Lupus Erythematous, Estrogen, Seizurs, Photophobia, Luupus Nephritis.

INTRODUCTION

Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by an unknown etiology that disrupts immune tolerance towards endogenous nuclear material. This disruption leads to systemic autoimmunity, which can cause damage to various tissues and organs.[1] Lupus nephritis (LN) is a form of glomerulonephritis and constitutes one of the most severe organ manifestations of SLE.[2] While most patients with SLE who develop LN do so within five years of their SLE diagnosis, it is not uncommon for LN to manifest at later stages. In fact, LN often serves as the presenting manifestation that ultimately leads to the diagnosis of SLE.

The incidence of SLE in the general population ranges from 1 to 8.7 cases per 100,000 person-years, while the prevalence ranges from 8 to 180 cases per 100,000 individuals. SLE exhibits a higher prevalence among women, particularly those in their reproductive years, compared to men, with a female-to-male ratio ranging from 6.1 to 13.3:1.[3] Additionally, gender may produce different characteristics in the manifestation of SLE. The diagnosis of SLE is based on characteristic clinical features and presence of auto-antibodies. SLE in males is uncommon, and we encountered five such cases in a 12-month duration, all of whom had Lupus Nephritis upon evaluation. The diagnosis of SLE was based, in all the five reported cases, on the the 2019 European League Against Rheumatism (EULAR)/ACR classification criteria for SLE. The histopathological diagnosis of Lupus Nephritis was based on the 2018 revised International Society of Nephrology/Renal Pathological Society classification.

Aim of the study

The aim of this study is to present a case series of 5 adult male patients with Lupus Nephritis so as to understand the spectrum of clinical and histopathological presentation of the disease.

Case descriptions

Case 1: A 40-year-old male, presented with history of bilateral symmetrical joint pains involving both large and small joints for 6 months and swelling of both feet for 3 months. He gave history of recurrent oral ulcers. His serum creatinine was 2mg/dl and Urinary spot protein creatinine ratio (UPCR) was 2.2. His Complete Blood Count showed Hemoglobin of 9.8 g/dl (Normochromic Normocytic type),

Lymphopenia and mild thrombocytopenia of 1.1 lakhs/cu mm. His ANA was positive and his ANA profile revealed Anti Sm positive and Anti U1RNP positive. Anti ds DNA was strongly positive. His C3 and C4 levels were low. His Renal biopsy revealed Diffuse Proliferative Glomerulonephritis pattern with wire loop lesions and full house on Immunofluorescence study. He was diagnosed as class IV LN with Activity Index of 9/24 and Chronicity Index of 2/12. He was given pulse steroids initially followed by oral steroids and was started on Mycophenolate Mofetil (MMF) 2 gm per day as Induction therapy and is presently on maintainance therapy with steroids and MMF and other supportive therapy with latest serum creatinine of 1.2 mg/dl and UPCR of 0.2

Case 2: A 26-year-old male, known case of SLE since 2017. He had initially presented with polyarthralgia involving both large and small joints for 6 months. He was found to be ANA positive and was diagnosed as a case of SLE by Rheumatologist and was started on low dose steroids and Hydroxychloroquine (HCQ). During routine evaluation he was found to have 24-hour urinary protein of 640 mg and referred to our centre. His Anti ds DNA was mildly positive (1:80) with Normal C3 and C4 levels. Urinalysis showed trace albumin and No RBCs. His Renal biopsy revealed class I LN. He was advised for conservative management with ACE inhibitors and HCQ.

Case 3: A 36-year-old male, presented with history of bilateral pedal edema for 2 months duration. His Urinalysis showed albumin 3+ and rbc 10-12 /hpf. His UPCR was 4.7 and his ANA was positive. His Serum creatinine was 1.2 mg/dl. His Anti ds DNA was strongly positive and complements low. His renal biopsy showed Class IV/V LN with Activity Index of 14/24 and Chronicity Index of 2/12. He was advised for NIH protocol but had defaulted on treatment and after 6 months presented with anasarca and severe renal insufficiency with sepsis. He died as a complication of sepsis.

Case 4: A 18-year-old male, presented with history of anasarca for 1-month duration. His UPCR was 2.2. His serum creatinine was 1 mg/dl. He had anemia with haemoglobin of 11.5 gm/dl which was normocytic normochromic but no lymphopenia and thrombocytopenia. His coombs test was negative. His ANA was positive. HisAnti ds DNA was mildly positive and Complements were low. His Renal Biopsy showed Class IV/V LN with activity index of 10/24 and chronicity index 4/12. He was started on steroids and MMF induction therapy along with other supportive therapy. He responded well to the therapy and he is presently in remission with UPCR of 0.2 and his serum creatinine is 0.9 mg/dl. He is on maintanence therapy of low dose steroids, MMF and HCQs and ACE inhibitors

Case 5: A 29-year-old male, presented with multiple hyperpigmented rash over the back and on face for 1 month and acute febrile illness with anasarca for 15 days along with reddish brown discolouration of urine. He gives history of photosensitivity. He was found to have lymphopenia and mild thrombocytopenia. His serum creatinine was 2.8 mg/dl. UPCR was 3.3. His Urinalysis showed plenty of RBCs, albumin 3+. His serum albumin was 1.3 g/dl. His ANA was positive. His Anti ds DNA levels were strongly positive and complements were low. His renal biopsy showed Class IV LN with Activity Index 9/24 and Chronicity Index 2/12. He was started on Steroids and Cyclophosphamide as per NIH protocol. His serum creatinine improved to 1.4 mg/dl and he is on follow up.

RESULTS

The Mean age of the patients was 29.8 years (18years to 40 years). 4 patients had symptoms suggestive of renal involvement at initial presentaion while the other patient developed LN five years into his disease. 2 patients had presented with only renal involvement with no other extra renal involvement. Two patients had synovitis at presentation. Two patients had mucocutaneous symptoms of which only one was photosensitive. 3 patients had hematological manifestations at presentation. 2 patients had renal insufficiency at presentation and both had responded to treatment. Most common pattern on Biopsy was class IV and IV/V. Activity index in biopsy correlated with Anti ds DNA levels. All the patients received supportive care in the form of Hydroxychloroquine and ACE inhibitors. Two patients were started on steroids and Mycophenolate Mofetil. One Patient was started on steroid and Cyclophosphamide as per NIH protocol. One patient was advised just supportive care with ACE inhibitors and HCQs. One patient defaulted on all treatment and later had come with sepsis with renal insufficiency, which resulted in his death.

DISCUSSION

In unselected patients with SLE, approximately 25–50% have signs or symptoms of kidney disease at SLE onset. As many as 60% of adult patients with SLE develop these renal signs or symptoms during the disease course.[4] Several observations point towards the presence of an estrogen effect, as evidenced by the varying female to male ratios of SLE across different age groups. In children, where sex hormonal effects are believed to be minimal, the ratio stands at 3:1. However, in adults, this ratio increases significantly to range from 7-15:1. Among older individuals, the ratio is approximately 8:1. Numerous cohort studies are in agreement that the prevalence of LN in patients with SLE varies by race and ethnicity. Most cohort studies report a tendency towards higher prevalence of LN in male patients than in female patients with SLE (27–75% versus 16–52%, respectively).[5]

The male-to-female ratio of LN prevalence in patients with SLE ranges from 1.1:1 to 1.7:1 and does

not vary with ethnicity,[6] Overall, SLE patients of younger age, male sex and African, Asian or Hispanic ethnicity are more likely to develop LN.[6] Male patients with SLE predominantly exhibit renal involvement, as opposed to photosensitivity and skin manifestations.[7]

Men with lupus tend to have a higher prevalence of serositis, older age at diagnosis and a higher one-year mortality,[6] In a study that included 1378 patients with SLE, with a median followup of 6.1 years, 118 patients died (8.6%) The overall cumulative probability of survival after disease diagnosis at 5, 10, 15 and 20 yrs was 95%, 91%, 85% and 78%. Based on a multivariate model, age at SLE diagnosis >50 years (hazard ratio = 5.9; P <0.001) and male gender (hazard ratio = 2.4; P = 0.004) were associated with poorer survival,[8] In 1999, the rheumatology clinic database for SLE patients at St. Luke's Hospital consisted of 62 individuals, with seven being male. It was observed that serositis, as the initial presentation, was more prevalent in males (29% vs. 2%, P <0.05).[9] A comparative analysis revealed that male SLE patients exhibit a disease spectrum similar to that of females, albeit with varying frequencies of organ involvement. Male SLE patients may experience either equivalent or more severe disease severity compared to females, potentially leading to a less favourable long-term prognosis. The majority of men with lupus maintain normal gonadal function.[10] Furthermore, a study investigating disease progression highlighted that lupus tends to be more severe in women over 40 years of age, male patients, and individuals with late-onset lupus.[11] The clinical tendency of male SLE cases has not been fully settled by now because the disease is uncommon.[12]

CONCLUSION

From this case series, we can see that male LN is not as uncommon as is thought. Unless we maintain a strong index of suspicion, the disease is generally missed and patients land up at late stages, which is invariably fatal. Male patients with systemic lupus erythematosus (SLE) predominantly exhibit renal involvement, as opposed to photophobia and skin manifestations. Furthermore, the prognosis appears to be more severe in males. Consequently, it is our contention that despite the relative rarity of male lupus patients, the manifestations they experience are potentially life-threatening. Therefore, early detection of the disease is crucial in order to improve the prognosis and overall outcome for these individuals.

Conflict of interest: None to declare.

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