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Internal Medicine

UNUSUAL PRESENTATION OF LUPUS NEPHRITIS IN A 22 YEAR OLD MALE:A CASE REPORT

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ABSTRACT Systemic lupus erythematosus (SLE) is an autoimmune disease in which organ and cell undergo damage initially mediated by tissue binding autoantibodies & immune complexes.In most patients, autoantibodies are present for a few years before the first clinical symptoms appears. It is five to six times more prevalent in women than in men .Nephritis is usually the most serious manifestation of SLE, particularly because nephritis and infection are the leading cause of mortality in the first decade of disease. We present a case of a 22 yr old male who came with complaint of bilateral pedal oedema and puffiness of face since 1 month . On examination, patient was stable hemodynamically with pulse of 88 per minute, blood pressure of 110/80 millimeter of mercury with room air saturation of 99 percent and jugular venous pressure of 6-7 millimeters of water. He also had pallor in lower palpebral conjunctiva and bilateral pitting pedal oedema.There was no clubbing, icterus,cyanosis or lymphadenopathy. His routine blood investigations showed anaemia , leucocytosis , elevated creatinine, hyperkalaemia , hypoalbuminemia, iron deficiency ,urine routine microscopy suggestive of RBC cast 60-70/high power field . Complement C3 and C4 were low, ANA positive grade 3(1:1000) homogeneous and cytoplasmic speckled, ANA BLOT positive for dsDNA, nucleosome, Histones, Sm/RNP,Mi2b.His ultrasound (USG) revealed bilateral bulky kidney and heterogeneous with raised cortical echogenicity and normal size. His renal biopsy was done which showed diffuse lupus nephritis(ISN/RPS2018 modification)class IV and indices(modified NIH) of activity 15/24 and chronicity 2/12, necrotizing vascular lesions along with evidence of vascular immune deposits in diffuse immunoflorescence studies and associated inflammatory cells are noted. Patient received intravenous pulse therapy of methyl prednisolone 1gram for 5 days with monitoring of kidney function test. Patient was put on cyclophosphamide with hemodialysis for immunosuppression because patient was not responding to steroids, as seen by rising serum creatinine and urea levels and declining urine output. The patient improved dramatically, urine output increased and serum creatinine and urea decreased, therefore haemodialysis was discontinued, and the patient was managed conservatively and discharged on oral prednisolone with a monthly cyclophospmide injection.

KEYWORDS :

INTRODUCTION

Lupus, also known as systemic lupus erythematosus (SLE), is a complex autoimmune disease that has a protracted relapsing-remitting course with a variety of symptoms that can range from moderate to life-threatening illness. The interplay of genetic predisposition with environmental, immunological, and hormonal variables leads to the clinical development of SLE, with a pronounced preference for females of reproductive age. Many autoantibodies (Ab) that result in the development and deposition of immune complexes (ICs) as well as other immunological processes are linked to the signs of SLE. The majority of SLE patients report constitutional, muco-cutaneous, and musculoskeletal manifestations as their first and most frequent symptoms. The epidermal, hematologic, renal, neuropsychiatric (NP), cardiovascular, and/or respiratory systems can all be impacted, in addition to any organ. Not all manifestations inevitably occur at once, and there may be a delay of several months or even years between the onset of certain symptoms (1).

Around 40 and 70 percent of SLE patients, lupus nephritis will manifest. Genes that breach immunological tolerance and encourage autoantibody production start the renal assault during SLE. These genes may work in tandem with other genetic components to increase IFN-I production and innate immune signalling, which can lead to an influx of effector leucocytes, inflammatory mediators, and autoantibodies into end organs like the kidneys. The development of the disease may be accelerated by the presence of cognate antigens in the glomerular matrix and inherent molecular abnormalities in resident renal cells.

A frequent side effect of SLE is lupus nephritis, an immunological complex GN. Several pathogenic processes are involved in the pathophysiology of lupus nephritis. Systemic lupus' extrarenal aetiology is based on numerous genetic variant combinations that impair the defences against immunological tolerance to nuclear autoantigens that are typically in place. Antinuclear antibodies enable the clinical detection of this lack of tolerance. Furthermore, innate and adaptive immunity are activated by nucleic acids released from apoptotic neutrophils via Toll-like receptors that are unique to viral nucleic acids. As a result, many of systemic lupus' clinical symptoms are comparable to viral infections. Endogenous nuclear particles in lupus, like viral particles during viral infection, cause IFN- signalling. Hence, the aberrant polyclonal autoimmunity is a result of the involvement of dendritic cells, T helper cells, B cells, and plasma cells. Rather than being caused by the deposition of circulating immune complexes, the intrarenal aetiology of lupus nephritis is caused by antibody binding to many intrarenal autoantigens. As renal immunopathology develops, tertiary lymphoid tissue development and local antibody production increase intrarenal complement activation (3).

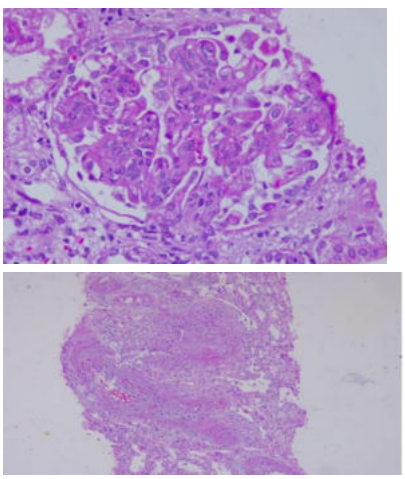
Autoantibodies interact intricately with nucleosomes, histones, inflammatory cells, activated resident cells, complement, cytokines, reactive nitrogen and oxygen species, and inflammatory cells to cause lupus nephritis. Anti-dsDNA antibodies that bind to cell surface targets and/or penetrate into the cell might affect cell activation, proliferation, and death, and induce expression of a large number of immunological mediators. Anti-dsDNA antibodies are thought to participate in the pathogenesis of LN by binding directly or indirectly with renal antigens. (4)

CASE PRESENTATION

A 22 year old male with no co morbidities presented with facial puffiness since 1 month and bilateral lower limb swelling since 1 month which was gradual in onset, progressive in nature, non painfu extending l up to knee joint with no aggravating and relieving factor. There was no history of fever,hematuria,breathlessness, decreased urine output or yellowish discolouration of eyes. His past and family history was unremarkable.There was no history of any drug or toxin ingestion. There was no history suggestive of autoimmune pathology like oral ulcers, photosensitivity, rash, alopecia.

The patient's social background was low, and he was accustomed to living in overcrowded conditions. He used to live in a slum having high endemicity for tuberculosis. There was no history of neck surgery, congenital defects or recurrent infections in the past.

The patient was hemodynamically stable, with a pulse rate of 88 beats per minute, a blood pressure reading of 110/80 millimetres of mercury, a room air saturation of 99 percent, and a jugular venous pressure of 6-7 millimetres of water. Moreover, he exhibited pitting pedal oedema on both sides extending upto the knees and pallor in the lower palpebral conjunctiva. Clubbing, icterus, cyanosis, or lymphadenopathy were absent. Examination of hands and nails was normal with no evidence of rash, alopecia, oral or genital ulcers and arthritis. His blood investigations showed hemoglobin of 8.8 gram per decilitre, white blood count of 17000 per cubic millimeters, platelets 15000 per cubic millimeters. Liver function test showed mildly elevated aspartate transaminase of 55 IU/L and alanine trasnaminase of 60 IU/L,low serum albumin of 2.8 gram per decilitre ,serum creatinine of 5milligram per decilitre and blood urea nitrogen ratio of 95, potassium of 6.8 milliequivalent per litre, sodium of 130 milliequivalent per litre.Random blood sugar was 110 milligram per decilitre with glycosylated hemoglobin of 5.4 percent.Arterial bloodgas analysis showed high anion gap metabolic acidosis. Inflammatory markers showed raised erythrocyte sedimentation rate of 65 millimeters per hour and C reactive protein of 12 milligram per decilitre.Fasting serum triglyceride was 110 milligram per litre.Serum procalcitonin was less than 0.5 nanogram per milliliters. Serology for HIV ,HBV,HCV, malaria and dengue was negative. Peripheral smear showed normochromic normocytic anemia with no signs of sickled RBCs. Urine routine microscopy suggested RBC cast 60-70/high power field with no pus cells. Urine culture sensitivity showed no growth. Serum Antistreptolysin O titres (ASO) were insignificant(100 IU/ml). 24 hour urine protein estimation revealed significant proteinuria in nephrotic range (3950 milligram per day).Further investigations showed C3 of 33.3 milligram per decilitre(90-180 mg/dl) and C4 of 2.2 milligram per decilitre(10-40 mg/dl) both of which were in the subnormal range.ANA was positive with titres of 1:1000 showing homogenous and cytoplasmic speckled pattern ,ANA BLOT positive for dsDNA, nucleosomes, Histones, Sm/RNP, and Mi2b. His ultrasonography of abdomen indicated heterogeneous, bilateral normal sized kidneys and elevated cortical echogenicity. A biopsy of his kidneys revealed diffuse lupus nephritis (ISN/RPS2018 modification)class IV with indices (modified NIH) of activity 15/24 and chronicity 2/12, necrotizing vascular lesions, and evidence of vascular immune deposits in diffuse immunoflorescence studies, as well as associated inflammatory cells.



Renal biopsy suggestive of diffuse necrotizing diffuse lupus nephritis

TREATMENT

The patient's urine output decreased during his stay at the hospital as his serum creatinine level rose.

Patient was given pulse therapy of intravenous methylprednisolone (1000 mg over 30 minutes for 5 days) along with immunosuppression by intravenous cyclophosphamide (0.5 mg per square metre) after taking consent.He was also given temporary renal replacement therapy with intermittent hemodialysis. Patient's daily creatinine and 24 hour urine output was monitored.

The patient improved dramatically, urine output increased and serum creatinine and urea decreased.Therefore, haemodialysis was discontinued, and the patient was managed conservatively and discharged on oral prednisolone with a monthly cyclophospamide injection.

He was advised to follow up with 24 hour urine proteins levels and ESR and CRP levels to monitor for response to therapy.

DISCUSSION

Systemic lupus erythematous and lupus nephritis (LN) are uncommon in men and are not well understood to us.The most common form chronic LN in boys is type IV LN, which typically manifests as nephrotic syndrome. A low estimated glomerular filtration rate at the time of the renal biopsy is linked to a poor prognosis for the kidneys.The most prevalent lupus symptom, lupus nephritis (LN), is seen in 30% to 75% of patients, either at the time of the disease's beginning or later on in the illness.(6)In numerous research on both men and women, it is thought to be the most significant predictor of morbidity and mortality since it suggests severity. (7,8,9)

When the information for men and women is compared, a significant dispute emerges. Traditionally, serositis and increased renal, neurologic, and hematologic damage have been associated with SLE in males being more severe and having worse prognoses. Nevertheless, a recent study with a 30-year follow-up failed to find any appreciable sex-related variations in the clinical symptoms of SLE and actually found that women were more likely to experience extreme renal failure and death.The small number of cases diagnosed each year contributes to the difficulties in determining the clinical characteristics and severity of LN in males.(10,11,12)

The patient had multiple organ involvement, primarily the kidney, and was identified as having SLE. He had unusual test results, including low albumin levels and urine protein with sediment that could have suggested active LN. Peripheral oedema induced by hypertension or hypoalbuminemia were symptoms of active nephritis. Due to the frequent association of diffuse or membranous LN with severe proteinuria, extreme peripheral oedema is more frequent in these renal lesions. Individuals with active LN frequently also exhibit other active SLE symptoms, such as fatigue, fever, rash, arthritis, serositis, or CNS disorders. They are more frequent in diffuse and focal proliferative LN, as in this instance.

By presenting this case report, we hope to analyse the disease pattern in a young male for whom there wasn't much reason to suspect lupus nephritis given the lack of additional signs of autoimmune multisystemic presentation and nephrotic range proteinuria. It is crucial to have a high suspicion for lupus nephritis in the young population because numerous studies have demonstrated a considerable mortality related with male lupus nephritis and the available preventive and rescue strategies to prevent end stage renal disease.

Normalizing renal function or, at the very least, halting its progressive decrease is the main aim of treatment for lupus nephritis . Depending on the pathologic lesion, the appropriate therapy varies. If a patient has clinically significant renal illness, corticosteroid treatment should be started. the use of immunosuppressive drugs, especially cyclophosphamide, azathioprine, or mycophenolate mofetil if the patient has proliferative renal lesions that are aggressive, as these medications enhance the prognosis for the kidneys. In addition, they may be utilised if a patient's reaction to corticosteroids is insufficient or they are too sensitive for the patient.

The duration between the commencement of the illness and the clinical diagnosis of lupus nephritis was reported to be longer in men because SLE symptoms were overlooked.This report cannot overemphasize the importance of early diagnosis and treatment of lupus nephritis urgently to prevent significant morbidity in young.

CONCLUSION

There is disagreement about the issue of whether male sex is a risk factor for higher rates of lupus nephritis, worse renal outcomes, and higher rates of mortality from lupus nephritis. To explain the function of the male gender in lupus nephritis, we contend that multicenter research involving a range of ethnicities, ages, mortality risk factors, and genetic backgrounds is required.

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