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RESEARCH ARTICLE

A CASE OF MALE SLE: AN UNUSUAL PRESENTATION

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Abstract

Systemic Lupus Erythematosus (SLE) is a chronic autoimmune diseasein which tissue-binding auto-antibodies and immune complex depositioncause damage to multiple organs and systems. We report a rare case of SLE in a 31-year-old male patient. He has a past history of unprovoked deep vein thrombosis of right lower limb for 8 years, treated with anticoagulant therapy but not evaluated further. The patient went on to develop recurrent symptoms of fever, rashes and joint pains which were also overlooked. ANA profile and APLA antibodies were positive and the patient was diagnosed with SLE after 8 years since onset of symptoms. He now exhibits renal manifestations in the form of anasarca and proteinuria and CNS manifestations in the form of seizures. We attribute the severity of his current condition to the delayed diagnosis.

Introduction:-

Like most rheumatic diseases, SLE has a higher incidence in females of reproductive age group(17-55y) than males with a ratio of 9:1, which falls to 2:1 with inclusion of pre-pubertal and post-menopausal women. This could be attributed to the possible immunosuppressive effect of androgens on T-cells. A number of studies have hypothesized that it could be due to differences in sex hormones or sex chromosomes but the exact reasons remain largely unknown[1][2]. It is observed that males have a higher risk of developing renal, cardiovascular, thrombotic, neuropsychiatric complications and death whereas women are more prone to developing skin (malar rash, photosensitivity), hematological, joint manifestations and Raynaud's phenomenon, much earlier in the course of the disease. One of the objectives of this report is to establish the grave importance of early diagnosis and management of SLE in males.

Owing to its multisystem involvement, patients present with a wide variety of non-specific symptoms, which seems to be the major cause of delayed diagnosis.

Upon clinical suspicion, patients are subjected to haematological investigations, most routinely the Anti-nuclear Antibody profile to test for auto-antibodies against cellular and nuclear components. Other tests like complete blood count, coagulation profile, Erythrocyte sedimentation rate (ESR), C-reactive protein andcomplement levels assess the degree of inflammation. Urinalysis is done to rule out lupus nephritis.

The 2019 EULAR/ACR classification criteria is used for diagnosis with a sensitivity of 96.1% and a specificity of 93.4%[3]. It requires a compulsory positive ANA at least once, and other signs and symptoms grouped under 7 clinical(constitutional, hematologic, neuropsychiatric, mucocutaneous, serosal, musculoskeletal, renal) and 3 immunologic(antiphospholipid antibodies, complement proteins, SLE-specific antibodies) categories. Patients with >10 points are said to have SLE.

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Case Report:
A 31-year-old male patientpresented with history of multiple joint pains, intermittent fever, increased frequency of micturitionfor one week.

He has a past history of DVT of right lower limb 8 years ago, andis on anticoagulant therapy and h/o multiple episodes ofrashes and small joint pains over the last few years. Physical examination showed low-grade fever, conjunctival pallor, non-pruritic maculopapular rash, right calf tenderness, anasarca. Cardiovascular, Respiratory and gastrointestinal examination were unremarkable. Neurological examination revealed no focal neurological deficits.

He was admitted for thorough evaluation. Routine blood investigations and special investigations were performed. **ANA profile** (using IMMUNOBLOT) showed high titres of Anti dsDna 3+, Anti-histone 3+, Anti-ribosomal P protein-3+, Anti-nucleosome – 2+, Anti JO1 – 1+, Anti RNP/SM – 1+, Anti mitochondrial – 1+, **APLA IgG**-98.85.Coagulation profile was abnormal with a high aPTT possibly due to chronic anticoagulant therapy and/or positive APLA titres**:** Platelet count: 2.61 lakh/mm3, PT: 19.5 seconds, INR: 1.7, APTT: 74.7 seconds. **Inflammatory markers** were elevated: CRP: 96 mg/L, ESR: 70 mm/h, LDH: 251 IU/L, Procalcitonin: 0.15 ng/ml.**Homocysteine**: 36 mg/dl. A negative rheumatoid factor and anti-CCP ruled out rheumatoid arthritis**. Urinalysis** showed nephrotic range proteinuria: protein 2+, no albumin, RBC 2-3/hpf, pus cells 2-4/hpf, **24h urinary protein of 4300mg/dl** and Urine PCR of 1.12. **Doppler of right lower limb**: chronic partial recanalization, suggestive of DVT (femoral and iliac vein) with incompetent perforators. Chest X ray and USG abdomen: normal. **2D echo**: normal valves, chambers, LV systolic function, EF:64%, no clot/vegetations. Complete blood count, iron profile, lipid profile, liver and renal function tests, and thyroid profile were normal. Serology was negative except for a false positive VDRL, discussed later. The chronicity of symptoms and notable diagnostic parameters led us to a diagnosis of SLE, as he met the ACR-EULAR criteria.

He was subjected to renal biopsy to assess the degree of involvement of the kidney, which revealed Lupus Nephritis class IV with AS 9/24 and CS 0/12, no crescents. He was started on **NIH protocol for lupus nephritis**: monthly intravenous pulses of Cyclophosphamide (0.5-1g/m^2) for 6 months. He received 5 doses, missed the last dose and was non-compliant to his oral medications for the next 1.5 years. He attained partial remission and has now come back with a nephrotic flare with anasarca and proteinuria and neurological symptoms in the form of one episode of generalised tonic clonicseizures. Biopsy was repeated which revealed Lupus nephritis **with diffuse endocapillary pattern/proliferative with membranous glomerulonephritis: CLASS IV G(A/C) +V, AS:9/24 and CS:2/12**.

MRI brain was normal with no evidence of thrombosis.

He was restarted on NIH protocol and daily oral medications: Hydroxychloroquine, Levetiracetam, Prednisolone, Ramipril, Thyroxine sodium and Acitrom (with Targeted INR between 2-3) and discharged with dietary advice, strict adherence to treatment and regular follow-ups. Warning signs such as haematuria and pain abdomen were explained and he was discharged in hemodynamically stable condition with adequate response to therapy.

Discussion:-

The earliest identifiable indication of SLE in this patient is unprovoked deep vein thrombosis, most likely due to the presence of APLA antibodies.

Hypercoagulability in SLE can be attributed to antiphospholipid antibodies (lupus anticoagulant, anticardiolipin antibodies, B-2 glycoprotein-1 antibodies) which target negatively charged phospholipids, initiating platelet activation. They also interfere with coagulation inhibitors like protein C and S, inhibit anti-thrombin and lead to the

formation of a thrombus. Chronic inflammation induces the expression of tissue factors which also activates the procoagulant arm of the coagulation system and inhibits anticoagulation and fibrinolysis. Lupus nephritis is thought to be associated with an elevated risk of thrombosis[4][5].

This can present in the form of deep vein thrombosis, superficial thrombophlebitis, transient ischemic attacks, recurrent miscarriages/intrauterine fetal demise (in females) or rapidly fatal conditions like stroke, pulmonary embolism and cerebral venous thrombosis (headache, focal/generalized seizures, cognitive disturbances, stroke like symptoms, cerebral edema, intracranial hypertension). A case series of 27 patients with CVT indicated a positive correlation between positive APL antibodies and risk of CVT[6]. Our patient should have been evaluated for causes of hypercoagulability. If APLA positive status had been suspected and diagnosed earlier, hecould have been started on treatment. The progression of SLE, although cannot be halted, can be slowed down by early diagnosis.

He also has an incidentally identified false positive VDRL status as the diagnosis of syphilis has been ruled out after careful examination for signs and symptoms. Gheorghe et al, in 2019 reported the case of a 32 year old male patient wrongly diagnosed to have syphilis owing to a false positive VDRL test, who was treated with penicillin for 5 years and showed no signs of improvement[7].He was later diagnosed to have SLE but by then, had developed renal, musculoskeletal and myocardialcomplications.

Another case report talks about a 25-year-old young male patient with pleuritis and pneumonitis. Malignancy, tuberculosis were ruled out[8]. A trial of antibiotics failed to improve his condition, after which an ANA profile was done and SLE was diagnosed. His condition improved with steroids.

We believe that primary care physicians with awareness regarding the vast spectrum of symptoms and rare presentations are less likely to miss the diagnosis and hence, play a major role in early management and better prognosis.

Conclusion:-

This case is an indicator of the consequences of delayed diagnosis of SLE. Even though the incidence is much lesser in males, the severity of the condition is much higher, contributing to the morbidity and mortality. Long termvague, constitutional and multi-systemic symptoms must be evaluated thoroughly, especially so in males where the disease may go undetected due to its rarity and negligence.

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