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A late diagnosis of Systemic lupus erythematosus diagnosed as rheumatism: A case series from Tumbi Regional Referral hospital in Pwani, Tanzania

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Abstract

Systemic lupus erythromatosus may not be as uncommon as it has been published in Sub-Saharan Africa. This case series represents a few cases among many that may be diagnosed late hence undesirable outcomes. Thus, this series calls upon a high index of suspiciousness among attending clinicians. Nevertheless, modalities of diagnosis in particular laboratory testing should be made available at a region hospital level to shorten delays of diagnosing such cases.

Keywords: Systemic lupus erythematosus; Late diagnosis; Autoimmune disease; Connective tissue diseases

1. Introduction

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease on unknown etiology that may affect any organ in the body. An outstanding immunologic feature of the disease is production of antinuclear antibodies (ANA) (1).

The burden of SLE worldwide remains undefined due to lack of studies particularly from developing countries. The highest burden has been reported in United Arab Emirates, Barbados and Brazil(2). On the other hand, in Sub Saharan Africa SLE is not a myth as it was beforehand reported. In some West African countries, the prevalence of SLE recorded has been ranging from 0.6% to 5.3%(3).

SLE has a protean presentation, in such a way it may present with mild skin and joint involvement to life threating complications in the central nervous, hematologic and renal system (1). Its capricious symptoms that mimic other autoimmune, infectious or hematological diseases possess a prodigious diagnostic and management challenge to most clinicians. Nevertheless, SLE clinical heterogeneity and lack of pathognomonic features or investigations make matters worse (1).

In this case series we present 2 cases that had a delayed diagnosis of SLE however, following adequate investigation and treatment all 2 cases had a remarkable clinical improvement.

2. Case 1

A 49-year-old female, with no previously known chronic illness, presented with progressive fatigue, generalized joint pain and skin rash (left arm and face) for a year. These symptoms were coupled with inability to walk and hold objects, significant weight loss, excessive oral cavity dryness, hair loss but she denied a feeling of numbness/pin and needles on the tips of toes or fingers, fever or drenching night sweats. Upon general examination, she was wasted with 45 kgs, hyperpigmented patches on the cheeks and left arm lateral aspect, patchy alopecia and slightly pale. Musculoskeletal examination, there was limitation on flexion and extension of almost all joints, tenderness along the thigh and calf

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muscles, however, no obvious joint deformities noted. Other systemic examination was unremarkable. A diagnosis of connective tissue disease with a differential of SLE, Sjogren syndrome, polymyositis and mixed connective tissue disease was made. The following laboratory investigations were ordered as per the table 1 below:

Table 1 Summary of laboratory investigations done at diagnosis

Investigation	**Results**
ANA profile	2+ Fine speckled nuclear Positive nRNP/sml, Sm and ribosomal P proteins
CK MB	Normal 2ng/ml
FBP	Mild anemia HB 10.9g/dl, normal white blood cells and platelets
Renal function tests	Normal Creatinine 79.4mmol/L
Urinalysis	Normal
Imaging chest radiograph and ECHO	Normal
CRP	Normal 3.3mg/L
Liver enzymes	Normal ASAT 21 ALAT 14

The patient was commenced on prednisolone 40mg od 2/52 then tapered off, rabeprazole 20mg bd 1/12, hydroxychloroquine 300mg od daily, nutritional counselling and walking exercises. A follow up clinic was set up at one month where the patient had marked improvement, body weight 48kg, no skin rash, improved appetite and resolved joint pain.

The second visit she had 52kgs, resolved alopecia and improved quality of life where she had resumed work.

3. Case 2

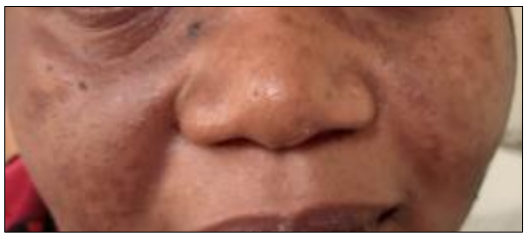

Figure 1 A picture displaying a malar rash

A 39-year-female presented with skin rash on the face, easy fatigue and joint pains for more than three months. The rash was hyperpigmented involving the cheeks and nose sparing the nasal labia folds and forehead whilst the joint pain involving joints of the fingers, wrist and toes intermittently rendering her unable to perform her daily chores. She denied excessive dryness of mucous membranes, myalgia or morning stiffness. Due to the complaints, she was attended and treated at a particular clinic with a diagnosis of osteoarthritis with no resolution of symptoms. On examination generally there was conjunctival pallor and tinge of jaundice on the sclera, skin and appendages she had a typical malar rash on the face, musculoskeletal examination limited flexion and extension on the wrist joint and carpal-metacarpal joints but

deformities. A diagnosis of systemic lupus erythromatosus was reached and a second diagnosis of hepatitis with differentials of viral vs autoimmune related was added.

The following laboratory investigations were ordered as per the table 2 below:

Table 2 Summary of laboratory investigations done at diagnosis

Investigation	**Results**
ANA profile	2+ Fine speckled nuclear Positive SS-A 2+, SS-B 2+, Nucleosomes 1+ and AMA M2 1+
CK MB	Normal <1ng/ml
FBP	Moderate anemia HB 8.9g/dl, normal white blood cells and platelets
Renal function tests	Normal Creatinine 88.2 mmol/L
Urinalysis	Normal
Imaging chest radiograph, abdominal ultrasound and ECHO	Normal
CRP	Normal 3.3mg/L
Liver enzymes	Elevated ASAT 195 ALAT 89
Hepatitis B and C serology	Negative

The patient was started on prednisolone 40mg od 2/52 then tapered off, hydroxychloroquine 300mg od daily, counselling and exercises.

A followed visit was set after two weeks where she had marked improvement of the joint pain and fatigue. A one month follow up the malar rash declined significantly and she was able to resume her usual daily activities. Currently the patient is on daily hydroxychloroquine.

4. Discussion

SLE may not be as rare as it has been documented in SSA. Aforementioned cases were misdiagnosed and wrongly treated for quite some time. These are among many other cases being delayed to treatment until severe form of the disease sets in. A dilemma to this clinical mystery was unanswered in most literatures, which patients to be screened for SLE. Various genes were linked to SLE however, current literature is not in favor to screen for them. Nevertheless, ANA testing in asymptomatic person is not useful as immune response to antinuclear antigens may not be SLE specific, it may be detected in healthy individuals or may precede SLE manifestation by many years (4).

A diagnosis of SLE should be suspected particularly in a female of reproductive age with following constitutional symptoms; fever, fatigue, weight loss and symmetrical or asymmetrical joint pains that might be coupled with morning stiffness affecting small to large joints. Erosion and large joint effusion are uncommon in SLE (9). Often, these constitutional symptoms are accompanied by other manifestation of SLE such as photosensitive rash on the face, neck and extremities (1). Similarly, in both cases presented here fatigue, skin rash on sun exposed areas and joint pain were prevailing symptoms.

Cutaneous manifestations in SLE are common in 75-80% of cases and are classified as acute, subacute, chronic and bullous lupus (4).

Table 3 Cutenous manifestations of SLE

Acute cutaneous lupus	Subacute cutaneous lupus	Chronic cutaneous lupus	Bullous lupus
Indurated or flat erythematous lesions on the malar eminences, scalp, arms, hands, neck, and chest	Annular lesions that may coalesce into a polycyclic (Overlapping ring-shaped) rash or papulosquamous lesions that do not scar and are distributed where light exposure is most frequent Commonly associated with anti-SSA antibodies	Verrucous lesions Smooth, shiny, red-violet plaques, usually on the head and neck Purplish-blue lesions on the fingers, toes, or ears	Blisters range from large, tense bullae (resembling bullous pemphigoid) to small, grouped vesicles (resembling dermatitis herpetiformis)

Additionally, in suspected cases of SLE the following systems should looked upon; hematologic: cytopenia is common in lupus patients whilst moderate to severe lymphopenia being associated with organ damage and high disease activity (1). Luckly, both of our patient had normal white cell and platelet count with exception of mild anemia in one patient.

On the other hand, SLE has renal manifestations affecting up to 50% of patients. It may be evidenced in urinalysis as hematuria, pyuria, proteinuria and/or cellular casts. In addition, renal function in particular creatinine may be deranged. Lupus nephritis has worse prognosis compared to other causes of end stage renal disease (4). Reflecting evaluation of our patients none had lupus nephritis presentations.

Furthermore, the respiratory system may be affected in 30-50% of patients. Clinically patients may present with dyspnea or pleuritic chest pain. When lupus pleuritis is suspected, other causes of pleural effusion such as infection, pulmonary embolism, liver disease, heart disease, and cancer should be excluded. Parenchymal lung involvement is a rare finding but it is associated with interstitial lung disease, acute pneumonitis and or bronchiolitis obliterans (1,4). Both of our patients had no respiratory presentation.

Nevertheless, the central nervous system involvement has a wide array of symptoms; headache, aseptic meningitis, vasculitis, movement disorder, seizure disorder, cognitive dysfunction, psychosis, demyelinating disease, myelopathy, autonomic disorder, and peripheral neuropathy(1).

Lastly, gastro intestinal manifestations are not uncommon among lupus patients. Some of the presentation includes; anorexia, nausea, vomiting, abdominal pain, and diarrhea. Similarly, anorexia was present in both of our presented patients (1).

The SLE diagnostic criteria has been going through modification to increase sensitivity and specificity so as to pick even the mild cases. In 2019, the European League Against Rheumatism (ELAR) and American College of Rheumatology (ACR) came up with a classification criterion to diagnose SLE. It requires a positive ANA as an entry criterion and a weight of 10 points from the 10 domains(5). Correspondingly, both presented cases qualified the entry criterion with a positive ANA test. Additionally, joints involvement (6 points) and acute cutaneous lupus (6 points) were among the initial presentations on both cases .

In order to affirm the diagnosis of SLE laboratory investigations have a crucial role. Antigen specific ANA such as double-stranded DNA (dsDNA) or ribonucleoprotein complexes (Ro/SSA, La/SSB, Smith, and RNP) have an essential role in adding weight to the diagnosis. Moreover, other supportive investigations are vital to ensure exclusion of target end organ damage as described in the SLE clinical presentation (6). Likewise, our presented cases had positive antigen specific ANA with preserved target end organ dysfunction.

In the treatment of SLE hydroxychloroquine is the cornerstone drug of choice. Other treatment options include; glucocorticoids, non-steroidal anti-inflammatory drugs (NSAIDs), immunosuppressive drugs and B-cell targeting biologics (7).

Approach to drug therapy in SLE is individualized and depends on organs involved, predominant symptoms, response to previous therapy, disease activity and severity. All patient patients with SLE regardless of degree and type of disease

activity hydroxychloroquine should initiated. In patients weighing 80kg and above 400mg once daily should be given whilst those below 80kg hydroxychloroquine 5mg/kg/day should be started. Hydroxychloroquine has the following crucial roles; prevents SLE exacerbations, reduces risks of heart block in congenital SLE, organ damage, cancer, antithrombotic effect by reducing platelets adhesion, aggregation and activation. Contrary, the reported adverse includes; retinopathy and skin pigmentation (7).

Treatment escalation depends upon the disease activity and severity. Mild disease; predominant skin, joint involvement, fatigue and mild leukopenia require solely hydroxychloroquine. Additionally, a short course of NSAIDs or prednisolone may be given (7).

In patients with moderate disease described as; significant but non-organ threatening disease e.g., constitutional, cutaneous, musculoskeletal or hematologic presentation responds to hydro chloroquine plus a short-term course of prednisolone 5mg -15mg daily. Hydroxychloroquine requires at least three months for clinical effect to be observed as a result, prednisolone should be tapered off once hydroxychloroquine has taken effect. Correspondingly, this treatment plan was employed in both of the presented cases above (7).

In severe cases defined as organ threatening manifestations such as renal or central nervous system involvement, require an initial period of intensive immunosuppressive therapy to halt tissue injury. In severely ill patient methylprednisolone 0.5-1g/day or oral prednisolone 1-2mg/kg/day in stable patients for 3 days may be given. These agents rapidly reduce inflammation hence, disease control. In addition, to reduce steroids related complications the doses may be tapered off while adding glucocorticoid sparing therapy such as mycophenolate (a dose of 500mg twice a day increase to 1000mg twice a day in 2 weeks), cyclophosphamide or rituximab (7).

Patient follow up is determined by disease severity. Patient with active lupus nephritis may require a week or two weeks follow up to monitor and guide therapy. On the other hand, those in remission with no symptoms expert groups recommends a three-four month follow up (7). Both of our cases were followed up for two weeks then four weeks for disease activity assessment and currently they are scheduled to come again after every three months.

The prognosis of SLE has markedly improved over the recent decades with 5-year survival rate increasing from 40% in 1950s to 90% in 1980s. Early disease recognition, advancement in diagnostic and treatment options are among the factors that have led to the increment in the survival rate. Increased risk of death occurs in cases with active disease or infection due to immunosuppression (7).

Various factors have been implicated to be associated with increased mortality to mention a few; kidney disease (especially diffuse proliferative glomerulonephritis), hypertension, male sex, young age, older age at presentation, low socioeconomic status, being a black person, presence of antiphospholipid antibodies, anti-phospholipid antibody syndrome and high overall disease activity (7).

5. Conclusion

In reference to these case series, SLE may not be as uncommon as it has been published in SSA. Clinicians should raise the index of suspicious in females of reproductive age reporting the constitutional symptoms aforementioned. Nevertheless, ANA profile is way far expensive on this side of the world, hence, policy makers should see the necessity of making these tests available at an affordable amount. Lastly, we recommend a registry of these cases to be started so that the real burden of SLE becomes well known.

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare no conflicts of interest.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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