Case report

Familial systemic autoimmune rheumatic disease in Nigerians: a case series

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Abstract

Systemic Autoimmune Rheumatic Diseases (SARD) are chronic disorders affecting multiple organs. Most SARDs have a female preponderance. SARDs have rarely been reported in African blacks, although there is increasing reportage of recent. Different SARDs are believed to have genetic predisposition and familial clustering.

SARDs occasionally run in families - among mothers and daughters, among siblings. Such clustering has however not been documented among black Africans. We present four Nigerian families with clustering of systemic autoimmune rheumatic disease.

Key words: Systemic autoimmune disease, Familial clustering, Nigerians

Introduction

Systemic Autoimmune Rheumatic Diseases (SARD) are chronic autoimmune disorders affecting more than one organ. This group of disorders comprise Rheumatoid Arthritis (RA), Systemic Lupus Erythematosus (SLE), Systemic Sclerosis, primary Sjogren's syndrome, inflammatory myopathies and systemic vasculitides, among others[1].

SARDs are being increasingly reported among black Africans[2-3]. This may be attributable to increasing awareness of these conditions among African physicians[4]. Its occurrence in more than one family member has been reported in literature, especially among female first degree relatives[5,6]. There have been reports of familial clustering from Japan Bangladesh and the USA[7]. There are no documented reports of such familial clustering in black Africans; hence this case series.

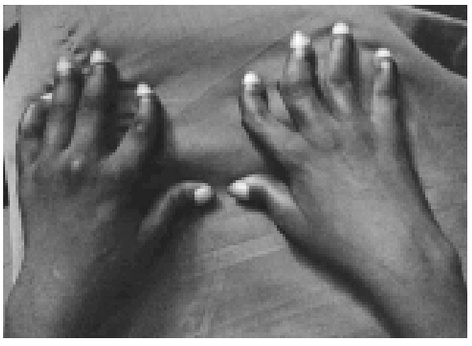
Family 1

Mrs JB, a 44-year old female presented with a 3-month history of alopecia, skin rashes and recurrent fever. She had multiple discrete lesions of scarring alopecia and atrophic lesions on both cheeks, bilateral pedal oedema, blood pressure was 110/60mmHg.

Investigations: Erythrocyte Sedimentation Rate (ESR) - 63mm/hr, proteinuria 3+. Urea and creatinine were normal. Antinuclear Antibody (ANA) - positive, (titre of 1:2,560; speckled pattern), anti-double stranded DNA antibody was positive. A diagnosis of SLE, with lupus nephritis was made - using the 1997 ACR criteria for SLE[7]. She was pulsed with intravenous methylprednisolone (500mg daily for 3 days), then continued with oral prednisolone (40mg daily, tapered over weeks), azathioprine and hydroxychloroquine. During one of her follow up visits, she mentioned that her daughter had deformed hands.

Her daughter, Miss JR, was 27 years old, and presented with a two-year history of pain in all joints of both hands. There was associated history of morning joint stiffness, swelling and deformities. Physical examination revealed swelling of all the Proximal Interphalangeal (PIP) joints of both hands and ulnar deviation at the PIP joints (Figure 1).

Figure 1: Picture of the hands (Daughter, Family 1)



Investigations: ESR - 132mm/hr, haematocrit - 26.9%, Rheumatoid Factor (RF) - positive (160 IU/ml). Anti-CCP-negative. Radiographs of both hands showed carpal and periarticular osteopenia; ulnar subluxation at the proximal and distal interphalangeal joints of 1st-4th phalanges; narrowing of the cartilage spaces and erosion of the heads of the phalanges with fusion of the carpometacarpal joints bilaterally (Figures 2 and 3). A diagnosis of

Rheumatoid Arthritis (RA) was made. She was managed with triple therapy, folic acid and low dose prednisolone.

Figure 2: Oblique radiographs of both hands (Daughter, Family 1)

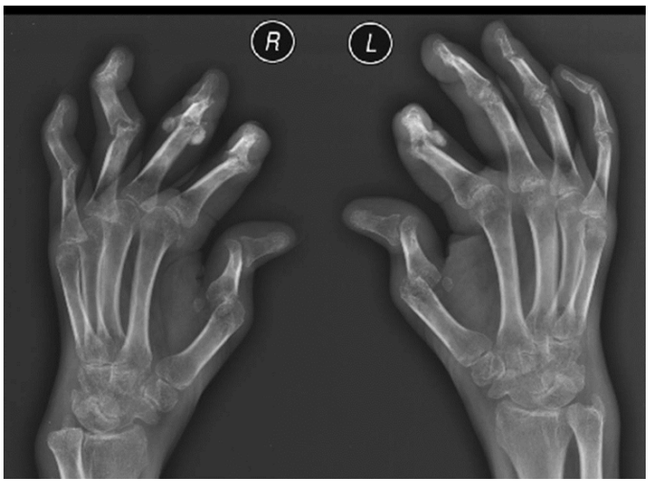
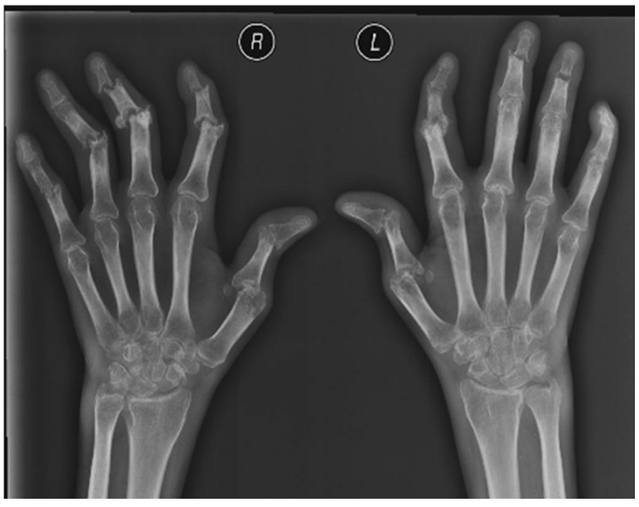


Figure 3: Posteroanterior radiographs of both hands (Daughter, Family 1)



Family 2

Mrs AO, a 58-year old female presented with a 5 year history of pain in the joints of her hands, wrists and ankles. There was a history of joint swelling with early morning joint stiffness lasting longer than 2 hours. Physical examination revealed swelling and tenderness of her wrists, MCPs, PIPs and ankle joints. Chest examination revealed crepitations in the middle and lower zones of both lungs.

Investigations: Elevated C-Reactive Protein (CRP) -71.6mg/L, anti-CCP - 94.0 EU/ml (ref. 0-30.0), RF - negative. Radiographs of both hands showed generalised osteopaenia of all the bones of the hands, narrowing of the PIP joints of the 2nd and 3rd digits bilaterally, and erosions in the first MCP joints. There was also subluxation of the MCP and PIP joints bilaterally and erosion of the medial part of the right ulnar bone. A chest radiograph showed bibasal alveolar filling opacities, mild cardiomegaly with left ventricular preponderance. The features were in keeping with pulmonary interstitial fibrosis.

An assessment of rheumatoid arthritis with interstitial pneumonitis was made. She was placed on hydroxychloroquine, sulphasalazineand prednisolone (which she took haphazardly). Her Clinical Disease Activity Index (CDAI) at the start of treatment was 35.0. She was changed to etanercept as her CDAI remained high even after one year. This was at a dose of 50mg weekly, but could only be given for 3 months because of financial constraints. She was subsequently lost to follow up, and was reported to have died from features suggestive of a myocardial infarction in another hospital 4 months later.

Her daughter, Mrs OO, was 34 years old and presented 2 months after her mother died. She had a history of polyarthralgia (wrists, knees and ankles) which started 3 months post-partum. She also had a history of fever, weight loss, and pedal oedema. On physical examination, she had synovitis of her wrist joints, both knees and ankles, and pitting pedal oedema extending up to both mid-thighs. Other systems were essentially normal.

Investigations: Haematocrit - 19%, ESR of 95mm/hr, dipstick urinalysis with 3+ proteinuria, 4+ haematuria, urine protein/creatinine ratio was 3.455g/g (reference range: 0.0-0.15). RF and anti-CCP both - negative, ANA positive (titre-1:640), Extractable Nuclear Antigen (ENA) screen –positive- at a level of 25.0 (reference range: 0.0-0.7). A diagnosis of lupus nephritis was made. She was pulsed with intravenous methyl prednisolone (500mg daily for 3 days) and thereafter commenced on intravenous cyclophosphamide (Eurolupus regimen). She is presently on mycophenolate mofetil.

Family 3

Miss OP, a 34-year old female - presented with a 3 year history of pain in the joints of her hands, elbows, shoulders and knees, with associated joint stiffness. She also had a previous history of a photosensitive rash, recurrent oral ulcers, and seizures. Physical examination revealed submandibular lymphadenopathy, tachycardia and bilateral loin tenderness.

Investigations: ANA- positive (titre 1:160, speckled pattern), anti-Sm antibody-positive, anti-nRNP antibody-positive, dipstick urinalysis - 1+ proteinuria.

An assessment of SLE was made and she was placed on hydroxychloroquine and prednisolone. Six years later, she had a left hemispheric CVD, with right-sided hemiparaesis. Anti-phospholipid antibodies were normal. Subsequently, on account of persistently high disease activity, azathioprine was added to her drug regimen. She is still being followed up.

Her younger sister, Mrs TR, was a 30-year old female who presented with a 2 year history of joint pain and swelling in the fingers of both hands, and early morning joint stiffness. On examination, she had subcutaneous nodules on the extensor aspects of both elbows, synovitis of the PIP joints of the 3rd and 4th digits of the right hand, and tenderness in her shoulders, elbows, wrists and knees.

Investigations: ESR 46mm/hr, RF72.9 IU/ml, anti-CCP 693 EU/ml. An assessment of RA was made and she was commenced on methotrexate, folic acid, and prednisolone. She is currently stable with low disease activity (CDAI-8.0) on this regimen.

Family 4

Mrs FO was a 32-year old woman who presented with a 6-month history of polyarthritis involving the joints of her shoulders, elbows, hands and ankles. There was associated joint morning stiffness lasting more than 1 hour in addition to dry eyes and dry mouth. On examination she had synovitis in all her MCP and PIP joints. She also had bilateral parotid enlargement.

Investigations: ESR-120mm/hr, CRP-15.5mg/L, ANA - positive (titre-1:640), Anti-SSA and Anti-SSB-positive, RF-marginally positive (23.6 IU/ml). Anti-CCP - negative (0.6 U/ml).

An assessment of Sjogren's syndrome was made, and she was commenced on methotrexate, prednisolone, folic acid, pilocarpine and hydroxychloroquine. She has had occasional flares and is presently on hydroxychloroquine. Her daughter, Miss CO, presented at 10 years with a history of polyarthralgia, passage of frothy urine and recurrent fever. On examination, she was febrile and had tenderness in her right knee and left ankle.

Investigations: Hct-30%, WBC-3.90 x 109/L (N-75%, L-25%), Platelets-283 x 10^9/L. ESR-90mm/hr.

Urinalysis: protein-2+, RBC-11-20/hpf, epithelial cells>10, specific gravity-1.030, pH-7.0. ANA was positive (titre-1:640), anti-dsDNA-negative. An abdominal ultrasound scan revealed Grade II renal parenchymal disease.An assessment of juvenile SLE was made. She was commenced on mycophenolate mofetil, prednisolone, calcium lactate, hydroxychloroquine and folic acid. She is stable, with low disease activity on this regimen.

Discussion

These cases are presented to illustrate the familial clustering of SARD in black Africans. There were three mother-daughter cases (mother with SLE, daughter with RA; mother with RA, daughter with SLE; and mother with Sjogren's syndrome, daughter with juvenile SLE). The fourth family comprised of two sisters (one with SLE, the other with RA). The family characteristics are shown in Table 1.

Table 1: Family characteristics

	First generation	Second generation	Number of siblings	Position of index patient
Family 1	Mother SLE	Daughter RA	4 2 males, 2 females	First
Family 2	Mother RA	Daughter SLE		
Family 3		2 Sisters SLE RA		First
Family 4	Mother Sjogren's Syndrome	Daughter SLE	2 One male, one female	First

There is increasing reportage of SARDs among black Africans, contrary to previously held notions that these conditions were rare[7]. There have been reports elsewhere of familial clustering of SARD: SLE in both mother and son in Japan[8], scleroderma in two members of the same family in Bangladesh[9], and juvenile dermatomyositis occurring in brother and sister in the USA[10].

It is believed that there are genetic predispositions to the occurrence of autoimmune disease as these diseases tend to cluster in families[4]. Ramos *et al*[7] have observed that the genetic overlap between SLE and other autoimmune diseases was however modest. It has been noted that there is an association of RA amongst the family members of patients with SLE[7,8]. As noted in this case series, 3 of the families had SLE in one member, and RA in another. It is believed that there is a familial aggregation of SLE and RA which could be due to the action of genes which predispose individuals to developing autoimmune disease. Such genes include PTPN22, CTLA4, STAT4 and TNFAIP3 which predispose to both SLE and RA[7].

In a study to determine whether transmission of SLE or RA from a parent to child was dependent on the sex of either party, it was documented that female offsprings are at greater risk of manifesting SARDs than their male counterparts[7]. There was no male subject among any of our cases.

Conclusion

We have presented four families which clearly demonstrate familial clustering of SLE and RA, and SLE and Sjogren's syndrome. It could be postulated that these patients have a genetic predisposition to these autoimmune diseases (SLE and RA).

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