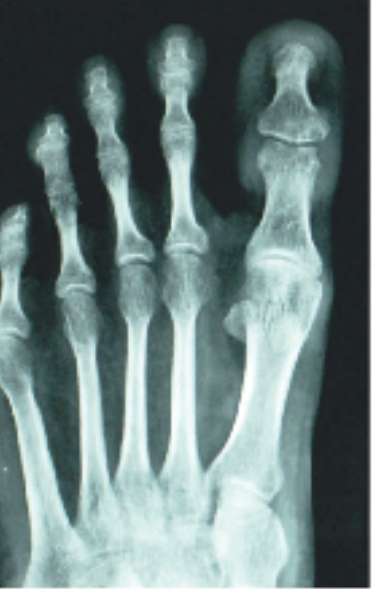

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Editorial

Welcoming an African asset: African Journal of Rheumatology

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It is with great pleasure that I allow myself to welcome the *African Journal of Rheumatology (AJR)* to our growing community of rheumatology journals. The AJR joins a highly competitive collection of more than 20 international journals in existence with some dating back more than 75 years and exclusively devoted to disseminate basic and clinical science developments of the specialty. On this era of global medicine and internet availability the AJR is a welcome addition as a representative of more than 50 African nations. A number of African national societies of rheumatology already have their own journal, but it is hoped the AJR will be representative of the African continent as a whole.

After reviewing the June 2014 issue of the journal I came across a variety of original clinical research and case report studies of great interest to clinical rheumatologists anywhere in the world, although some studies may be more representative of the rheumatic pathology seen in certain geographic areas of the African continent. Case in point, the two research articles on HIV infection and associated clinical manifestations. The first article describes the prevalence of HIV infection among a population of patients with avascular necrosis of the femoral head in Ouagadougou, Burkina Faso[1]. Findings showed that HIV infection accounts for 4.25% of avascular necrosis in a total of 141 patients seen at two medical centers in Burkina Faso, with alcohol consumption and steroids being the most common risk factors on this population. These findings are similar to what has been described in Western populations, but strongly indicates that patients exhibiting avascular necrosis on this highly endemic HIV infection area of the world should be screened for underlying HIV infection[2].

The second study that caught my attention originated in Nairobi, Kenya, another highly endemic area of HIV infection and reporting a high prevalence of fibromyalgia, 17.9%, among the HIV population and associated risk factors, WHO clinical stage 3 and a mean CD4 cell count of 276.2, comparable to what has been reported in Western countries[3-5].

Barasa *et al*[6] study on anti-phospholipid antibodies in patients with venous thrombosis at Kenyatta National Hospital, Nairobi, Kenya, is also of great interest. The study evaluated 60 patients, most of whom were females (86.7%), and their findings demonstrated that anti-phospholipid antibodies (Lupus anticoagulant and anti-β2glycoprotein I IgG antibodies) are present only in a minority of patients with venous thrombosis. In contrast, anti-cardiolipin IgG antibodies were present in the majority of patients, but their clinical significance was not entirely ascertained. As the authors acknowledged a number of issues hampered interpretation of the data. However, the study is one of a handful ever performed in the African continent, and points the way for the performance of more studies of this nature on similar, and more importantly in other populations of patients with anti-phospholilpid antibody syndrome exhibiting a myriad of clinical manifestations such as pregnancy loss, thrombocytopenia, thromboembolic disorders, autoimmune disorders. In addition, it would have been of great interest and importance that the authors of the study would have performed repeated anti-phospholipid determination several months after the initial episode of venous thrombosis. Another aspect that requires further investigation is the study of anti-phospholipid antibodies of IgM and IgA isotypes. The latter would have been of great interest, considering that our group and others have reported the IgA isotype to be the immunoglobulin isotype most commonly prevalent in anti-phospholipid antibody positivity in African American patients with systemic lupus erythematosus (SLE)[7,8].

A fascinating case report of a young 22-year old female exhibiting a systemic illness with renal involvement complicated with diffuse alveolar hemorrhage (DAH) in which a final diagnosis of SLE was made, promptly treated with a successful outcome also merits some comments[9]. DAH is an unusual complication of lupus that is accompanied by a high fatality rate if not recognized early and properly treated, and the authors should be commended for recognizing this complication and more importantly initiating rapid and aggressive therapy despite not counting with proper and adequate ancillary procedures and facilities. This case also brings forward the issue of how common or uncommon is lupus among black Africans. This topic

is superbly summarized and discussed by Professor Adelowo in his editorial in the same issue of the AJR[10].

Africa is the second-largest and most populous continent in the world and with over 1 billion people and more than 50 fully recognized countries surely deserves to have its own rheumatology journal. It should become a rich source of information about rheumatic disorders in the continent and it is a timely addition to our worldwide rheumatology community. It is my hope that the AJR parallels the rapid grows already in progress by the continent as a whole and becomes competitive on its own right. The editors and editorial board should be commended for their efforts in initiating this worthwhile academic enterprise.

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When is the last time you looked for diffuse infiltrative lymphocytosis syndrome in HIV patients?

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Abstract

Background: Diffuse Infiltrative Lymphocytosis Syndrome (DILS) is characterised by a persistent $CD8^+$ lymphocytosis and lymphocytic infiltration of various organs. The exact prevalence isn't known but some studies have reported between 0.85 – 3%, and appears to be more common in African population. Patients with DILS tend to have higher CD4 cell counts and survive longer than those patients without DILS. Most patients present with bilateral parotid gland enlargement and features of the Sicca syndrome. Common sites of extra glandular involvement are the lungs being the most common site, followed by peripheral neuropathy and liver. With the high incidence of HIV in our population it is likely that DILS is under diagnosed probably due to our ignorance of this disease. Awareness of its various presentations may bring to light undiscovered patients with DILS.

Objective: To review pathogenesis, diagnostic approach and current trends in the management of diffuse interstitial lymphocytic syndrome.

Data source: Literature review of relevant published literature from both Africa and the rest of the world.

Data synthesis: Pathologically, under light microscopy, DILS resembles the focal sialadenitis seen with Sjogren's syndrome, although it tends to be less destructive of the glandular architecture than in Sjogren's syndrome. Most of the inflammatory infiltrate is composed of $CD8^+$ lymphocytes unlike Sjogren's which are $CD4^+$. Lymphoepithelial cysts are frequently observed in the parotid glands of patients with DILS. The variation in $CD8^+$ count in the course of HIV disease is less understood. The variation in $CD8^+$ lymphocytes is implicated in the pathogenesis of a number of clinical manifestations in HIV diseases including Diffuse Infiltrative Lymphocytic Syndrome (DILS) and HIV associated $CD8^+$ lymphocytosis syndrome. Parotid gland enlargement in a patient with HIV infection should prompt clinicians to suspect DILS. In addition, clinicians should be aware that the pulmonary process associated with DILS may mimic clinically and radiographically the pneumonic process caused by *pneumocystis carinii*. Other manifestations of DILS to consider include a severe form of peripheral neuropathy; lymphocytic infiltration of the liver, evident as hepatitis; myositis; and lymphocytic interstitial nephritis. Management of DILS is determined by the severity of glandular and extra glandular features. Data on therapeutic trials are lacking although there are isolated reports of good response to antiretroviral and steroid therapy.

Conclusion: DILS, a subset of HIV disease manifestation, may present as parotid gland swellings. In general, an HIV patient presenting with DILS has a better prognosis than a patient with HIV alone. With the high incidence of HIV in our population it is likely that DILS is under diagnosed probably due to our ignorance of this disease. Awareness of its various presentations may bring to light undiscovered patients with DILS. Clinicians should watch for the possible transformation into B-cell lymphoma. There is still paucity of data about this disease from pathophysiology to treatment to studies correlating the plasma viral load with $CD8^+$ lymphocyte count in patients with HIV disease.

Introduction

The Diffuse Infiltrative Lymphocytosis Syndrome (DILS) in HIV-infected persons is characterized by a presence of circulating $CD8^+$ lymphocytosis. Their response to the HIV infection is to developing an oligoclonal expansion of $CD8^+$ lymphocytes. These cells infiltrate multiple organs with the salivary glands and the lungs being the major sites involved

in this process. This infiltrative process resembles in the salivary glands many aspects a Sjogren's-like syndrome, owing to the visceral lymphocytic infiltration. Clinicians should suspect DILS in HIV patients who present with unilateral parotid gland enlargement. In addition, clinicians should be aware that the pulmonary manifestation associated with DILS may mimic clinically and radiographically *pneumocystis carinii* infection. Other ways in which it manifests of DILS include peripheral neuropathy; lymphocytic infiltration of the liver as a hepatitis; myositis; and lymphocytic interstitial nephritis. It was first reported in 1989 from New York in a cohort of 12 patients who were HIV positive with parotid gland enlargement, pulmonary insufficiency and lymphadenopathy[1]. There is limited literature on the exact prevalence of the disease with estimates ranging from 0.8% to 7.8% in HIV-infected persons[2,3]. In West African review it was reported to be as high as 48% in HIV patients with features of DILS on lymph node biopsy[4]. The prevalence in the United States of America (USA) was found to be 3% (definitive) and 3.4% (possibly) in an HIV positive outpatient population[3]. It is reported to be more common in African Americans (60%) than American whites (26%)[2, 4]. A French retrospective study found a prevalence of 2.5%[5].

Pathophysiology

The histopathogenesis is however, still uncertain. Analysis of the $CD8^+$ lymphocytes infiltrating the salivary glands of patients who have DILS has provided evidence that DILS represents an MHC-restricted, antigen-driven oligoclonal selection of $CD8^+CD29^+$ lymphocytes that express selective homing receptors, such as CD29, the integrin CD11a/CD18 (lymphocyte function-associated antigen-1 [LFA-1]), and CD57. These receptors allow $CD8^+$ to become sequestered and infiltrate the salivary glands, lung, and other organs. There is also a strong expression of CD54 (intracellular adhesion molecule-1 [ICAM-1]) molecules on post-capillary venule endothelium within lymphoid aggregate. Therefore, the entry of lymphocytes into tissues involves interactions between specific cell adhesion molecules and their ligands, such as between LFA-1 and ICAM-1[6]. Research has suggested that both the circulating and the infiltrative $CD8^+$ lymphocytes in HIV-infected persons with DILS represent an antigen driven and immunogenetically determined host response to HIV infection. The cellular and molecular responses described above together with presence of HIV-encoded proteins in salivary gland macrophages localized in close proximity to lymphoid aggregates suggest that the systemic response to HIV infection, in certain immunogenetically predisposed persons, gives rise to a specific oligoclonal $CD8^+$ T-cell response that infiltrates certain tissues, such as the salivary glands[7]. The variation in CD8 count in the course of HIV disease is less understood. The variation in $CD8^+$ lymphocytes is implicated in the pathogenesis of a number of clinical manifestations in HIV diseases including Diffuse Infiltrative Lymphocytic Syndrome (DILS) and HIV associated $CD8^+$ lymphocytosis syndrome.

Clinical presentation

It commonly presents with features similar to Sicca Syndrome. Patients typically presents with bilateral parotid gland enlargement with xerostomia in 82% and xerophthalmia in 35%. It's rarely unilateral parotid swelling[1,2,8]. Generalized lymphadenopathy is seen in 80-100% of the patients[9,10]. How to differentiate it from Sjogren's syndrome?? Degree of gland enlargement (firm and tender) and extra glandular involvement together with relative of antibodies and differing HLA associations[11]. The lung is the most common extra glandular site of disease, affecting 31% of patients in the largest patient group investigated for DILS to date[3]. Clinicians should be aware that the pulmonary process associated with DILS (lymphocytic interstitial pneumonitis) may mimic clinically and radiographically the pneumonic process caused by *pneumocystis carinii*. The most common presenting symptoms are cough (71%) and worsening dyspnea (61%) which is slowly progressive over months and in rare cases several years[12-14]. Other symptoms and/or signs include weight loss (16%), fevers (10%), pleuritic chest pain (6%), fatigue and arthralgia. Examination findings are finger clubbing, cyanosis though rare and crackles on respiratory system. One should also look out for extra respiratory findings that may point towards LIP which are hepatosplenomegaly, lymphadenopathy, parotid gland enlargement, and arthritis. Peripheral nervous system involvement has been reported in association with DILS. Both a symmetric sensorimotor neuropathy and an asymmetric neuropathy have been described[15-17]. These polyneuropathies might be confused with the very common distal sensory polyneuropathy of late HIV infection or with a toxic polyneuropathy related to antiretroviral nucleoside analogue drugs. Both of the neuropathies associated with DILS may present with predominating distal sensory symptoms and (less commonly) with either mononeuritis multiplex or a demyelinating polyneuropathy. Peripheral neuropathy has been reported with DILS occurring in approximately 20–25% of patients[4,5]. Other extraglandular manifestations of DILS to consider include seventh nerve palsies due to compression by the parotid gland; lymphocytic infiltration of the liver, evident as hepatitis; myositis; interstitial gastrointestinal disease and lymphocytic interstitial

nephritis[18]. Curiously, the natural history of patients with DILS includes the relatively slow progression of their underlying HIV infection but with a high frequency of high-grade lymphoma.

Diagnosis

Diagnosis should be suspected in a HIV-patient with parotid gland enlargement and/or marked $CD8^+$ expansion in peripheral blood combined with a minor salivary gland biopsy demonstrating a $CD8^+$ predominant sialadenitis. Itescu and Winchester[19] developed a diagnostic criteria that requires a subject to be HIV-seropositive, have bilateral salivary gland enlargement or xerostomia for more than six months, and have histologic confirmation of salivary or lacrimal gland lymphocytic infiltration in the absence of granulomatous or neoplastic involvement. The diagnosis of DILS can be made from a labial salivary gland biopsy by demonstrating a $CD8^+$-predominant focal lymphocytic infiltrate unlike the $CD4^+$-predominant infiltrate in Sjögren syndrome[4,20]. MRI and CT scans can be of use in the diagnosis. They may reveal benign lymphoepithelial cysts, which can be a feature of DILS. Scintigraphy with gallium citrate Ga 67 has been shown to be extremely useful as a substitute for salivary gland biopsy in two different studies in which a classic, intense uptake of tracer occurred, provided that the patient has persistent bilateral parotid gland enlargement[2,3]. The intense gallium activity in DILS patients reveals the extensive lymphocytic infiltration of the salivary glands

Therapy

There are no randomised controlled trials that have evaluated therapy for DILS. Surgical removal of the superficial lobe of the gland was abandoned because the danger of this treatment was the possible surgical damage of the facial nerve and possible morbidity in an immunocompromised patient[21]. Enucleation, low-dosage radiation, and aspiration all have been reported with some success. Radiation therapy should generally be avoided because of concerns regarding malignant transformation. For treatment of the parotid gland enlargement, which is frequently cystic and occasionally highly disfiguring, antiretroviral therapy has been associated with a major degree of clinical regression. Medications such as combination of AZT with the newer protease inhibitors seem to be the most successful measures in treating the parotid swellings of patients with DILS. Therapy for DILS focuses on the use of prednisone and antiretroviral drugs[24]. Corticosteroids in moderate to high doses tend to elicit a good response, but their use is recommended only for patients with significant symptoms[20.22]. The lymphocytic interstitial pneumonitis associated with DILS requires higher doses of corticosteroids (up to 60 mg/d), as suggested by Reveille[20]. Reports of low-dose radiotherapy suggest good short-term efficacy in reducing parotid gland enlargement in DILS patients but with frequent relapses occurring in patients with less favourable initial responses[22,23]. The prevalence of DILS seems to be decreasing since the advent of HAART[2,20]. This supposition is based on the results of T-cell receptor analyses that show oligoclonal expanded $CD8^+$ T cells to be significantly diminished during HAART[24], with the entire $CD8^+$ T-cell repertoire decreasing after 8 weeks[25]. These results suggest that with HAART, there may be an interruption of chronic antigenic stimulation and that persistently replicating viral populations are required to maintain elevated levels of HIV-1-specific $CD8^+$ lymphocytes[24,26]. The response of $CD8^+$ lymphocytes to antiretroviral therapy was seen even from the onset of use of antiretroviral therapy, when monotherapy with zidovudine was used for HIV-related Kaposi's sarcoma[27]. In addition, many reports have shown significant improvement in $CD8^+$ lymphocytosis and reversal of visceral infiltration with the institution of antiretroviral therapy[20,21,28]. Others have shown that HAART is also effective in resolving parotid epithelial cysts[29]. The initiation of HAART seems to be the best modality for treating DILS in patients with HIV infection. The possibility of transformation into a B-cell lymphoma should be kept in mind by the clinician. The patient should be examined periodically at six-month intervals. In general, an HIV patient presenting with DILS has a better prognosis than a patient with HIV alone. The reasons for the better prognosis have not been identified.

Conclusions

DILS, is a subset of HIV disease manifestation and is characterized by the presence of dryness of the eyes and mouth and often massive enlargement of the parotid glands. Other manifestations of DILS include lymphoid interstitial pneumonitis, peripheral neuropathy; lymphocytic infiltration of the liver, evident as hepatitis; myositis; and lymphocytic interstitial nephritis. The histopathologic findings in the minor and major salivary glands are similar to those in Sjogren's syndrome, but the conditions differ in their underlying immunopathology and genetics. Few reports of DILS have been made from southern Africa. This may be due to a lack of knowledge concerning this disease or that in our population of patients with HIV. DILS may be an uncommon complication or presentation. Treatment often is not necessary due to the benign nature of this disease, unless cosmetics become a concern. Clinicians should watch

for the possible transformation into B-cell lymphoma. A six monthly check-up is recommended, supplemented by a fine needle aspiration biopsy when indicated by the clinical behavior of the lesion.

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Juvenile dermatomyositis in Africa

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Abstract

Background Juvenile Dermatomyositis (JDM) is a rare inflammatory myopathy of childhood that occurs in all racial groups and regions of the world. However, it has rarely been reported from Africa. Understanding the epidemiology and treatment outcomes of this disease in children is important for better planning of appropriate diagnostic and treatment interventions.

Objective To describe the demographic and clinical characteristics of patients diagnosed with JDM from Africa and highlight some challenges to their management.

Data source Published articles in Medline and Scopus data bases including case reports and case series on juvenile dermatomyositis from African countries.

Data synthesis: Forty four cases were identified from 13 studies: 29 females and 11 males. The sex of four of the patients could not be determined from the available information. Their racial distribution was 29 blacks and 15 others or unknown ancestries. Six of the patients died (13.6%) from respiratory failure, sepsis and severe myocardial disease.

Conclusion: Few case reports of JDM have been published from Africa though the relative paucity of published case reports is probably the result of underreporting. Mortality seemed to be higher among reported cases of JDM from Africa compared to those from other regions. Challenges to patient care include inadequate access to essential diagnostics and drugs; as well as inadequate skilled human resource.

Key words: Juvenile dermatomyositis, Africa

Introduction

Juvenile Dermatomyositis (JDM) is a rare inflammatory myopathy of childhood. It presents with skin and internal organ involvement with the lungs, gastrointestinal tract and heart among the systems that are often affected. It occurs in all racial groups and regions of the world and is at least twice as frequent in females as males in reports from most parts of the world[1-3] except India where reported incidence in males exceeds that in females[4,5].

The aetiology of JDM is not fully understood but genetic and environmental factors are known to play a role in its pathogenesis[6]. Therefore, regional and racial differences may occur and affect the incidence rates, clinical manifestations and even treatment outcomes. In Africa, only a few case reports of JDM have been published and the epidemiology, burden and clinical characteristics of the disease are not well understood. This article summarizes the reported cases of JDM from Africa and compares the demographic, clinical presentation and treatment outcomes with those from other regions of the world.

Materials and Methods

A case based review of Juvenile dermatomyositis in Africa was conducted by searching the Medline and Scopus data bases for cases of JDM published from Africa using the broad search terms "dermatomyositis" and "Africa". The article titles and abstracts were then scrutinized for relevance. Case reports, case series or any descriptive study that included a case of juvenile dermatomyositis from an African country were included with no restriction on language or year of publication. Studies for which we were unable to access the abstracts or full articles were excluded. Further cases were identified by modifying the search terms to include country names (e.g "Dermatomyositis" and "Algeria"). We also searched regional journals such as the *South Africa Medical Journal* (SAMJ), *East African Medical Journal* and *Nigerian Journal of Paediatrics* (NJP) for additional cases.

Results

Search results: A total of 39 articles were retrieved. Nine studies satisfied the criteria for inclusion but three articles published in the 1960s that did not include abstracts or full articles were excluded as we could not scrutinize the content for paediatric cases among the reported cases of dermatomyositis. Using the modified search strategy, four further studies were identified from Algeria and Egypt. Two

other case reports were identified; one each from the SAMJ and NJP which were not captured in the Medline and Scopus data base search.

Patient characteristics and treatment outcomes: A total of 44 cases were identified from the 12 studies: 29 females and 11 males (Female: Male ratio 2.6:1). The sex of four of the patients could not be determined from the available information. Their racial distribution was 29 blacks and 15 others or unknown ancestries. The mean age at diagnosis of 40 patients for which age was reported was 10.7 years.

Twenty eight (63.6%) of the patients had at least one of the markers of severe disease including calcinosis and ulceration (17); gut perforation (1); dysphagia/ dysphonia (2); nasopharyngeal carcinoma (1); interstitial lung disease (2) and myocardial disease (1). Six of the patients died (13.6%) while the outcome for 12 could not be determined as they were lost to follow up (3 cases) or inadequate information to determine survival status (9 cases). The causes of death were sepsis (one patient); respiratory failure due to muscle weakness (one) and lower respiratory tract infection in 3 (pneumonia in 2 and TB in 1); and severe myocardial disease (1 patient). One of the patients with fatal pneumonia had underlying interstitial lung disease. The characteristics of the JDM patients from the studies are summarized in Table 1.

Table 1: Summary of JDM cases reported from Africa

Country	Reference	Age	Race	Number (Sex)	Associated manifestations	Treatment outcome
S Africa	*S Afr Med J* 1965	5	Black	1 (F)	General edema, weak tender muscles	Recovered
		11	Black	1 (F)	Gottron's, Oedema, contractures, TB	Recovered
		16	Black	1 (F)	TB	Died
		10	Black	1 (F)	Pneumonia	Died
S Africa	*S Afr Med J* 1969	11	Black	1 (F)	NA	Recovered
		7	White	1 (M)	Myocardial disease on autopsy	Died
		17	White	1 (M)	NA	Recovered
Cameroun	*Med Sante Trop* 2013	9	Black	1 (F)	Calcinosis universalis	NA
S Africa	*Ped Rheum Online J.* 2014	9.8*	Black	16 (F) 5 (M)	Arthritis (42%), calcinosis (71%), Ulceration (43%)	2 deaths; 3 lost to follow up
Tunisia	*Tunis Med* 2007	NA	Arab	4 (NA)	amyopath1; MCTD1	NA
Tunisia	*J Am Acad Dermatol* 2003	16	Arab	1 (M)	Nasopharangeal Ca	Recovered
Egypt	*Eur J Pediat* 2008	3.5	Arab	1 (M)	Anasarca, dysphagia	Recovered
Egypt	*Paed Allergy Immun* 2000	9*	Arab	4 (F)	2 of 4 patients had Raynauds phenomen	NA
Algeria	*Joint Bone Spine* 2010	14	Arab	1 (M)	Calcinosis universalis	Recovered
Nigeria	*BMJ Case Rep.* 2014	11	Black	1 (F)	Dysphagia, dysphonia, proximal weakness, heliotrope	Recovered
Nigeria	*Nigerian J Paediat* 2011	10	Black	1 (F)	Dysphonia, abdominal pain	Died
S Africa	*S Afr Med J.* 2010	14	Mixed	1 (M)	Normal CK	Recovered
S Africa	*Pediatr Surg Int.* 2002	6	NA	1 (F)	Recurrent gut perforation	Recovered

*Mean age of the patients reported in the study NA: Information not available

Table 2: Comparison of characteristics and treatment outcome of JDM

Country (Reference)	African patients	USA/ CARRA(3)	Australia (1)	Western India (7)	UK/ Ireland (2)	Europe/Latin America(8)	USA (9)
Number (N)	44	384	57	22	120	390	329
Age (years) at diagnosis	10.7*	6.1	7.1	7.5	7.7	NA	7.4
M:F	1:2.6	1:2.5	1:2	1.4:1	1:2.2	1:2	1:2.5
Mortality %	13.6	NA	0	0	0.7	3.1	2.4

* Mean age of 33 of the patients for whom age was documented. NA: Information not available

Discussion

Demographic and clinical characteristics

Even though JDM is rare, it is the most common inflammatory myopathy in children with an estimated incidence rate of 1.9-4.1 cases per a million. There is female preponderance with a female to male ratio (F: M) of 2-5:1 in most studies[10-12]. In this series of patients from Africa, the gender distribution (F:M) was 2.6:1 similar to that from most parts of the world. The patients from Africa also appear to be older at diagnosis (Mean 10.7 years) compared to the mean of about 7 years reported from other parts of the world[1,2,7,13].

JDM occurs in all racial groups and available data do not support significant racial differences in incidence rates though Mendez *et al*[10] reported lower incidence rates among individuals of Hispanic descent compared to those of African and Caucasian descent in the USA. Some authors have also reported differences in phenotypic manifestations in different racial groups. Hoeltzel *et al*[14] reported a higher incidence of calcinosis among individuals of black African descent. A recent study from Johannesburg, South Africa among black children with JDM also found a high incidence of calcinosis (71%)[15] compared to that reported from other parts of the world (12-18%)[1,2,3,7].

Even though only a few studies have described the occurrence of JDM in Africa, cases have been reported from as far back as the 1965. Horsfall[16] described two Juvenile patients among a group of four patients with dermatomyositis in South Africa in 1965. Findlay *et al*[17] described five further cases among a group of 17 patients with dermatomyositis in 1969. The first study that systematically analyzed data from a cohort of children with JDM from Africa has only recently been published[15]. This study described 21 cases of JDM among black African children and reported higher incidence of severe forms of disease associated with vasculitis, calcinosis and *staphylococcus aureus* infection compared to disease manifestations in patients from other regions of the world.

Recently, clinical manifestations of JDM that confer increased risk of mortality have been described. These include dysphonia, dysphagia, Raynaud's phenomenon, older age at diagnosis, presence of interstitial lung disease, gastrointestinal perforation and presence of anti-aminoacyl tRNA synthetase antibodies[9]. Among the patients in this review, 28 (63.6%) had at least one of these markers of severe disease. Calcinosis occurred in at least 17 (38.6%) of the patients compared to that reported by other authors (5-24%)[1,3,8]. Six out of the 44 patients died giving a mortality rate of 13.6%. This is higher than the 0-3.1% mortality rate reported in cohorts from other regions of the world[1,3,7-9] (Table 2). However, the deaths include three patients reported in the 1960s when less aggressive therapy may have been the norm. But even the only systematic study from Africa that included 21 JDM patients reported a mortality of 2 (9.5%) patients. As noted above, African patients presented with severe disease that put them at greater risk for disability and death.

Challenges with diagnosis and management of JDM

The diagnosis of JDM still relies on the Bohan and Peter criteria published in 1975. The criteria include two procedures [muscle biopsy and electromyography (EMG)] that are not routinely performed in current practice. Instead, Magnetic Resonance Imaging (MRI) has gained popularity as a non-invasive alternative for assessing muscle inflammation[18,19]. In many African settings, access to these diagnostic facilities is poor. A working group of the Paediatric Rheumatology European Society (PReS) proposed additional clinical criteria including dysphonia, calcinosis and abnormal capillaroscopy that could be valuable in the diagnosis of JDM especially in the resource constrained settings[20]. Difficulties with diagnosis of JDM may also result from inadequate knowledge and skills. Further, difficulty with identifying cardinal features of JDM such as heliotrope rash in dark skinned (black) people has been reported[16,21]. These may result in delay in instituting appropriate treatment and associated increased risk of serious complications such as calcinosis[8,22].

Steroids remain the mainstay of JDM treatment and have contributed to significant reduction in JDM mortality from about 30% to less than 4% (Table 2). Toxicity from long-term steroid use however remains a major concern. To induce early remission and minimise steroid dose and duration, early institution of DMARDs such as methotrexate has been recommended[23-25]. Intravenous Immune Globulin (IVIG) and biologics such as rituximab are often used to induce remission in severe cases and as second line agents. In Africa, access to agents such as (IVIG) and biologics is limited by prohibitive costs, inadequate laboratory support and lack of qualified staff to supervise their use. In many regions of sub-Saharan Africa, poor access even to the most basic drugs such as NSAIDs, steroids and methotrexate means that even when the correct diagnosis is made, appropriate treatment may often remain a mirage[26].

In some African societies, the concept of chronic disease is not well appreciated and cures rather than disease control is always anticipated. Thus high dropout rates from follow up and poor adherence to treatment often remain major challenges in the management of chronic diseases. A study evaluating the clinical patterns of JIA in Zambia[26] reported that majority of patients were lost to follow up; while in the only case series of JDM reported in Africa so far[15], 3 out of the 21 (14.3%) patients were lost to follow up reducing the ability to reliably determine the treatment outcome rates.

Opportunities to mitigate the challenges

Despite the challenges alluded to above, opportunities exist for improving the diagnosis and management of JDM. Initiatives such as the University of Cape Town's APFP (African Paediatric Fellowships Program) and SHEPPHERD (Southern Hemisphere Educational Partnership for Paediatric and Adolescent Rheumatic Diseases) may help with training and improved human resource availability[27]. Further, JDM is mainly a clinical

diagnosis and most cases can be diagnosed with minimal laboratory and radiologic support. Additionally, many tertiary centres in Africa increasingly have access to MRI facilities.

Drugs such as methotrexate, cyclophosphamide and prednisone are already widely used for malignancies, asthma and renal diseases. Clinical and laboratory monitoring could also benefit from capacity that has been improved especially courtesy of the HIV programs. Routine X-rays and barium studies are also available in many centres that have supported various services. Pulmonary function testing may not be widespread but is available in most large tertiary centres for monitoring asthma and other respiratory conditions. Despite the poverty levels, a few patients may be able to afford second line treatments including biologics. Where appropriately trained personnel and adequate support services are available, these should be availed so that their benefits may be apparent at the local level. This could provide valuable tools for advocacy to improve access to these treatments.

Conclusion

JDM cases are increasingly being reported from Africa. Lack of published reports on the occurrence of the disease in Africa has made the estimation of the incidence rates and treatment outcomes difficult. Inadequate or inappropriate case management combined with apparently higher prevalence of the more severe forms of JDM among the African JDM patients may be contributing to comparatively higher morbidity and mortality rates. Key challenges to the diagnosis and management of JDM include lack of trained personnel; inadequate access to appropriate diagnostic and therapeutic facilities; low prioritization of non-communicable diseases by health authorities in the region and sociocultural factors.

Declaration: Kindly also note that the article forms part of my literature review for my MPhil thesis in Paediatric Rheumatology at the University of Cape Town.

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Hip osteoarthritis in Douala General Hospital: Clinical, radiological patterns and treatment options

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Abstract

Background: Hip osteoarthritis is a chronic debilitating disease that is treatable surgically by total hip replacement, sparingly available in developing countries, particularly in Africa. Few data are available on clinical patterns of hip OA in Cameroon.

Objectives: To describe the epidemiological, clinical and radiological profile of hip OA, and also treatment options offered to patients presenting with this condition at the Douala General Hospital, Cameroon.

Methods: After prior ethical clearance, a hospital-based cross sectional descriptive study was carried out, including all patients (one patient = one file) diagnosed with symptomatic hip OA during a 10 year period between January 2004 and December 2013 in Rheumatology and Orthopaedic Units at DGH. The Kellgren-Lawrence classification was used. Data was collected using pretested questionnaires and analyzed using Epi info version 7 and Microsoft excel 2007.

Results: Of the 9615 cases reviewed, 258 (2.7%) had symptomatic hip OA. The mean age was 53.3 ± 16.3 years (16 – 85 years). Females were more affected (56.4%). The mean BMI was 27.0 ± 4.3 (19.7 – 41.9) Kg/m^2. The prevalence increased with age over 50 years. The most frequent clinical findings were pain in the inguinal area, morning stiffness, limping, and limited range of internal rotation hip motion. Pain was usually moderate to severe in intensity. The most frequent radiological grade was K-L grade 4 (39.3%). The condition was unilateral in 73.1% of cases; it was unipolar in 65.4% (superior pole most affected); bicompartmental in 14.1%; tricompatmental in 20.5% of cases. There was no association between pain and radiologic grade of symptomatic hip OA. Out of the hundred with indication of hip arthroplasty, only forty-seven patients underwent surgical hip replacement therapy. The main limitation was financial.

Conclusion: Symptomatic hip OA has a female predominance. From the age of 50 years, females are more likely to develop the condition. There is poor correlation between symptoms and radiological findings.

Key words: Hip osteoarthritis, Pain, Joint replacement, Africa

Introduction

Osteoarthritis (OA) is a chronic degenerative joint disease[1] which affects more than 60% of the population older than 60 years and is associated with pain, disability, poor health status, and the frequent use of health care providers[2,3]. The worldwide prevalence of symptomatic OA is estimated at 9.6% in men and 18% among women. The burden of OA can be measured by its impact on both quality of life and psychosocial status due to pain, impaired mobility and decrease in functional capacities[1,2]. Although the spectrum of degenerative musculoskeletal disorders may be similar in developing and industrialized countries, the burden tends to be higher in developing countries due to delays in diagnosis and lack of access to specific interventions such as arthroplasty, joint replacement and rehabilitation[4]. Total joint replacement therapy in some cases (eg hip joint), known to provide relief and improve the quality of life in patients, is common in developed countries but not readily available and financially accessible to patients in low-income countries. Of 291 conditions evaluated as the cause of the global burden of disease and disability, hip and knee OA were ranked as the 11th highest contributors[5]. A hospital based study on OA in Cameroon showed that the hip is the second most affected site after the knee[6]. While the clinical characteristics of knee OA has been described in our setting, little is known about patterns of hip OA. Few orthopaedic centers offer total joint replacement therapy in

Cameroon making standard of care recommended for hip OA difficult to achieve[7]. The study aimed to describe the epidemiological, clinical and radiological profile of hip OA, and also identify treatment options offered to patients presenting with this condition at the Douala General Hospital, Cameroon.

Materials and Methods

Setting: The study was conducted in the Douala General Hospital, a 320 bed tertiary health center serving approximately 8 million inhabitants living in Douala, the economic capital of Cameroon, and the neighbouring regions. The DGH is a referral center, for rheumatology and orthopaedic patients with a well-equipped radiology service. Total hip replacement surgery is also routinely performed.

Study design: After prior approval from the local Ethical Review Board (ERB), a cross-sectional descriptive study was conducted to determine the main epidemiological, clinical and radiological characteristics of hip OA and the therapeutic options available in a tertiary referral health care center in Douala-Cameroon.

Data was retrospectively collected from the files of patients (one file=one patient) diagnosed with Symptomatic Hip Osteoarthritis (SHOA) at the Rheumatology and Orthopaedic Units between January 2004 and December 2013. Data was also collected directly from patients diagnosed with SHOA at the Outpatient Department (OPD) of these units, between April 2013 and December 2013. Clinical diagnosis of SHOA was based on the ACR criteria and radiographic classification was done using Kellgren-Lawrence classification. Patients with past or recent history of trauma, infection of the hip, and other inflammatory joint diseases were excluded.

Assessment: Data collected from each patient included; age, sex, residence, height in centimeters and weight in kilograms, past and recent medical history, duration of mechanical hip pain, visual analogue scale (VAS in millimeters ranging from 0 to 100) for pain during the last week, disease related clinical findings; pain was classified as low, moderate and severe when VAS ranged respectively from 0-49, 50-79 and 80-100. To define overweight and obesity, the body mass index [weight / (height^2) in Kg/m^2] was used. Overweight was defined as a BMI $\geq$ 25.0 Kg/m^2 while obesity as a BMI $\geq$ 30.0 Kg/m^2. Radiographic assessment was done using weight bearing anteroposterior and lateral views of the hip. Radiographs were read by the principal investigator, using Kellgren and Lawrence grades (0-4). Kellgren and Laurence (KL) staging of OA was calculated including joint space measurement with identification of Joint Space Narrowing (JSN), subchondral bone thickening and the presence of osteophytes.

Statistical analysis: Categorical variables were presented as frequencies and continuous variables as mean and standard deviation. Statistical significance was considered at p values < 0.05. Data were analyzed using the Stata® software (College Station, Texas, USA).

Results

A total of 9615 cases were reviewed during the study period and 156 fulfilled our inclusion criteria: 59.6% (93/156) from the Orthopaedic Unit and 40.4% (63/156) from the Rheumatology. The mean age was 53.3 ± 16.3 years (16 – 85 years), and the most affected being in the 60 – 69 year age group. Females were more affected than males; 56.4% and were significantly more likely to develop the condition than males at 50 years or older (OR = 0.7; 95% CI = 0.02-0.20; p<0.01); 61.5% patients were overweight. The mean BMI was 27.0 ± 4.3 (19.7 – 41.9) Kg/m^2. Twenty two (14.1%) patients had a history of trauma to the affected hip. Twenty eight (18%) patients had a family history of symptomatic hip OA. The right hip was affected in 73.2% (123/156) of cases. The pain was unilateral in 95.5% (149/156) of cases. The mean duration of symptoms was 4.1 ± 3.5 (3 months – 15 years). Pain was graded as moderate to severe (55.1% and 38.5% respectively); with the most common location being the inguinal area in 140 (89.7%); radiating to the knee in 28 (18.0%), the anterior thigh in 24 (15.4%). Ninety four (60.3%) of our patients had a limp. The most frequent was the antalgic limp, occurring in 82 (52.6%) of our patients (Table 1).

Table 1: Clinical characteristics of symptomatic hip OA

Characteristics	Items	Frequency
Age (years, %)	<40	34(21.8)
	40-49	26(21.6)
	50-59	34(37.8)
	60-69	40(21.6)
	70-79	20(12.2)
	>80	2(3.4)
Sex	F/M	88/68
BMI, mean		27.0 ± 4.3
BMI, n (%)	< 25	60 (38.5)
	>25	96 (61.5)
Symptoms pain†, n (%)	Inguinal region	140 (89.7)
	Low back	18(11.5)
	Buttocks	6 (3.9)
	Knee	2(1.3)
Pain duration, n (%)	<1 year	20 (12.8%)
	1-5years	98 (62.8)
	6-10 years	26 (16.7)
	>10 years	12 (7.7)
VAS pain, n (%)	Low (0-4)	10 (6.4)
	Moderate (5-7)	86(55.1)
	Severe (8-10)	60(38.5)
Other symptoms††, n (%)	Limping	94(60.3)
	Limb length discrepancy	31 (19.9)
	Muscle wasting	13(8.3)
	Low back pain	25 (16.0)
	Coarse crepitus	9 (5.7)

† A patient could have more than one location of pain at a time

†† A patient could present with more than one symptom at a time

Table 2 : Range of movements in our study participants

Range of movement	Frequency (n = 156)	(%)
*Limited ROM	108	69.2
Limited flexion	65	41.7
Limited internal rotation	97	62.1
Limited external rotation	54	34.6
Limited abduction	32	20.51
Limited adduction	9	5.8
Limited extension	11	7.1
Normal ROM	48	30.8
Total	156	100

Table 3: Radiographic findings in the study population

Poles involved	Frequency (n = 156)	(%)
Unicompartmental (n=102)		
Superior only	72	46.2
Medial only	18	11.5
Axial only	12	7.7
Bicompartmental (n=22)		
Superior + medial	18	11.5
Superior + axial	2	1.3
Medial + axial	2	1.3
Tricompartmental (n=32) (Superior + medial + axial)	32	20.5
Total	156	100

One hundred and eight (69.2%) of our patients had limitations in the range of movement in the affected hip joint(s). The most involved planes of movement were internal rotation in 97(62.1%) (Table 2).

Radiological findings were unilateral in 92.3% of cases. The most frequent radiological grade was K-L grade 4 (39.3%). Grade 3 and grade 2 occurred in 44 (26.2%) and 58 (34.5%) patients respectively. It was unipolar in 65.4% (superior pole most affected); bicompartmental in 14.1%; tricompatmental in 20.5% of cases (Table 3).

Table 4: Association between age and sex

Age	Female (%)	Male (%)	P value	Total (%)
< 50	12 (20.0)	48 (80.0)	< 0.001	60 (100)
≥ 50	76 (79.2)	20 (20.8)	< 0.001	96 (100)
Total	88 (56.4)	68 (43.6)		156 (100)

Table 5: Relationship between radiologic grades and severity of pain

KL Grade	Mild pain	Moderate pain	Severe pain	P – value	Total
Grade 2	2 (3.5)	34 (58.6)	22 (37.9)	0.69	58 (100)
Grade 3	6 (13.6)	28 (63.6)	10 (22.7)	0.09	44 (100)
Grade 4	4 (6.1)	30 (45.5)	32 (48.5)	0.29	66 (100)

Compared to males, females below the age of 50 years were less likely to have symptomatic hip OA (OR = 0.7; 95% CI = 0.02 – 0.20, p < 0.001) whereas at 50 or above, females were 15 times more likely to have symptomatic hip OA (OR = 15.2; 95% CI = 4.8 – 47.2, p < 0.001) (Table 4). There was no association between pain and radiologic grade of symptomatic hip OA (Table 5).

Treatment of OA in our study population included those in use of NSAIDS in 140 (89.8%), analgesics in 156 (100%), walking aid and braces in 30 (19.2%). Indication for THR was established for 100 (64.1%) patients, all with radiological KL grade III to IV associated to moderate and severe pain. Total joint replacement therapy was performed on 47 (30.1%) patients. The procedure used was Kocher-Langenbeck surgical approach with cemented implant in all the cases. Immediate postoperative complications were few (one massive hemorrhage and pulmonary embolism). One case of femoral component loosening was observed, treated by surgical revision.

Discussion

The aim of this study was to describe the clinical and radiological characteristics as well as the treatment options of patients with SHOA in Douala-Cameroon. The results revealed that SHOA (symptomatic hip OA) was more common in females, in or around their fifth decade. K-L grade 4 and superior pole involvement were the most frequent radiographic findings, and there was a poor association between the severity of radiological stage and the intensity of pain.

The study findings of SHOA being more common with increasing age are similar to that in other studies[4,8,9]. This is probably due to ageing related changes that occur in the cells and extracellular matrix of the articular cartilage such as decreased thickness, increased proteolysis, advanced glycation and calcification, which lead to biomechanical dysfunction and tissue destruction[9]. Mean age was 53.3 years in our study and this was similar to that in Togo but lower than in the USA and Italy, 63 and 74 years respectively[4,11,12]. Community based studies are determinant to make a true appraisal of the age of SHOA in African populations. Worth noting is the fact that the mean age of patients with rheumatic conditions in hospital based study in Yaoundé was 52.7 years[6].

Females were more affected in this study. More recent studies[2,5,9,13] report similar findings. In addition, females were significantly more affected at 50 years or older. This may be related to hormonal changes as women enter menopause. However, a few authors[8,14] showed no clear relationship between female hormonal tendencies and hip OA and they suggested that the relationship was probably too complex or other factors yet to be determined were responsible for the increased prevalence in females above 50 years.

Being overweight or obese probably increases the mechanical load across the hip joint. The findings of the study was consistent with other studies[6,15,16] that reported a significant association between being overweight/obese and developing hip OA. Even though the association of increased BMI and knee OA is certain[17], some authors debate about overweigh and SHOA[2,18].

Hip pain in this study as in others was described as anterior, at the inguinal area, and radiating to the anterior thigh and knee[15,19,20]. Chronic long standing pain and limping were the most frequent presenting complains, similar to what was described in other African studies, and this may be consistent with lack of accessibility to adequate health care facilities and delays in seeking specialized health care providers[4,6]. This point is confirmed by the fact that most of our patients are seen with severe radiographic changes (KL Grade 4) at the first consultation, and supported by the lack of association between pain and radiologic grade[20]. This raises the problem of inadequate care provided to patients seen late in the course of this disease, thereby making it difficult to prevent aggravation of ongoing degenerative processes in weight bearing joints. This highlights the need to create awareness amongst patients on the importance of early consultation in order to promote strategies for controlling risk factors. Symptoms can be reduced by information on importance of changes in lifestyle, adequate and regular exercises, braces and other forms of joint protection; All these measures are useful to reduce OA progression[1,16,21,22] particularly in an environment where joint replacement is not readily accessible.

Among the patients suitable for THR, only 1/3 benefited from surgical treatment of SHOA. Even though the surgical procedure is offered by the General hospital, very few could access the financial requirements, rending the standard care at this stage of the disease difficult[21,22]. It becomes important to emphasize on early detection of SHOA, to ensure effective low progression of joint lesions through simple measures accessible in low-income countries. Advocacy may also be important in training adequate health care providers in rheumatology, orthopaedic surgery and physiotherapy in our African setting to make recommended standard of care available and accessible to our patients.

The main limitation of this study was the lack of information about functional impairment related to SHOA and also the primary or secondary aetiology of SHOA. Severity of radiographic changes of knee OA in Cameroon has been associated with functional impairment rather than pain, this is still to be analyzed in the case of hip OA.

Conclusion

SHOA appears more prevalent in women older than 50 years. There was a poor association between the severity of radiological stage and the intensity of pain. Early intervention through reduction of factors associated with OA progression may improve outcome in sub-Saharan countries where surgical therapeutic interventions are not readily accessible. Community-based prospective studies are needed to better appreciate risk factors and functional impairment associated with SHOA.

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Research Article

Cardiovascular risk factors and carotid atherosclerosis in patients with systemic lupus erythematosus at Kenyatta National Hospital

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Abstract

***Background*:** Cardiovascular disease is now acknowledged as a primary cause of morbidity and mortality in patients with Systemic Lupus Erythematosus (SLE). The risk of developing coronary artery disease in these patients is four to eight times higher than that in the normal population. Prior to this study there was no data regarding cardiovascular risk in SLE patients in our setting.

***Objective*:** To determine the prevalence of selected cardiovascular risk factors and carotid atherosclerosis in patients with systemic lupus erythematosus at Kenyatta National Hospital.

***Methods*:** This was a cross-sectional survey carried out in patients with SLE and age- and sex-matched controls at the Kenyatta National Hospital. The SLE patients underwent clinical assessment of their blood pressure, weight, height, waist and hip circumferences as well as laboratory testing to determine their fasting blood sugar and fasting lipid profile. In addition, measurement of carotid Intima-Media Thickness (IMT) and assessment for presence of carotid plaque was done for the lupus patients. The controls had similar clinical and laboratory assessment done as for patients. Carotid ultrasonography was however not done for controls.

Results: Sixty six SLE patients and 66 healthy controls participated in this study. Mean age of the patients was 35.9 years, with a female to male ratio of 21:1 and median duration of illness of two years. Hypertension prevalence was 42.4% in the patients and 24.2% in the controls (p=0.027), dyslipidemia occurred in 74.2% of the patients and 62.1% of the controls (p=0.135) while diabetes prevalence was 4.5% in patients and 1.5% in controls (p=0.619). Obesity by Body Mass Index (BMI) assessment was found in 12.1% of patients and 21.2% of the controls (p=0.330) whereas abdominal obesity (by waist: hip ratio) occurred in 33.3% of patients and 24.2% of controls (p=0.249). Mean carotid IMT in SLE patients was 0.63mm (SD=0.15) with 9 (13.6%) patients having IMT readings of 0.8mm and above. Carotid plaque was detected in 15 (22.7%) patients. Carotid IMT and BMI significantly correlated with disease duration (p values= 0.006 and 0.021 respectively).

Conclusion: There was a high prevalence of atherosclerosis and selected cardiovascular risk factors in this population of SLE patients. Hypertension was significantly more common in the lupus patients than controls. Cardiovascular risk assessment and appropriate treatment of risk factors identified should be enhanced in patients with SLE.

Key words: Systemic lupus erythematosus, Cardiovascular risk factors, Carotid intima-media thickness, Carotid plaque

Introduction

Systemic Lupus Erythematosus (SLE) is a multisystemic autoimmune disease whose reported prevalence in different parts of the world ranges from 20-150 cases per 100,000[1,2]. It has been reported to occur infrequently among blacks in Africa[3]. Median age at diagnosis tends to be in the early thirties as shown in studies in Africa; 33 years in Nigeria[4] and 34 years in South Africa[5]. Lupus is known to occur predominantly in females worldwide.

Risk of death in lupus patients is two to five times higher than that in the general population, with a bimodal pattern of mortality described. Early mortality (less than one year since diagnosis) has been associated with severe disease activity while later mortality tends to be secondary to complications of longstanding disease and treatment options used in controlling the illness[6,7]. Accelerated atherosclerosis and consequent cardiovascular disease contributes to the causes of late mortality in these patients[8]. Furthermore, in comparison to other races, black women with lupus have been shown to die of cardiovascular disease much earlier than sex- and race-matched controls.[9] Whereas the pathogenesis of accelerated atherosclerosis in these patients is still incompletely understood, three contributing factors have been well described. These include the inflammatory

nature of SLE, the higher burden of traditional cardiovascular risk factors and the use of corticosteroids which are pro-atherogenic[10].

In the INTERHEART study, abnormal lipids, smoking, hypertension, diabetes, abdominal obesity, inadequate consumption of fruits and vegetables, alcohol intake, psychosocial factors and sedentary lifestyle (commonly referred to as the traditional cardiovascular risk factors) accounted for over 90% of the risk of myocardial infarction in the general population[11]. In the John Hopkins lupus cohort, 53% of the SLE patients had three or more of the classic cardiovascular risk factors[12] while in the Toronto Risk Factor study, hypertension, diabetes, elevated triglycerides and elevated low density lipoprotein were significantly more common in the lupus patients than controls[13]. This increased prevalence of cardiovascular risk factors in these patients means their risk of coronary disease is higher than that in the general population. Another important factor is the chronic inflammation that occurs in SLE. Chronic inflammation is central in the pathogenesis of atherosclerosis which begins with endothelial injury. A number of factors inherent in SLE such as autoantibody formation, impaired immune clearance, complement activation, elevated homocysteine levels among others contribute to endothelial injury and ultimately to atherogenesis[14]. Steroid therapy in lupus patients has been associated with an increase of traditional cardiovascular risk factors and atherosclerosis[15,16].

This study sought to assess the burden of selected cardiovascular risk factors and carotid atherosclerosis (as a marker of atherosclerotic disease) in SLE patients at Kenyatta National Hospital with the aim of providing a basis for primary and secondary interventions to reduce cardiovascular morbidity and mortality in the population.

Materials and Methods

This was a cross-sectional survey in SLE patients and controls at the Kenyatta National Hospital. The SLE patients were above 18 years of age and fulfilled the ACR criteria for diagnosis of lupus[17]. They were recruited into the study at the Rheumatology Out-Patient clinic, the Renal Clinics and the medical wards over a period of nine months. Controls were staff and students at the institution who were sex- and age-matched (to the nearest 5 years) to the SLE patients in the study. They were screened to exclude symptoms of SLE in the present or past.

The SLE patients and the controls had anthropometric measurements taken to assess for obesity as per WHO guidelines. Blood pressure readings were taken and hospital records assessed to determine those who were hypertensive. The patients and controls also had fasting blood sugar and fasting lipid profile assays done. Bilateral carotid ultrasonography was subsequently performed on the SLE patients by a team of consultant radiologists to evaluate for the presence of carotid plaque and for Carotid Intima-Media Thickness (CIMT) measurement. Carotid plaque was defined as the presence of focal wall thickening that was at least 50% greater than that of the surrounding vessel wall or as a focal region with CIMT greater than 1.5millimeters that protruded into the lumen from the adjacent boundary. Mean maximum CIMT was derived using images from all the carotid artery segments bilaterally; including the common carotid artery, carotid bulb and the internal carotid artery. Carotid atherosclerosis definition was the presence of carotid plaque and/ or an abnormal CIMT reading (≥0.8mm).

Data collected was coded, entered and managed in a pre-designed Microsoft Access database. Data entry was done continuously during the research period and data cleaning performed at the end of entry. After the data was cleaned, it was exported to the SPSS version 17.0 software for analysis. Demographic and clinical characteristics of the patients were summarized into means, medians and proportions for continuous and categorical variables respectively. Prevalence findings for carotid atherosclerosis (abnormal CIMT and carotid plaque presence) and cardiovascular risk factors were analyzed and presented as proportions. Anthropometric measurements were classified as per the World Health Organization (WHO) guidelines and analyzed with prevalence findings for obesity presented as proportions. Prevalence of cardiovascular risk factors in the SLE patients and controls were compared using the chi-square or Fischer's exact tests where appropriate. Comparison of anthropometric measurements between the two groups was done using the Student's t-test. Odds ratios were calculated to estimate the risk among SLE patients as compared to controls. All statistical tests were performed at a 5% level of significance.

Results

Between January and September 2013, a total of 66 SLE patients and 66 healthy controls were recruited into the study. Sixty three (95.5%) SLE patients and a similar number of controls were female; with a female to male ratio of 21:1. Mean age of the patients was 35.9 years (±10.9SD) and 35.7 years (±10.2SD) for the controls. Fifty percent of the patients and a similar proportion of controls were married. Median duration of illness for SLE patients was 2 years and the mean age at diagnosis 33.1 years. Only one of the SLE patients had confirmed secondary antiphospholipid antibody syndrome. A total of 58 of the 66 patients (87.9%), took steroids regularly as part of their treatment. Of these most (55.2%) were on a prednisone dosage of 10–20 milligrams per day. Nearly half of the patients (31 of the 66), were on treatment with either methotrexate, azathioprine, mycophenolate mofetil or a combination of the immunosuppressants. Only one patient was on a statin and another four were on anti-platelet agents (aspirin or clopidogrel).

Carotid atherosclerosis occurred in 19 (28.8%) of the 66 lupus patients. Nine patients (13.6%) had abnormal CIMT and carotid plaque(s) was found in 15 (22.7%) patients.

Twenty eight patients (42.4%) with lupus had hypertension compared with 16 (24.2%) controls and the difference was statistically significant {O.R. 2.3, CI: (1.1-4.9), p-value = 0.027}. Dyslipidemia occurred in 49 (74.2%) SLE patients and 41(62.1%) of the controls (p-value = 0.135). Twenty two patients (33.3%) and 23 (34.8%) controls had elevated total cholesterol levels (p-value=0.078); hypertriglyceridemia occurred in 36.4% of patients and 27.3% of controls (p-value= 0.350); risk indicator levels of HDL were found in 50% of patients and 34.8% of controls (p-value=0.078) while elevated LDL levels occurred in 30.3% of both patients and controls. Three patients and one control had diabetes. There was no statistically significant difference in the occurrence of obesity in lupus patients compared to controls. Among the SLE patients, 12.1% had obesity as per the WHO BMI classification compared with 21.2% of controls. Twelve (18.2%) of SLE patients were underweight (i.e. with BMI<18.5) compared to only two controls and this was significant; p-value = 0.010. Abdominal obesity as assessed by the waist to hip ratio was more frequent among the patients (33.3%) than the controls (24.2%) but this difference was not significant (p-value = 0.249) (Table 1).

A total of six SLE patients (9.1%) had already had a cardiovascular event(s) in the past; one patient had both stroke and myocardial infarction in the previous 2 years, another patient had stroke only, and four patients had experienced angina.

Table 1: Cardiovascular risk factors in SLE patients and healthy controls

Variable	SLE patients (n=66) No. (%)	Controls (n=66) No. (%)	OR (95% CI)	P-value
Hypertension	28 (42.4)	16 (24.2)	2.3 (1.1 - 4.9)	0.027
Dyslipidemia	49 (74.2)	41 (62.1)	1.8 (0.8 – 3.7)	0.135
Diabetes	3 (4.5)	1 (1.5)	3.1 (0.3 – 30.6)	0.619
Obesity by BMI BMI ≥ 30	8 (12.1)	14 (21.2)	0.6 (0.2 – 1.7)	0.330
Obesity by W:H ratio Females ≥ 0.85 Males ≥ 0.90	22 (33.3)	16 (24.2)	1.6 (0.7 – 33)	0.249
Obesity by waist circumference Females >80cm Males >94cm	22 (33.3)	27 (40.9)	0.7 (0.4 – 1.5)	0.368

Table 2: Carotid intima media thickness and carotid plaque in SLE patients

Variable	Frequency / Value
Mean CIMT(millimeters)	
Mean (SD)	0.63 (0.15)
Min - Max	0.35 -1.06
CIMT Status	
Normal (<0.8mm)	57 (86.4%)
Abnormal (≥ 0.8mm)	9 (13.6%)
Presence of carotid plaque	
Present	15 (22.7%)
Absent	51 (77.3%)

Three male SLE patients were on follow-up at the rheumatology clinic at the time of the study. None of these men (mean age of 34 years) were hypertensive, diabetic or obese. Two of the three had dyslipidemia, one had an abnormal CIMT (≥0.8mm) and another had carotid plaque (Table 2).

Lupus patients with carotid atherosclerosis and obesity had significantly longer duration of illness compared to those without these findings (p-values = 0.040 and 0.021 respectively). Analysis to assess for correlation between carotid atherosclerosis and the use of corticosteroids or other immunosuppressants and the traditional cardiovascular risk factors did not yield any significant findings. Similarly there was no statistically significant correlation between the presence of traditional cardiovascular risk factors and regular use of steroids or other immunosuppressants.

Discussion

This study population consisted predominantly of young females in the reproductive age group with a relatively short median duration of SLE (2 years since diagnosis). The mean age at diagnosis of lupus was 33.1 years with a female to male ratio of 21:1. Other studies within the African continent have had similar findings such as a mean age at diagnosis of 33 years and female to male ratio of 21:1 in Nigeria[4] and mean age of 33 years at diagnosis in a South African study with a female to male ratio of 18:1[5].

The prevalence of hypertension in this study was 42.4% amongst the lupus patients and 24.2% in the controls with the difference being of statistical significance (p=0.027). Vascular stiffness has been associated with the inflammatory process in SLE and is thought to contribute to the higher rates of hypertension in lupus patients than the general population[18]. Other factors that have been associated with hypertension in these patients include lupus nephropathy and steroid intake[19, 20]. This study neither assessed for level of inflammation nor evaluated for lupus nephropathy and thus such correlations could not be pursued. It is however notable that up to 87.9% (58 out of 66) of SLE patients used corticosteroids on a regular basis. Probably due to the fact that almost all the patients were on steroids no correlation was shown between regular intake of steroids and hypertension or other study variables. In the Toronto Risk Factor Study, hypertension occurred in 33% of the lupus patients compared with 13% in the controls[13] while 41% in the John Hopkins Lupus cohort were hypertensive[12].

Dyslipidemia occurred in about three quarters of SLE patients (74.2%) compared to 62.1% of the controls (p=0.135). A third of the lupus patients (33.3%) had hypercholesterolemia, 50% had low HDL levels, 30.3% had elevated LDL and 36.4% had hypertriglyceridemia. Only one patient was on a statin, indicating that dyslipidemia in this group was largely untreated. These findings were similar to those in a study that evaluated the proportions of dyslipidemia in SLE patients in Indonesia[21]. In that study, dyslipidemia prevalence was 75% with hypercholesterolemia in 43%, low HDL in 26%, elevated LDL in 26.4% and raised triglycerides in 44.2%. Of note, all the patients in that study were on corticosteroids and lupus duration less than three years correlated with dyslipidemia prevalence. No association between steroid use and dyslipidemia was demonstrated in our SLE patients, majority of whom used the corticosteroids regularly. It was also observed that a big proportion (62.1%) of controls who were staff or students at the Kenyatta National Hospital had dyslipidemia. An earlier study by Kirui *et al*[22] that assessed the prevalence of cardiovascular risk factors in rheumatoid arthritis patients and healthy staff at our institution as controls found 73.8% of the control population to have dyslipidemia. This raises concern that this population probably has some undescribed characteristics that may put them at risk of dyslipidemia and thus cardiovascular disease.

Diabetes was not a frequent finding in the study population. Three (4.5%) of the lupus patients and one control were diabetic. All the three patients had recently been hospitalized and were on high doses of prednisone, above 20 milligrams per day which may have contributed to their hyperglycemic states. Other studies have found similar proportions of diabetics among lupus patients. In the Toronto Lupus cohort, 5% were diabetic[13] comparable to 7% in the John Hopkins lupus cohort[12].

Obesity defined as BMI ≥ 30, occurred in eight (12.1%) of our patients and 14 (21.2%) of the controls and correlated with longer disease duration in the SLE patients. Abdominal obesity which has been strongly associated with cardiovascular disease[11], occurred almost similarly in the lupus patients (33.3%) and controls (24.2%). About a fifth (18.2%) of the lupus patients were actually underweight (BMI <18.5) compared to only 3% of controls (p=0.011) which may point to active disease rather than stable chronic disease in that proportion of our patients. The association between obesity and longer disease duration may be attributable to longer exposure to steroids and possible reduction in physical activity that may occur in these patients especially those with musculoskeletal involvement. In the John Hopkin's lupus cohort, 38% of patients were obese and 70% had a sedentary lifestyle while 15.6% in the Toronto Risk Factor study had abdominal obesity[12,13]. Variation in obesity prevalence in these studies is partly due to use of different cut-offs to define obesity.

Prevalence of carotid atherosclerosis in this study was 28.8%. Carotid plaque(s) occurred in 22.7% of the patients and abnormal CIMT in 13.6% of the lupus patients. In a study that assessed for the prevalence and correlates of accelerated atherosclerosis in SLE patients in New York, Roman *et al*[23] found a higher prevalence of carotid plaque, occurring in 37.1% of the patients whose mean age was 44 years with a mean duration of illness of 10.75 years. Another study in British women with SLE that sought to evaluate the health-related quality of life, smoking and atherosclerosis found carotid plaque in 26%

of the patients and abnormal CIMT (cut-off >0.51mm as per studies in their general population) in 35% of the patients whose mean age was 47.6 years and mean duration of illness 11.4 years[24]. Our study population therefore had lower rates of carotid plaque and abnormal CIMT than those in the aforementioned studies and this was probably a consequence of our lupus patients being younger and having had the disease for shorter duration than those in the other two studies.

Carotid atherosclerosis was associated with a longer duration of illness, a finding that was also observed in the study by Roman *et al*[23] and in a more recent study that assessed the progression of carotid atherosclerosis in SLE patients[25]. Whereas longer disease duration also results in advancing of age which is known to be associated with progression of atherosclerosis in the general population, the above two studies found longer disease duration independently correlated with carotid atherosclerosis.

A total of six patients (9.1%) in this study already had a cardiovascular event; one patient had both stroke and myocardial infarction in the previous two years, one patient had stroke only and another four patients had experienced angina. These findings in a population with a relatively short duration of SLE affirm the need to pay attention to cardiovascular risk in our patients.

Conclusion

Patients with SLE had a high prevalence of atherosclerosis. Hypertension was more common in these patients than the controls. Both the lupus patients and the controls had high prevalence of dyslipidemia. There was no significant difference in the occurrence of diabetes, dyslipidemia and obesity in the SLE patients and controls.

Study limitations

Due to financial constraints, comparison of atherosclerosis in SLE patients and controls was not done. It is acknowledged that doing so would have given more information on cardiovascular risk in patients with lupus. Furthermore, disease activity and damage scores were not established for the patients thus assessment for correlation of atherosclerosis and traditional cardiovascular risk factors to these parameters could not be done. We also did not evaluate for the presence of lupus nephropathy in the patients.

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Musculoskeletal disorders in the elderly in rheumatology practice in Burkina Faso

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Abstract

Objective: To study the frequency of musculoskeletal (MSK) disorders in the elderly in Ouagadougou, Burkina Faso.
Patients and methods: A retrospective study was conducted from February 2006 to March 2011 in the University Hospital Yalgado Ouédraogo in Burkina Faso. All patients aged over 65 years seen at the Department of Rheumatology were included.
Results: Four hundred and twenty-four patients (11.85%) aged over 65 years were identified among the total of 4084. The mean age was 70.15± 23.26 years with a range of 65-95 (mode: 70 years, median 69 years). There were 336 (69.4%) women and 148 men (30.6%). Rheumatic diseases were dominated by osteoarthritis(OA) and degenerative disease: low back pain / sciatica: 117 (24.17%) cases, OA of the knee: 111 (22.93%), tendinitis of the shoulder: 52 (10.74%), several OA (6%). Polymyalgia rheumatica was diagnosed in 15 (3%) patients. Only two cases of Rheumatoid Arthritis (RA) and one case of ankylosing spondylitis were noted. Osteoporosis was reported in three patients. Fifty-five (11.36%) had diabetes mellitus (type 2), 221 (45.66%) had hypertension and 15 (3%) heart disease.
Conclusion: The elderly have an important place in rheumatology practice in Ouagadougou. Osteoarthritis and degenerative MSK disorders are common and osteoporosis, chondrocalcinosis and RA rare. Polymyalgia rheumatica was the most common inflammatory disorder. Comorbidities were dominated by hypertension and diabetes mellitus.

Keywords: Musculoskeletal diseases, Elderly, Osteoarthritis, Low back pain

Introduction

In the next forty years, the population of people aged over 60 years is expected to triple worldwide including Africa[1]. The increase will inevitably come with its burden of musculoskeletal (MSK) disorders. Rheumatic diseases of the elderly are well documented in developed countries and include brachialgia (29%), osteoarthritis and osteoporosis (17%), rheumatoid arthritis (8%), ankles/ foot pain (8%), knee pain (6%), hip pain (5%), shoulder pain (5%), hand/wrist pain (3%) and elbow pain (3%)[2]. Women typically report problems more than men, regardless of the MSK condition[2]. Few studies have addressed this issue in sub Sahara Africa. However, it has been projected that the aging of the population will be the largest and fastest in this part of the world[1]. The aim of this work was to study the frequency and characteristics of MSK disorders in the elderly in the setting of rheumatology practice in a sub-Saharan country.

Materials and Methods

This was a retrospective study of case record files conducted from February 2006 to March 2011 in rheumatology consultation (Internal Medicine Department) at the University Hospital Yalgado Ouedraogo in Ouagadougou, capital city of Burkina Faso. Ouagadougou is the only city in the country that has a specialized rheumatology service. In 2006 the general population of Burkina Faso was estimated to be 14,017,262 including 473, 611 people aged 65 years or above; 53.2% of whom were women and 46.8% men[3]. The "elderly", met the definition given by the World Health Organization (WHO) ie 65 years and above.

All (inpatients and outpatients) aged over 65 years seen at the Internal Medicine Department for rheumatologic disease during the study period were included. Case records were retrieved and the following data extracted: age, gender, disease duration before the consultation, medical history, and MSK diagnosis. The diagnosis of mechanical and degenerative diseases was clinico-radiological. The diagnosis of inflammatory and infectious diseases was clinico-biological and radiological. Rheumatoid Arthritis (RA), ankylosing spondylitis and polymyalgia rheumatic fulfilled the appropriate diagnostic criteria[4-6].

Blood count, erythrocyte sedimentation rate, C reactive protein, serum transaminases, and creatinine were measured in all patients and rheumatoid factor, anti-citrullinated peptide antibodies, antinuclear antibodies including, DNA and Extractable Nuclear Antigen (SSa, SSb, Sm, RNP, Scl70, centromer, Jo1) antibodies in cases of suspected RA or–connective tissue disease. Radiographs of affected joints were performed in all patients and bone densitometry in ten. Joint aspirates were subjected to cytobacteriological examination and a search for microcrystals using polarized microscopy.

Results

There were 484 patients (11.85%) aged 65 years and over among 4084 patients seen in the clinic; 148 were men (30.6%) and 336 women (69.4%) (M/F 0.4). The mean age was 70.1 ± 4.8 years. Figure 1 shows the distribution of patients by age and sex. The average disease duration was 376.45 weeks (7.8 years) with range of 1 to 2600 weeks and a median of 48 weeks.

The diagnostic categories are shown in Table1. Mechanical and degenerative disease ranked first in rheumatic diseases, found in 401 patients (82.8%). Spinal tuberculosis (Pott's disease) was diagnosed in four patients. Polymyalgia rheumatica (27 cases, 5.54%) was the main inflammatory arthritis; the average age of patients was 70 years; it was seen in only women. No clinical evidence of giant cell arteritis was found. Only two cases of Rheumatoid Arthritis (RA) and one of ankylosing spondylitis were noted.

The metabolic pathology was dominated by gout (6 cases) and chondrocalcinosis (4 cases). Two cases of multiple myeloma and one of bone metastasis constituted malignancy disease; the average age was 67.0 ± 2.8 years for multiple myeloma and 73 years for bone metastases. Table 2 shows the distribution of patients with a diagnosis of OA and tendinitis. Other diagnoses included 12 cases of diffuse pain, 4 cases of algodystrophy, 13 females with non specific arthralgia and 3 cases of osteoporosis. Three hundred and eighty-seven patients (79.9%) had co-morbidities (Table 3).

Figure 1: Distribution of patients by age and gender

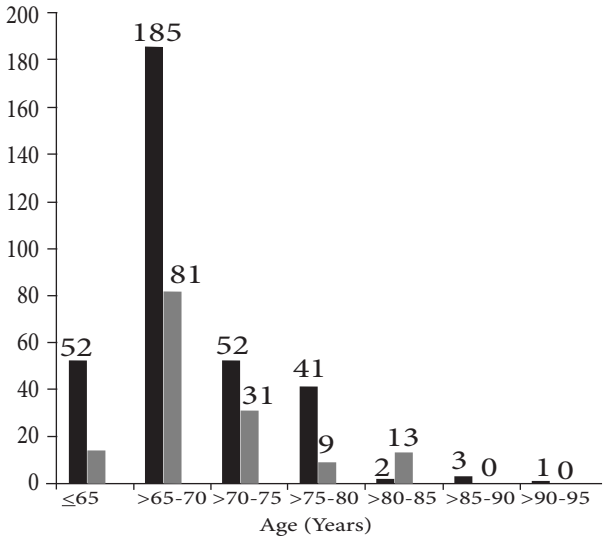

Table 1 : Distribution of patients according to the different disorders

	No.	(%)	Average age	Standard deviation	Sex-ratio M/F
Mechanical and degenerative pathologies	401	82.8	69.9	3.9	0.8
Infectious diseases	6	1.2	69	4.1	0.2
Chronic inflammatory arthritis	30	6.2	69.4	2.1	0.03
Metabolic diseases	10	2	67.8	3.9	2.3
Malignancies	3	0.6	69	1.4	0.5
Soft tissue rheumatism	19	3.9	70.8	4.1	0.05
Unclassified arthropathies	13	2.6	65	0	0/13
Total	484	100	70.1	4.8	0.44

Table 2: Distribution of patients according to OA and tendinitis

	No·	(%)	Average age	Standard deviation	Sex-ratio (M/F)
Neck pain	15	3.1	71	5.4	0.1
Cervico-brachial neuralgia	4	0.8	66	1.1	3
Cervical spinal stenosis	6	1.2	73.5	5.5	5
Back pain	15	3.1	79.7	4.7	15/0
Low back pain	83	17.1	71.3	4.7	0.5
Sciatica	34	7	67.9	3	0.9
Lumbar spinal stenosis	20	4.1	68.5	1.5	0/20
Forestier's disease	2	0.4	75	1.4	1
Shoulder OA	4	0.8	69.5	5.7	3
Fingers OA	2	0.4	70	7.1	1
Hip OA	8	1.7	71.4	5	0.6
Knee OA	111	22.9	70.3	4.6	0.4
Several OA	29	6	73.8	3.6	0.2
Shoulder tendinitis	50	10.3	67.6	3.3	0.1
Tunnel syndrome carpal	15	3.1	68.7	4.8	0/12
Bursitis/Ténosynovitis	3	0.6	67	1.4	1

Table 3: Frequency of patients according to comorbidities

	No.	(%)
High Blood Pressure	221	56.8
Heart disease	15	3.8
Arrhythmia atrial fibrillation	1	0.2
Angina	11	2.8
Arrhythmia	1	0.2
Myocardial infarction	1	0.2
Heart failure	1	0.2
Gastroduodenal ulcer	34	8.7
Epigastralgia	25	6.4
Kidney failure	1	0.2
Gout	7	1.8
Diabetes mellitus	69	17.7
Sickle cell disease	13	3.3
Tumours	1	0.2
HIV*	1	0.2
Total	387	100

*HIV : Human Immunodeficiency virus

Discussion

MSK disorders in our elderly patients accounted for 11.85% of 4084 rheumatology patients, proportions similar to a study from the Ivory Coast, which recorded 12.83% (over 60 years) of 2294 rheumatology patients[7].

Mechanical and degenerative disease accounted for over three quarters of the MSKs in our study. The full range of spinal disorders was encountered and low back pain with and without sciatica dominated with a female majority. A female predominance was noted throughout this series. This finding could be related to a selection bias in terms of distribution (52% women) of the general population further modified by strong domestic and more labour intensive activity in women in our context[3]. In studies from the developed world the explanation for the predominance of females with MSK disorders is considered to be multifactorial including biological, psychosocial and obesity factors[2]. A recent Chinese study has shown a higher frequency of intervertebral space narrowing in older women compared to men ($p < 0.0001$)[9].

The functional consequences of low back pain were not assessed in our study however, low back pain significantly affects the quality of life of older people[10,11]. Osteoporosis is a common cause of back pain in the aged Caucasian[2]. However malignancy and not osteoporosis was the main cause of compression fracture of the dorsal vertebrae in this series, with only three cases of osteoporosis confirmed by bone densitometry. However the risk of osteoporosis and future fracture increases with age and therefore it is reasonable to predict a future increase in fracture prevalence related to osteoporosis in elderly black Africans.

Osteoarthritis seems, indeed, to be the main cause of pain in the elderly[8]. The knee (22.9%) was by far the commonest location of OA in our patients. Large variations in prevalence are found in the literature according to the criteria used and gender: (54 to 74% in women over 60 years against 4 to 35% for men of the same age)[2]. As the knee is a weight bearing joint, degenerative disorders cause varying degrees of functional impairment which may be improved by the persistence of physical activity and an effective analgesic treatment regime[12].

Osteoarthritis of the hip appears to be rare in comparison with Caucasian series[2]; this low frequency

appears to be associated with the scarcity of primary hip osteoarthritis[13]. However, in a recent Togolese study, a high hospital frequency (46.1%) of primary hip OA was found[14]. Aging also affects tendon structures. Tendinitis was dominated by shoulder tendinitis; old age could be a factor but there is also diabetes mellitus found in 17.7% of the elderly in our series[15].

In addition to the mechanical and degenerative diseases, inflammatory rheumatism seems less frequent[2]. Polymyalgia rheumatica was the most common inflammatory arthritis encountered. This confirms that polymyalgia rheumatica is not so rare in the black African and is likely to increase as the population ages. An increased awareness is required to allow early diagnosis and treatment[16]. We did not detect clinical evidence of cranial arteritis in this series (cranial headache, temporal artery pain swelling, jaw claudication). However temporal artery biopsy and/or ultrasound of the temporal arteries might have increased the diagnostic yield among those with polymyalgia rheumatica[17]. Only two cases of RA were reported in our series[18]. Cardiovascular risks associated with inflammatory rheumatism and the low life expectancy of our general population (50 years) may explain the low incidence of RA in our series[3,19].

High Blood Pressure (HBP) was the most common co-morbidity reported in half of the patients. The well established increased risk of cardiovascular disease with chronic inflammatory rheumatism especially Rheumatoid Arthritis (RA) may also extend to osteoarthritis[19]. In the elderly the use Non Steroidal-Anti- inflammatory Drugs (NSAIDs) carries a significantly increased risk of hypertensive crisis and stroke, precipitating cardiac failure and bleeding from gastric erosions and peptic ulcers[20,21].

Conclusion

The elderly contribute to a significant and increasing workload in rheumatology practice in Ouagadougou. Osteoarthritis and age related degenerative MSK disorders predominate. Polymyalgia rheumatic was the most common inflammatory disorder. Osteoporosis, chondrocalcinosis and RA were rare. Comorbidities were dominated by high blood pressure and diabetes mellitus.

Acknowledgments

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Disclosures : None

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Research Article

Occurrence of crystal arthropathy in patients presenting with synovitis in Nairobi

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Abstract

Background: Crystal arthropathies represent a heterogeneous group of skeletal (musculo-skeletal) diseases associated with the deposition of mineralized material within joints and periarticular soft tissues. Gout is the most common and pathogenetically best understood crystal arthropathy, followed by basic calcium phosphate and calcium pyrophosphate dihydrate deposition diseases, and, in very rare cases, calcium oxalate crystal arthropathy. In Kenya there are no studies to demonstrate the prevalence of these diseases. This study endeavored to describe the different types of crystals seen in patients with synovitis in Nairobi from 1st January 2012 to 31st January 2014.

Objective: To describe different types of crystals seen in patients with synovitis in Nairobi.

Design: Descriptive prospective cross sectional study.

Results: There were 260 samples received from patients with synovitis. Of them, 61 (23.5%) were from males while 199 (76.5%) were from females. The age range of the patients was from 14 – 110 years. The mean, median and mode were 59.6, 60 and 55 years respectively. Majority of the patients were in the 51-60 years age category. Most of the patients recruited had no crystals (n=211; 81.2%) diagnosed, with 14.2%(n=37) having uric acid crystals and 4.6 % (n=12) having CPPD crystals. For the patients who had uric acid crystals (n=37), when gender was cross tabulated against microscopy, males (n=32; 86.5%) were noted to have more uric acid crystals than females (n=5; 13.5%). Among patients diagnosed with CPPD (n=12), there were more females (n=9; 75%) patients compared to males (n=3; 25%). From the total population recruited (n=260), when age range categories were cross tabulated against microscopy, the age ranges 41-50 (n=9; 3.5%) 51-60 (n=12; 4.6%), and 61-70 (n=6; 2.3%) were noted to have more uric acid crystals than any other age category recruited. Patients in the age category 61-70 (n=6; 50 %) had more CPPD crystal detections than any other age category from the patients recruited.

Conclusion: Crystal arthropathy is a major cause of synovitis in patients seen in Nairobi.

Introduction

Synovial fluid analysis may be diagnostic in patients with bacterial infections or crystal-induced synovitis. The white cell count, differential count, cultures, Gram stain, and crystal search using polarized light microscopy are the most valuable studies[1,2]. Noninflammatory fluids generally have fewer than 2000 white blood cells/mm^3, with fewer than 75% percent polymorphonuclear leukocytes[2].

Synovial fluid aspiration and analysis is the gold standard for diagnosis of crystal arthropathies. The objective of this study was to describe the occurrence of crystal arthropathy, using polarizing microscopy technique, among patients presenting with synovitis in Nairobi and to characterize the different types of crystals seen.

Materials and Methods

This was a prospective study of consecutive patients presenting with joint effusion in Nairobi. The patients were seen between 1st January 2012 and 31st January 2014. The aim of this study was to describe different types of crystals seen in patients with synovitis in Nairobi, with the following specific objectives: to characterize the demographic profile of the patients, to describe the types of crystals found in the synovial fluids and to determine the association between the age and gender and the types of crystals found.

Informed consent was obtained from the patients for athrocentesis and their sociodemographic characteristics obtained. The affected joints were then cleaned with alcohol swabs and the overlying skin anaesthetized using 1% lignocaine. A needle was then inserted and about 2ml of synovial fluid aspirated and fluid collected in a sterile bottle. The samples were then sent to the laboratory for analysis. The samples were prepared and examined for crystals using polarizing microscope and a first order red plate inserted between the polarizer and analyzer. This turns the background red. The crystals seen were described by their characteristic shape and sign of birefringence on microscopy.

Results

During the 24 month study period, a total of 260 patients with joint effusion were

enrolled into the study with their synovial fluid collected and analyzed for crystals. The gender distribution was; 61 (23.5%) males while 199 (76.5%) were females.

The age distribution of the patients is depicted in Figure 1. The age range of the patients was from 14 – 110 years. The mean, median and mode were 59.6, 60 and 55 years respectively. Majority of the patients were in the 51-60 years age category.

Out of the total 260 patients sampled, no crystals were seen in 211 (81.2%) synovial fluid samples. Uric acid crystals were seen in 37 (14.2%) and CPPD crystals in 12 (4.6%) of the samples analyzed.

From the total population recruited (n=260), when gender was cross tabulated against microscopy, males (n=32; 12.3%) were noted to have more uric acid crystals than females (n=5; 1.9%). For the patients with CPPD (n=12), there were more females (n=9; 75%) compared to males (n=3; 25%).

As depicted in Table 1, the males had significantly higher risk (RR 8.16) occurrence of any type of crystal arthropathy. The males also had a significantly higher risk (OR 45.54) of uric acid crystal arthropathy. There was however no significant gender difference in the patients with CPPD crystal arthropathy.

From the total population recruited (n=260), when age range categories were cross tabulated against microscopy (Table 2), the age ranges 51-60 (n=12; 4.6%), 41-50 (n=9; 3.5%) and 61-70 (n=6; 2.3%) were noted to have more uric acid crystals than any other age category recruited. Occurrence of CPPD crystal arthropathy was seen among the elderly (over 83% of the cases seen in patients aged above 61 years).

Figure 1: Distribution of patient age ranges

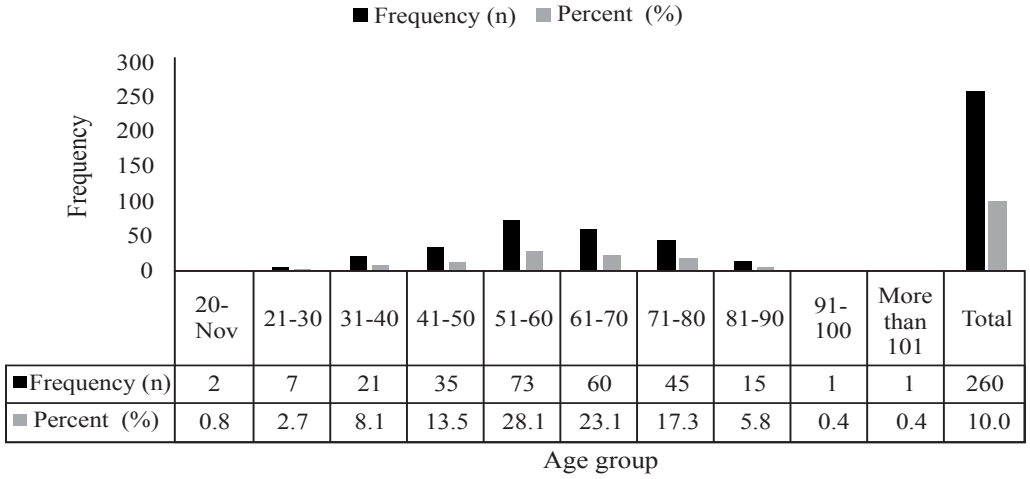

Table 1: Univariate analyses of gender vs. occurrence of crystal arthropathy

	Crystal arthropathy	No crystal arthropathy	Relative Risk	P value
Male	35	26	8.16	0.000001
Female	14	185		
	Mono sodium urate crystal	No crystal	Odds Ratio	P value
Male	32	26	45.54	0.000001
Female	5	185		
	CPPD crystal	No crystal	OR	P value
Male	3	26	2.37	0.204
Female	9	185		

Table 2: Age range categories versus microscopy cross tabulation

		Microscopy			Total
		Uric acid crystals	CPPD Crystals	No crystals seen	
Age categories	11-20	0	0	2	2
	21-30	1	0	6	7
	31-40	4	0	17	21
	41-50	9	1	25	35
	51-60	12	1	60	73
	61-70	6	6	48	60
	71-80	4	1	40	45
	81-90	1	2	12	15
	91-100	0	1	0	1
	More than 101	0	0	1	1
Total		37	12	211	260

Discussion

The understanding of the burden of crystal arthropathy in our setting remains limited. Moreover the diagnostic ability to diagnose crystal arthropathy is quite limited with only one functional polarizing microscope in the country. Thus the burden of this group of diseases is poorly understood. This study, set in Nairobi thus set to establish burden of crystal arthropathy in patients presenting with synovitis. Of all the samples taken for analysis, 49(18.2%) had crystals identified by polarizing microscopy.Those with Mono Sodium Urate (MSU) crystals were 37(75.5%) with Calcium Pyrophosphate Dehydrate (CPPD) crystals accounting for 12(24.5%).

There are no published population surveys on the burden of crystal arthropathies. There is also no published study that has looked at the prevalence of crystal arthropathy amongst patients presenting with synovitis. However there have been several case series reports on the occurrence of gout in Africa. Lowenthal *et al*[3] reported only 2(1.4%) patients with gout out of a total of 138 rheumatology cases seen in 1982 at a University Teaching Hospital. There has been doubling of gout prevalence in the last 2 decades in the United States[4], and the clinical complexity of gout has increased over this same period. Underlying these developments is a perfect storm of convergent factors that have changed the landscape of gout patients and how we treat them. Petersel *et al*[5], observed that in hospitalized patients with acute gout, significant renal impairment was present in approximately 65% of subjects. The increase in population longevity and the high prevalence of chronic kidney disease in the aged are of particular concern because renal insufficiency renders the management of both gouty inflammation and hyperuricemia more difficult.

In this evaluation, male gender was significantly associated with crystal arthropathy of any type (RR 8.16, p 0.000001). Occurrence of MSU crystal was significantly higher in the male gender (OR 45.2, p 0.000001) whereas there was no significant difference between the males and females in the occurrence of CPPD crystals (OR 2.37, p 0.204). This observation is consistent with many studies[4] that have shown the male to female ratio of gout to be up to 20:1, with the disease being rare in premenopausal women. The gender distribution of CPPD crystal deposition disease has differed among large series [6-9], but no major sex predominance appears likely.

A total of 12 patients were found to have CPPD crystals with most of them (10 patients) occurring in patients above 60 years of age. Rosenthal *et al*[7] reported more than 80% of cases of CPPD in patients aged above 60 years with an average age of occurrence of 72 years. Although this was an urban based evaluation, it can be deduced that crystal arthropathy is a major cause of arthritis in patients presenting with synovitis. A larger study will be needed to generalize these findings to the general population.

Conclusion

Crystal arthropathy is a major cause of arthritis in patients presenting with synovitis in Nairobi, with monosodium urate crystals accounting for most of the crystals seen.

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Spontaneous resolution of a case of anti-retroviral treatment-naïve HIV-associated polymyositis

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Abstract

Autoimmune Rheumatic Diseases (ARD) have been described in individuals with Human Immunodeficiency Virus (HIV) infection. However, the incidence of ARD in individuals with HIV has evolved since the introduction of Highly Active Anti Retroviral Therapy (HAART) for the treatment of HIV. Clinicians face a therapeutic dilemma regarding the use of potent immunosuppressants when managing ARD in individuals with HIV infection. The disease activity of ARD varies during the natural course of HIV infection and its treatment with HAART. The outcomes of some ARDs may be better in individuals with HIV when compared with individuals without HIV. Here we report the first case of spontaneous resolution of HIV-Associated Polymyositis (HAM) presenting with profound proximal muscle weakness occurring in a treatment-naïve patient with HIV and discuss the possible treatment options of HAM based on evidence from the literature.

Keywords: HIV, Polymyositis, HIV-associated myositis, HAART, Highly Active Antiretroviral Treatment and anti-retroviral drugs

Introduction

Autoimmune polymyositis is a chronic condition that affects muscles and vital organs such as lungs and heart. However, polymyositis may be caused by infections with bacteria or viruses. Polymyositis (PM) may resolve with successful treatment of bacterial infection whereas the course of PM in the context of viral infections such as Human Immunodeficiency Virus (HIV) is usually chronic, probably because the virus persists in the host. The course of PM in an individual may undulate consequent to a continual change in the host's immune system toward containing the HIV. Therefore, a better understanding of the dynamics of the host's immune system in the course of HIV infection would be of clinical relevance to guide the use of immunosuppression to control PM. To this end, we present a case of spontaneous resolution of a case of HIV-associated anti-retroviral treatment naïve PM. We show that with careful monitoring during an initial presentation allowed us to cautiously withhold immunosuppression and introduce anti-retroviral treatment. We discuss the pathways of Immunopathogenesis of HIV-associated PM and highlight that immunosuppression may be withheld for HIV-associated PM.

Case Report

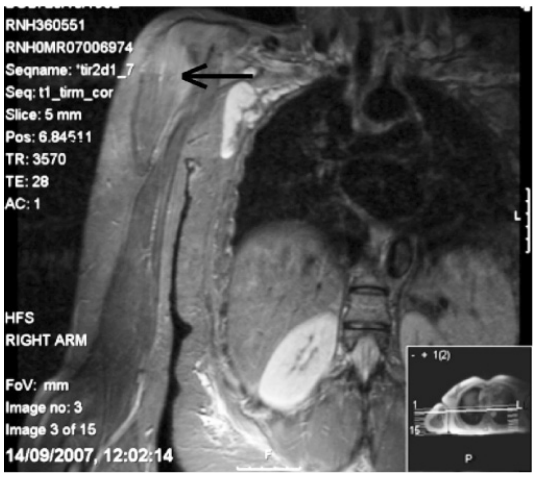
A 44-year-old Nigerian lady presented with an acute history of generalised weakness, painful legs and joint pains. She found it difficult to manage routine daily activities due to severe weakness of arms and legs. She could no longer carry on working as a domestic cleaner. There was no preceding history of intercurrent illness. She had no respiratory, cardiovascular or gastrointestinal or any neurological symptoms. There was no history of smoking, alcohol or other drug abuse. Past medical history included hypertension and uterine fibroids. Five months prior to her presentation she was diagnosed with HIV-I infection (asymptomatic). Her CD4 count was greater than 280 (reference range 500-1600) cells/mm^3 and CD8 count was 1280 (reference range 375-1100) cells/mm^3. She had not needed any antiretroviral treatment. There was no family history of autoimmune diseases. On examination, she looked generally unwell. She was afebrile and had non-tender cervical, axillary and inguinal lymphadenopathy. There was no evidence of any rash, parotid enlargement, mouth ulcers or hair loss. There was no joint swelling or tenderness. There was erythema and oedema of both upper and lower limbs. The proximal muscles of upper and lower limbs were also tender and weak with their power limited to 3/5. Sensation, muscle tone and reflexes were normal. Respiratory and cardiovascular examination was unremarkable.

Initial blood tests revealed a Creatinine Kinase (CK) level of >90,000

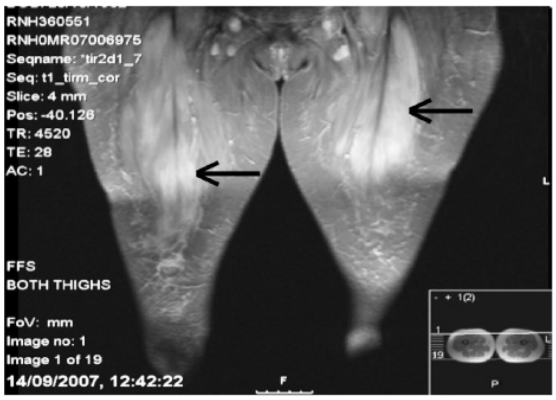
IU/L. Erythrocyte sedimentation rate was 44 mm/hour and C reactive protein was 22g/L (normal <5). Full blood count, urea, electrolytes, thyroid function tests, chest X-ray, electrocardiogram, spirometry and echocardiography were normal. Antinuclear antibody, extractable nuclear antibody and anti Jo-1 antibody were negative. Hepatitis serology was negative. Urine dipstick analysis was normal. Electromyography revealed subtle evidence of myopathy but no evidence of neuropathy. MRI findings revealed widespread patchy hyperintense lesions affecting the proximal muscles of both upper and lower limbs indicative of active PM (Figure 1).

Figure 1: Active proximal myositis detected by magnetic resonance imaging. T1 weighted image of the right upper limb showing patchy areas of hyperintense signal in the deltoid, supraspinatus (black arrow) (A). T1 weighted MRI of lower limbs showing patchy areas of hyperintense signal (black arrow) (B)

A



B



Whilst waiting for the results of the muscle biopsy, she received physiotherapy and her power gradually improved in both upper and lower limbs to 4/5. A MRI-guided targeted muscle biopsy was performed after 2 weeks. The histological features of which were diagnostic of autoimmune polymyositis. There was evidence of CD8+ T cell and macrophage infiltration surrounding the MHC-I- expressing muscle fibres, similar to that in seronegative myopathies. Clusters of CD3+ and CD8 +ve T lymphocytes were also seen in the endomysium and around blood vessels. Few CD20 +ve lymphocytes were also seen perivascularly. Further, there were regenerating muscle fibres and some atrophic fibres but no features to suggest drug induced or nemaline rod myopathy. No inclusion bodies were seen.

Highly Active Antiretroviral Treatment (HAART) with a combination of abacavir and limuvidine was initiated. Under close monitoring including 6-hourly spirometry, immunosuppressive therapy was judiciously withheld. Within three weeks of the onset of symptoms, she was able to carry on with her daily activities. On further review, at five weeks from the onset of symptoms, her power continued to improve and CK levels normalised, at 146 IU/L. She has continued to be asymptomatic on follow up at 72 months since the initial presentation.

Discussion

This case report illustrates that spontaneous remission can occur in HIV-Associated Myositis (HAM), even in individuals with profound weakness and HAART therapy may aid in sustaining remission.

ARD in an HIV-infected individual: The outcomes for individuals with HIV infection have remarkably improved, since the introduction of anti-retroviral drugs in 1987 and HAART in 1996[1]. However, HAART therapy is associated with the occurrence of IRIS and an increase in certain Autoimmune Rheumatic Diseases (ARD)[2]. Factors related to HIV such as the viral load and genotype, and the susceptibility of the infected individual to develop ARD such as HLA B27 positivity, determine the outcomes of HIV-associated ARD. For example, the estimated risk of developing Reiter's syndrome in HIV infected individuals is many fold (up to 140) higher than in seronegative population and the risk is linked with HLA B27 positivity[3]. This estimate was prior to the introduction of HAART and could be lower, since the introduction of HAART in 1996[4]. ARDs occurring in individuals with HIV and their relationship to HAART are summarised in Table 1.

Table 1: Common ARD associated with HIV and their relation to HAART

Condition	Comments	Relation to HAART	Reference
Polymyositis		Occurs de novo or exacerbates	(2)
Dermatomyositis		?	(48)
Reiter's syndrome	Up to 140 fold higher, HLA B27 linked susceptibility	Risk reduced	(3), (4)
Rheumatoid Arthritis		Tends to improve	
Spondyloarthropathy		Tends to improve	(2)
DILS	CD8+ T cell infiltration of tissues	Improves	(2)
Antiphospholipid syndrome/ antibodies	Positive antibodies high, however, clinical syndrome is rare		
Autoimmune thrombocytopenia	Up to 40% estimated	Improves with HAART	(49)
SLE	Extremely rare	Occurs de novo or exacerbates	(2)
TTP	Very rare	Tends to improve	(50)
Vasculitis		Occurs de novo	

HAM may be the presenting manifestation of HIV infection[5]. Rarely, the manifestations can be severe with life-threatening myocardial and oesophageal involvement[6]. Antisynthetase syndrome with positive anti-Jo 1 antibodies and pulmonary fibrosis has also been reported[7]. HAM has been reported to result in myoglobinuric renal failure[8], although myoglobinuria could occur even in the absence of muscle inflammation[9]. The creatine kinase levels in HAM could be normal[10] or modestly elevated (two fold increase above normal) and almost four fold lower than the CK levels in autoimmune polymyositis[11]. Although, radionuclide scan has been used as non-invasive diagnostic modality in the diagnosis of HAM[12], MRI-guided muscle biopsy demonstrating characteristic Immunohistochemical changes in the affected muscle remains the investigation of choice to diagnose HAM.

The effect of HAART on the prevalence and prognosis of HAM: Since the first report of PM in a patient with Acquired Immunodeficiency Syndrome (AIDS) in 1986[13], several independent groups have confirmed PM in HIV as a distinct condition, HIV-associated (HAM)[14-17]. The estimated prevalence of polymyositis in HIV varies from 2-7%[15,18]. Since the introduction of HAART, a study of 888 individuals from 1995 to 2006 estimated the overall prevalence of rheumatic manifestation in HIV infection is approximately 9%, only one patient in this cohort was diagnosed with polymyositis and there were no cases of seronegative spondyloarthritis or Sjogren's syndrome[4]. PM has been reported to occur during immune restoration with HAART therapy[19,20]. The prevalence of HAM was found to be higher in symptomatic individuals not previously treated with HAART[21]. As in the case of most ARDs, a higher prevalence was noted in women and younger individuals[11]. A possible explanation for the observed discrepancy in the estimated prevalence rate of HAM in various studies is the introduction of HAART for the treatment of HIV. Taken together, the difference in the estimated prevalence of HAM between studies undertaken prior to and following the introduction of HAART suggest that HAART treatment influences the development of clinically evident HAM. HAART therapy reduces the viral load and consequently, the disease activity of HAM. Further, asymptomatic individuals or those with milder symptoms may not seek specific medical attention and remain undiagnosed.

Immunopathogenesis

What factors regulate the outcome in HAM? HIV infection activates both cellular[22] and humoral immune response; the latter is indicated by the presence of hypergammaglobulinemia[23,24]. The net effect of these responses determines the timing and the severity of ARD. Both the viral load and its sensitivity to HAART therapy determine the outcome of HIV infection. It has been suggested that the natural course of HIV infection and its response to HAART could be represented as stages of the infection. For example, Zandman-Goddard *et al*.[25] suggest that the occurrence of ARD in HIV relates to the stage of infection and the viral load.

Defective classic apoptosis of T cells in the muscle: HIV has a predilection to infect CD4+ T cells inducing their activation and apoptosis[26]. Rawson *et al*[27] proposed that the dendritic cells phagocytose T cell apoptotic material and process it in their proteasome where caspases break down the proteins into peptides (self antigens), which are then coupled with MHC before presenting to the effector cells. This hypothesis is supported by the observed correlation between the T cell-apoptotic load and the number of autoreactive CD8+ T cells. With effective therapy using HAART, the apoptotic load is reduced

which results in decreased number of autoreactive CD8+ T cells. In contrast in HAM, there is differential lack of T cell apoptosis (predominantly CD8+ T cells) in the neuromuscular tissues when compared with lymph nodes[28]. The mechanisms that underlie this differential anti-apoptotic T cell survival are not clearly understood. However, there is some indirect evidence that suggests an increased expression of classic anti-apoptotic proteins and the up-regulation of the Fas/Fas ligand system in HIV[29].

Myocytes act as antigen presenting cells and sustain local inflammation: The striking histological similarities between HAM and PM suggest that HIV inflicts widespread muscle inflammation using the same immune effector pathway as PM. However, the precise mechanism by which this immune response is triggered remains undefined. Based on the histological findings demonstrating the presence of effector cells around the site of muscle damage, it has been suggested that HIV virus could infiltrate myocytes. The infected myocytes act as non-professional antigen presenting cells and recruit immune effector cells, which amplify the immune effector response at the site. Using *in situ* polymerase chain reaction-amplification Seidman *et al*[30] have detected the presence of HIV nucleic acids in the muscle fibres of individuals with HAM. However, another group found fewer CD4+ cells in muscle biopsies from 19 individuals with HAM when compared with five individuals with seronegative PM. Further, they detected the presence of HIV antigens (p24, gp 120 and gp41) in the interstitial mononuclear cells but not in the muscle fibres. There was no quantitative difference in B cells, natural killer cells, interleukin-2 receptor positive cells or macrophages[31]. Another study found evidence of HIV antigen (gp41) in muscle macrophages[32]. However, other groups have not been able to demonstrate the presence of HIV in myocytes using *in situ* hybridisation[16] and polymerase chain reaction[33]. Based on this, the authors concluded that it is not likely that HIV virus infects or replicates in myocytes. Similarly, in the case of PM in individuals with HTLV-I infection the histological features are indistinguishable from autoimmune PM[34], where it has not been possible to detect the HTLV-I in the affected myocytes[35] . Further, HIV infection and hepatitis C infection may coexist, and myositis in this context may present with atypical multinodular polymyositis[36]. Thus the data on direct infiltration of myocytes by HIV remains contentious. Alternatively, this conflicting evidence could be due to a limitation of the technique used for the detection of the virus and does not exclude a transient infection of myocytes.

Role of cytokines and toll-like receptors: Proinflammatory cytokines are thought to play a key role in sustaining a state of chronic inflammation in PM. Several cytokines have been implicated to play a functional role. Evidence from immunohistochemical study of damaged muscle fibres implicates a functional role for Tnf-alpha. Further, the expression of endothelial cell adhesion molecules (ICAM-1) and LFA-1 (the main counter-receptor for ICAM-1) on effector cells such as monocytes and lymphocytes is up-regulated[37]. In the presence of IFN-γ, the muscle fibers up regulate TLR-3, which renders the muscle fibers more receptive to stimulation by viral ds-RNA. Furthermore, there is up regulation of NKG2D-ligand on myoblasts, which attract counter-receptor bearing effector cells such as NK cells, cytotoxic CD8 T lymphocytes and macrophages[38]. Thus, direct infiltration is not essential to initiate the self-sustaining inflammatory.

Differential diagnosis: Individuals infected with HIV are susceptible to myositis from HIV, its treatment with anti-retroviral drugs, autoimmune, inflammatory and infective causes (Table 2).

Table 2: Muscle involvement in HIV

Differential diagnosis for myositis in HIV
Infective
Bacterial (*staphylococcus*)
Tuberculosis
Toxoplasmosis
Pyomyositis
Autoimmune
Polymyositis
Dermatomyositis
DILS
Miscellaneous
Drug induced myopathy
Non infective necrotising myopathy
HIV myopathy/ wasting disorder

Anti-retroviral drugs and HAM: Anti-retroviral drugs such as Zidovudine (AZT) affect the mitochondria resulting in myopathy[39]. It is difficult but important to distinguish ARV-induced myositis from HAM[40].

Non-autoimmune polymyositis associated with HIV: Diffuse Infiltrative Lymphocytosis *(DILS)* is a multisystem inflammatory condition occurring in individuals with HIV, characterised by persistent CD8 T lymphocyte infiltration of the involved organs. Polymyositis as a manifestation of DILS is a distinct entity, histological features may be very similar to autoimmune polymyositis, but can be differentiated on electron microscopy[41]. A study of 35 individuals with DILS from a cohort of 4,100 HIV-infected subjects found biopsy-proven evidence of polymyositis in four individuals[42].

Infections: Reduced number of T cells, common in HIV infection or from other causes, increases the host's susceptibility to opportunistic infections. Infections of the muscle or pyomyositis may mimic polymyositis. Toxoplasmosis is one such infection to be considered in the differential diagnosis[43]. *Staphylococcal polymyositis* may complicate HIV infection[44]. HIV infected individuals are susceptible to tuberculosis, which can cause tuberculous polymyositis[45]. Both MRI and CT scans can be used to diagnose range of muscle/soft tissue

involvement including polymyositis, pyomyositis and necrotising fasciitis associated with HIV[46].

Treatment: Available evidence appears to suggest that HAM usually runs a milder course[18]. Standard immunosuppressants used to treat PM have all been used for the treatment of HAM and appear to be effective[18]. HAM has also been effectively treated with intravenous immunoglobulins[47]. Our patient with HAM who presented with profound weakness the symptoms resolved spontaneously over a 3-4 week period. She has tolerated the introduction of HAART initiated at this time and remains asymptomatic at 36 months since diagnosis. In conclusion, HIV-associated myositis may resolve spontaneously and HAART may be used for sustaining remission.

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Adult onset polyarticular pigmented villonodular synovitis

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Abstract

Pigmented Villonodular Synovitis (PVNS), typically, presents as a chronic monoarthritis affecting medium to large joints or tendon sheaths. Polyarticular presentation of PVNS is extremely rare, mostly reported in children and has not yet been reported in adults. We report a case of polyarticular PVNS, presenting in adulthood. We made the diagnosis based on characteristic MRI findings and typical histopathological changes. Patient was successfully managed with synovectomies and was not subject to inappropriate DMARDs. We suggest, that PVNS should be considered in the differential diagnosis of seronegative polyarthropathy, to avoid a delay in diagnosis and consequent delay in appropriate treatment. To our knowledge, this is the first case report of PPVNS presenting in adulthood, and serves as an example of atypical presentation of a rare condition.

Introduction

Symmetrical polyarthritis in the absence of rheumatoid factor and/or anti-CCP (cyclic citrullinated peptide) antibody may be diagnosed as seronegative arthritis. Seronegative arthritis encompasses several differential diagnoses including seronegative rheumatoid arthritis and inflammatory arthritis secondary to infections such as tuberculosis, hepatitis and human immunodeficiency virus. In children, pigmented villo nodular synovitis has been reported to manifest as polyarthropathy. Therefore, early diagnosis is of high importance in the management of seronegative arthritis.

Here we present a case polyarticular PVNS presenting for the first time in adulthood. We discuss useful investigations in the setting and emphasise on typical radiographic findings. Finally, we show that unjudicious use of Disease Modifying Anti-Rheumatic Drugs (DMARDs) could be avoided by careful consideration of differential diagnosis. Further, we show that even polyarticular presentation is amenable to succesful surgical intervention. Thus our case highlights the importance of considering PVNS in the differential diagnosis of seronegative arthritis.

Case Report

A 38 year old Bangladeshi gentleman was referred to our rheumatology department, with a 6 week history of bilateral painful and swollen knees. He experienced early morning stiffness in his knees, lasting for up to an hour. He had been involved in a road traffic accident seven years earlier, but could not recollect any injury to his knees. Systems enquiry was normal. There was no history of Raynaud's phenomenon, mouth ulcers, hair loss, photosensitivity, dry eyes or dry mouth. There was no history of weight loss, fever or night sweats. He had no symptoms suggestive of tuberculosis and had no contact with patients suffering from tuberculosis. His past medical history was unremarkable. He was not taking any medications. He worked as a chef in a restaurant.

On examination he looked systemically well. There was no lymphadenopathy, edema, pallor or icterus. Respiratory, cardiovascular and abdominal examination was unremarkable. Musculoskeletal examination revealed prominent swelling of the right knee. This was associated with reduced range of movements. He had no features suggestive of systemic lupus erythematosus or connective tissue disease.

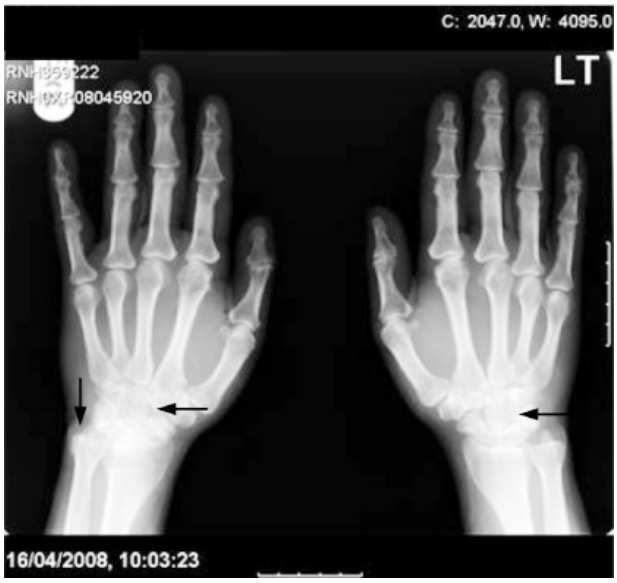
Full blood count, urea, electrolytes, liver function tests, erythrocyte sedimentation rate, c-reactive protein were normal. Rheumatoid factor and anti nuclear antibody were negative.

X-rays of the knees showed minor osteoarthritic changes. Analysis of his knee fluid aspirate, revealed a few pus cells, but no crystals. Cytology was negative. AFB was negative on both microscopy and cultures. MRI of his right knee demonstrated changes typical of PVNS (Figure 1). Arthroscopic examination of the right knee showed synovial thickening, moderate effusion, generalised extensive proliferative villous vascular synovium.

Medial menisectomy was performed. Biopsy findings were suggestive of pigmented villonodular synovitis. A year later, due to persistent pain, a total synovectomy was performed. Histology revealed changes of chronic synovitis.

A few months later, he presented with painful wrists. Both wrists were tender and movements were restricted. The left wrist showed advanced osteoarthritic changes with erosive changes of the proximal row of carpal bones.

Figure 1: X-ray images of hands demonstrate erosive changes (black arrow) of the carpal bones and radiocarpal and radioulnar joint

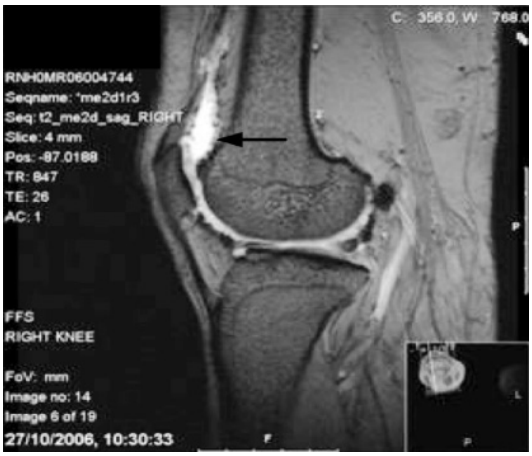


Two years later, he experienced severe pain, swelling and stiffness of right wrist. A total synovectomy was performed. Histological examination revealed diffuse chronic inflammatory cell infiltrate, rich in plasma cells, marked synovial hyperplasia with surface fibrin deposition. Collections of haemosiderin laden macrophages were present. Appearances were those of chronic synovitis with features suggestive of pigmented villonodular synovitis.

Seven years later, he experienced worsening pain in his right knee and left wrist. Magnetic resonance images of his right knee and left wrist showed changes consistent with pigmented villonodular synovitis in both knees and the left wrist.

Figure 2: Magnetic Resonance Images (MRI) of the right knee demonstrates an effusion with low signal areas (black arrow) due to haemosiderin (A). MRI of the left wrist demonstrates low signal areas (black arrow) due to haemosiderin and erosive changes.

A



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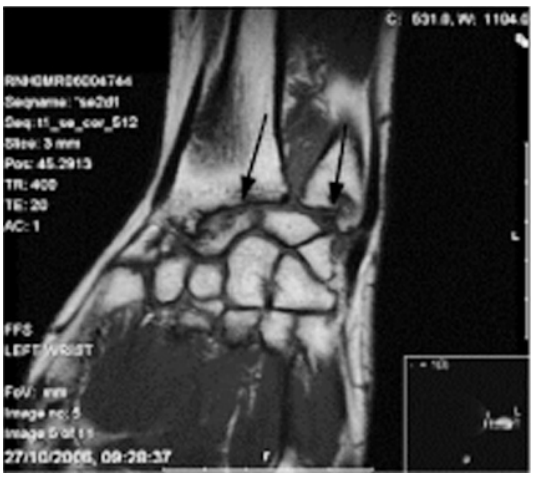

A year later, he was admitted with abdominal pain, when a diagnosis of pleural and peritoneal tuberculosis was made based on the clinical findings, pleural biopsy, computerised tomogram of chest and abdomen. Anti-tuberculous medication was started with good response.

In summary, our patient had chronic polyarticular PVNS, affecting multiple joints over a period of 7 to 8 years. On each occasion, a diagnosis was based on the characteristic radiographic (MRI) or histopathological features. Synovectomy proved to be effective, to treat both large and small joint disease. Immunosuppressive therapy was appropriately avoided.

Discussion

Pigmented Villonodular Synovitis (PVNS) is a benign proliferative disorder affecting synovial joints, bursae and tendon sheaths. Typically, it presents as a chronic monoarthritis of large joints, in the second to fifth decade, however, it has been described in paediatric as well as elderly patients. . A case of acute onset mono-arthritis has been described[1]. The annual incidence is estimated to be two cases per million population. There may be a long delay in presentation, particularly in children, as the joint pain is often mild and is disproportionate to the swelling[2]. Most commonly, it affects the knee (80%) and less frequently involves hips, ankles and shoulders. Multiple joint involvement has only been reported in younger patients and to our knowledge it has not yet been described in adults.

Aetiopathogenesis is poorly understood. A neoplastic aetiology has been suggested based on the findings of aneuploid DNA, chromosomal abnormality and malignant potential[3]. Reports of PVNS occuring in association with congenital anomalies raises a possible genetic link[4,5].

Diagnosis is made on the typical histopathological and radiographic (MRI) features. MRI findings of synovial proliferation, joint effusion and erosion of bone are common. Haemosiderin deposits in the synovial masses, appear as low signal areas, best seen on Fast Field Echo (FFE) sequence and are diagnostic of PVNS[6]. However, MRI may not differentiate PVNS from other causes of chronic hemorrhagic synovitis.

The prognosis is generally good, but may cause erosive arthritis. Localized lesions may be amenable to arthroscopic interventions, however, diffuse form may need total surgical synovectomy. Relapse is a frequent problem, and has been treated with either intrarticular radioactive Yttrium or anti-TNF agent, following athroscopic surgery[8,9] and Imatinib[10]. Anti-TNF therapy has been used to treat a case of PVNS, although it took few months to achieve disease control[11]. Therefore, surgical removal of the lesion appear to be associated with low risk of relapse whereas medical interventions including biological treatments appear to have variable benefit.

In conclusion, our case highlights, that atypical presentation of PVNS, needs to be considered in the differential diagnosis of a patient with seronegative arthropathy. We suggest that careful consideration of this rare condition may avoid unjudicious use of DMARDs and that even polyarticular PVNS is amenable to successful surgical intervention. The study shows that polyarticular pigmented villonodular synovitis may present as symmetrical seronegative arthropathy even in adults.

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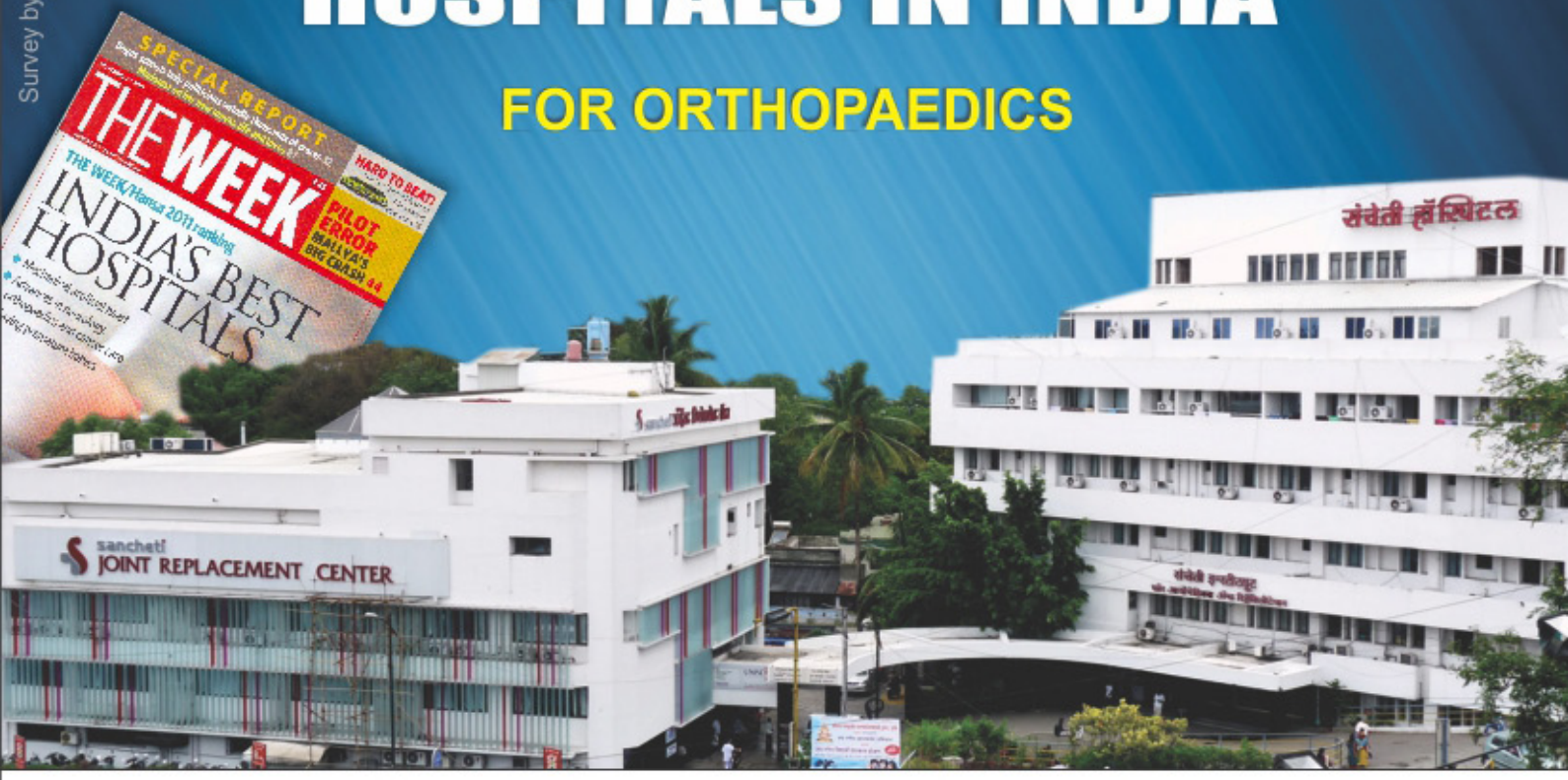

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