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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