Original article

Podoconiosis: an important but forgotten cause of non-filarial lymphoedema

ABSTRACT

Podoconiosis is a preventable, non-infectious and non-communicable cause of lymphoedema leading to chronic swelling of the foot and lower leg. Most prevalent in Africa, Central America and India, it is caused by long-term exposure to irritant red volcanic clay soil. Risk factors for disease are related to the absence or inadequacy of footwear. However, not all those at risk develop the disease, indicating that both genetic and environmental predispositions contribute to disease development.

Symptoms of podoconiosis include asymmetrical limb swelling with associated itching, burning sensation and lymphatic ooze. Late stages are characterised by irreversible swelling and joint fixation. Due to the disfiguring nature of the disease, those affected often experience social stigmatisation. Associated economic losses result from reduced productivity and absenteeism. The disease must be differentiated from conditions such as filarial lymphoedema and congenital lymphoedema, which can have similar presentations, such that appropriate therapy can be implemented.

Primary management of podoconiosis is prevention which involves the regular use footwear such as shoes and education of the disease. In the early stages of podoconiosis, compression therapy and limb elevation delays clinical progression in affected individuals. In later stages, changes are irreversible; however, additional therapy can include surgical intervention and limb elevation for symptom control. Psychosocial care is also needed to address the mental distress associated with the disease. Despite the preventable nature of podoconiosis, it remains prevalent in developing countries, necessitating further investment of resources.

Keywords Podoconiosis, lymphoedema, elephantiasis

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INTRODUCTION

Podoconiosis is a form of non-filarial (infectious disease) lymphoedema and is a debilitating chronic swelling of the foot and lower leg. Podoconiosis occurs with long-term exposure to irritant red volcanic clay soil in the highland regions of Africa, Central America and India[1]. It is caused by the passage of microparticles of volcanic silica and aluminum silicates through the skin of those walking barefoot in areas with a high content of volcanic soil[2]. Podoconiosis is a non-communicable (no person-to-person spread) tropical disease with high potential for eradication, but it remains a neglected condition.

Globally, it is estimated that there are four million people affected with podoconiosis[3]. The highest reported prevalence values are in Africa, including 8.08% in Cameroon, 7.45% in Ethiopia, 4.52% in Uganda, 3.87% in Kenya, and 2.51% in Tanzania[4]. In India, the prevalence was estimated to be 0.21%, primarily from Manipur, Mizoram and Rajasthan States[4]. The prevalence is higher in adults compared to children or adolescents, and is likely due to a longer duration of exposure to volcanic soil[4].

Several risk factors have been implicated in the development of podoconiosis such as a family history of the disease, absence of footwear, poor foot hygiene and low frequency of wearing shoes[5]. Other factors, such as being from a medium income household and having primary education, lower the risk of developing podoconiosis[5]. Studies have shown, however, that even in those with risk factors, podoconiosis develops in only

Merna Adly
MD candidate
Cumming School of Medicine, University of Calgary, Calgary, AB, Canada

Kwadwo Mponponsuo
MD
Department of Medicine, University of Calgary, Calgary, AB, Canada

Ranjani Somayaji*
BScPT, MD, MPH, FRCPC
Departments of Medicine; Microbiology, Immunology & Infectious Disease; Community Health Sciences, University of Calgary, Calgary, AB, Canada
Email rsomayaj@ucalgary.ca

** Corresponding author*

a subgroup of people. One study conducted in Ethiopia found familial clustering, with a high heritability of 63%[6]. A genome-wide scan of 194 cases and 203 controls, alongside family-based testing, demonstrated association between variants in HLA Class II loci with podoconiosis, suggesting that the condition may be a T cell-mediated inflammatory disease[6].

Social stigma of patients with podoconiosis is widespread. It is, at times, erroneously believed to run in families – which may occur due to the same exposures and not due to person-to-person spread – leading to isolation of those afflicted[7]. However, the diagnosis of podoconiosis is linked with a lower quality of life. Additionally, similar to other chronic illnesses, a recent study identified depression prevalence to be 12.6% amongst individuals living with podoconiosis[8]. Factors associated with this include social stigmatisation, living in an urban area, being illiterate, and being single[9]. Economic losses are also enormous since it mainly affects adults. This leads to reduced productivity and absenteeism, and contributes to the disease–poverty–disease cycle[10]. The estimated productivity losses per patient amount to 45% of working days per year, causing a significant economic impact[11].

CLINICAL FEATURES

Podoconiosis presents as bilateral asymmetrical lower limb swelling below the knee lasting more than a month, plus any one of the following symptoms – skin itching or burning, foot oedema, lymph ooze (due to build-up and overflow of lymph fluid from the vessels), prominent skin markings, rigid toes and/or mossy papillomata[12] (Figures 1 & 2). Podoconiosis has a curable pre-elephantiasic phase but causes lifelong disability once the elephantiasis phase is established. Progression to chronic disease (incurable state) occurs over years and has five stages (Table 1). Podoconiosis demonstrates changes of chronic lymphoedema with extensive sclerosis (hardening of tissue), loss of elastic fibres, verrucous acanthosis (hyperpigmented and hyperkeratotic plaques), and reactive changes of eccrine structures (destruction of sweat and sebaceous glands)[13,14,15,16].

PATHOPHYSIOLOGY

Traditionally, it has been identified that silicate particles absorbed via the skin induce an inflammatory process of the lower leg lymphatics. However, more recent work has identified that minerals enriched in incompatible elements such as calcium, potassium, magnesium and sodium are strongly implicated in the development of the disease[14]. Persons with dry skin have a greater risk – due to skin cracking or splitting – of particle absorption, lymphoedema and infection[15]. Silicate particles entering through skin are then thought to be taken up by macrophages in the lower limb lymphatics, causing subendothelial oedema, lymph inflammation and, eventually, destruction of the lymphatic lumen. In addition, immune cells are activated which contribute to ongoing inflammation. Eventually, these changes lead to clinical lymphoedema. The chronic inflammation transforms the swollen soft tissues

Table 1. Stages and management of podoconiosis[15,16].

Stage-specific clinical features	Treatment approach (all stages)	Treatment approach (stage-specific)
Stage 1: Swelling limited to below the ankle and is reversible overnight[15].	• Protective footwear. • Foot hygiene (daily washing with soap, water and antiseptics). • Soaking foot in 2% glycerin for 30 minutes, and vaseline application with each wash. • Emollient in order to improve the skin barrier and prevent cracking, as well as reduce the risk of infection. • Compression therapy. • Limb elevation at night to improve drainage and reduce limb size. • Exercise to enhance distal lymphatic drainage of the affected limbs. • Manual lymphatic drainage involving light superficial massage of the affected limb in order to enhance lymph drainage.	None.
Stage 2: Irreversible swelling limited to below the ankle. It may be complicated with bumps and knobs which occur below the level of the ankle. Nail dystrophy may develop.		Minor shaving surgery to reduce nodules, hyperplastic and verrucous bumps which prevent patients from wearing shoes.
Stage 3: Irreversible swelling limited to below the ankle. It may be complicated with bumps and knobs which occur above and below the level of the ankle.		Minor shaving surgery to reduce nodules, hyperplastic and verrucous bumps which prevent patients from wearing shoes. In severe cases, extensive surgical techniques involving the removal of redundant tissue, skin grafting, and then prolonged limb elevation during recovery may be utilised. However, results are usually short-term and skin scarring may cause further problems. Limb elevation at night may be suggested for several hours per day.
Stage 4: Irreversible swelling above and below the ankle. It may be complicated with bumps and knobs which occur above and below the level of the ankle.		
Stage 4+: Joint fixation of the ankle as a result of surrounding soft tissue overgrowth. Sensation is still preserved. Irreversible swelling above and below the ankle.		

Table 2. Differential diagnosis of podoconiosis and comparison of the diseases.*

	Filarial lymphoedema	Congenital lymphoedema	Podoconiosis
Pathogenesis	Filarial lymphoedema is transmitted through mosquitoes. The most common nematode species causing it is *Wuchereria bancrofti*[20]. Larvae entering humans grow in the lymphatics to adult worms, resulting in damaged lymphatic vessels[20].	Congenital lymphoedema is a genetic disorder of the lymphatic vessels[21]. It is ascribed to mutations, including those that inactivate the VEGFR3 tyrosine kinase signaling mechanism that is believed to be specific to lymphatic vessels[24].	Podoconiosis is an immune disease caused by heavy metals affecting the lymphatic vessels[22]. These particles, absorbed via the skin, are thought to induce an inflammatory process and a consequent endo-lymphangitis of the lower leg lymphatics[11].
Presenting features	May present as asymptomatic, acute or chronic infection. When it develops into a chronic condition, it leads to lymphoedema, as well as elephantiasis of limbs and hydrocele (scrotal swelling)[20]. Filarial lymphoedema most commonly has descending and unilateral progression of lymphoedema. It often affects the lower limbs and, to a lesser degree, the arms. It is uncommon for male genitalia to be involved and rare for breasts and genital regions in females[20].	Swelling may involve a single leg, but oedema of multiple limbs, the genitalia, and even the face can be seen. Bilateral leg swelling and involvement of the entire lower extremity is more likely in congenital cases than in other forms of primary lymphoedema[21].	Presents first in the foot and progresses up to the leg to the knee but rarely involves the groin. It usually has an ascending progression, and is most often bilateral[11].
Age distribution	Infection is acquired in childhood but the disease occurs later in adulthood[20].	May be apparent at birth, and becomes recognised within the first 2 years of life[21]. However, depending on the genetics, patients can present in childhood, adolescence or later in life.	Occurs more commonly in adults than in children or adolescents[4].
Geographical distribution	Prevalence of 120 million affected people in 83 countries, with up to 16 million having lymphoedema[20].	Prevalence is 1 in 6,000 individuals in the general population. Hereditary lymphoedema type II (Meige syndrome) is the most common form of congenital lymphoedema[21].	Prevalence estimate of four million persons affected globally. Occurs in highland areas of tropical Africa, Central America and northwest India where there is high seasonal rainfall[10]. More common at higher altitudes (>1000 metres above sea level)[10].
Diagnosis	Diagnosis is made through the identification of microfilariae antigen in a blood smear via microscopy.	Diagnosis is made through clinical evaluation (age of presentation) as well as various specialised investigations including lymphoscintigraphy, ultrasound and MRI[23].	Diagnosis is made clinically considering geography after exclusion of other causes (filarial lymphoedema).
Treatment	Diethylcarbamazine (DEC) is the drug of choice when there is active infection from *W. bancrofti*, *B. malayi* and *B. timori*[20] – other agents are based on geography and risk of co-infections.	No gene therapy for hereditary lymphoedema is available. Treatment aims at reducing swelling (compression) and infection prevention[23].	Treatment involves – foot hygiene; covered footwear; compression bandaging; and emollient usage to improve skin barrier.

**All forms of lymphoedema will require lymphoedema-specific care, including compression, once present, in addition to disease-specific treatments.*

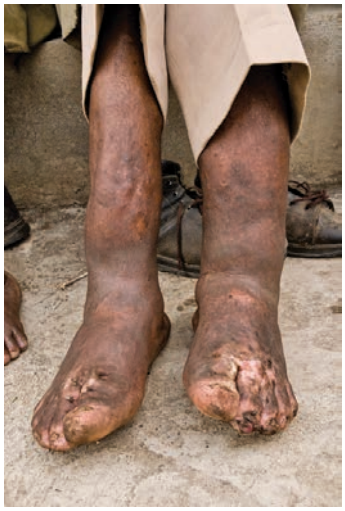

Figure 1 Podoconiosis with foot and lower limb deformity.

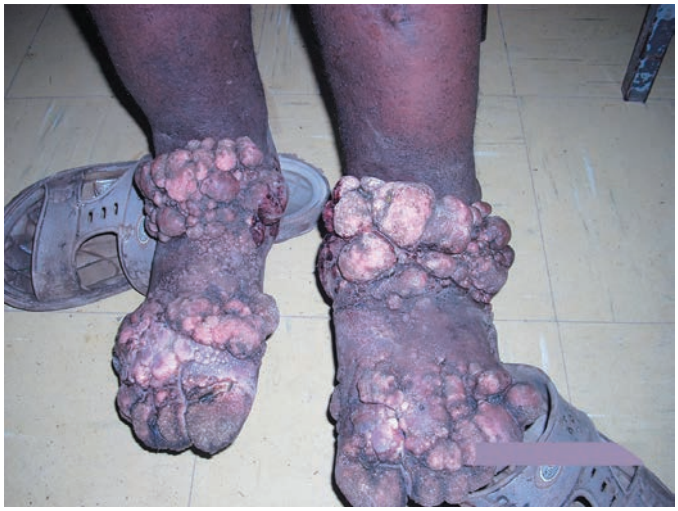

Figure 2: Podoconiosis with gross nodular involvement.

to hard and thickened skin over time, contributing to the irreversibility of the condition.

APPROACH TO TREATMENT

Research has shown that the provision of a simple, inexpensive package of lymphoedema self-care has considerable impact on both clinical progression and self-reported quality of life of affected individuals[2]. Several qualitative research studies show that culturally-informed education programmes that increase the perceived controllability of stigmatised hereditary health conditions like podoconiosis have promise for increasing preventative behaviours and reducing interpersonal stigma[17]. Additionally, several factors have been described as barriers to preventive behaviour, including uncomfortable footwear for farm activities and sports, affordability of shoe wear, shortage of soap for washing, as well as cultural influences promoting gender inequality which result in women being least able to access shoes[18]. As a result, it is essential to link podoconiosis-affected families with local governmental or non-governmental organisations providing socioeconomic support for households so families are able to better engage in behaviours that will reduce the risk of podoconiosis[18]. Finally, in order to address the high burden of mental distress among people with podoconiosis, it is essential to integrate psychosocial care into the current morbidity management of podoconiosis[19].

DIFFERENTIAL DIAGNOSIS

Accurate diagnosis of podoconiosis is essential for appropriate patient management and treatment. The diagnosis is established clinically as there is no gold standard diagnostic tool. It is a diagnosis of clinical exclusion based on history, physical exam, and certain antigen-antibody specific tests to exclude diseases included in the differential diagnosis such as filarial (infectious) lymphoedema and congenital lymphoedema. The differentiating features of filarial lymphoedema, congenital lymphoedema and podoconiosis are detailed below (Table 2).

CONCLUSION

Podoconiosis is a chronic swelling of the foot and lower leg caused by long-term exposure to irritant red volcanic clay soil in the highland regions of Africa, Central America and India. Those affected by podoconiosis have significant morbidity, loss of productivity, and frequently experience stigma and isolation. As there are simple measures for prevention, the elimination of podoconiosis is feasible. Global and local advocacy efforts for shoe provision and education are therefore urgently needed.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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