Puffy Foot Syndrome: An Important Often Overlooked Clinical Entity

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**ABSTRACT** The puffy foot syndrome, a novel clinical entity, describes the complication of secondary lymphedema with chronic progression in the feet, a finding that has often been overlooked in the non-tropical setting. While previously well described in the upper extremities, this complication has not been fully explored in the lower extremities. However, given increasing rates of diabetes mellitus, obesity, and a myriad of other possible etiologies in the United States, it is important to understand this entity and its non-viral, non-parasitic causes in non-tropical regions. This review delineates common illustrative properties of this syndrome observed in clinical practice as well as long-term complications, including Ruocco’s immunocompromised cutaneous district, that are often overlooked. Furthermore, a novel method of staging is suggested for this condition, reflective of increasing risk of complication, infection, and malignancy. We also highlight the increased need for improved detection and recognition of this condition to avoid possibly deleterious outcomes.

**KEY WORDS:** lymphedema, diabetes mellitus, obesity, Ruocco’s immunocompromised cutaneous district, neoplasia

**SIGNIFICANCE:** Puffy foot syndrome describes the complication of secondary lymphedema with chronic progression in the feet. Secondary lymphedema is common in urban areas often due to non-tropical causes such as diabetes mellitus and obesity. Puffy foot syndrome is a disease of neglect and early recognition is key to prevent progression in patients to malignant or vascular neoplasms and end-organ damage. Physician awareness of this syndrome can help improve recognition and treatment in earlier stages of disease.

**INTRODUCTION**

Lymphedema of the feet, typically associated with filariasis seen in tropical areas of the world, is widespread, affecting 120 million people and 83 countries [1]. However, there is a tendency to overlook lymphedema in non-tropical regions [2, 3]; we emphasize its non-parasitic causes [4]. Complications of this lymphedema often arise due to chronic neglect, and, as its causes are multi-factorial, we suggest placing these cases under the umbrella term “puffy foot syndrome”, similar to “puffy hand syndrome” used to identify a similar complication of lymphatic obstruction of the upper extremities [5]. As previously described by Yeh et al. [6], puffy hand syndrome often arises in individuals with poor glycemic control and obesity, typically in non-tropical urban areas. Irreversible consequences or emergent treatment at presentation is often needed as initial symptoms had been ignored [7]. It has been characterized as a disease of urban communities [8].

Beyond immediate consequences of the obstructive nature of puffy foot syndrome, it produces an immunologically vulnerable site for development of neoplasms, Ruocco’s immunocompromised
cutaneous district, including vascular tumors such as Kaposi’s sarcoma if the affected individual is human herpes virus-8 seropositive [9]. Herein, we evaluate the possibility of obesity and diabetes mellitus as important causes and associated pathophysiology of complications resulting in puffy foot syndrome, or lymphedema of the lower extremities, in a non-tropical context, and the dangers that may arise with continued neglect of this condition.

Figure 1 shows the foot of an obese, diabetic female patient. Commonly, these women develop cellulitis which quickly turns into recurrent lymphangitis; this lymphangitis eventually manifests itself as cobblestone-like nodules of the feet, appearing similar in presentation to the elephantiasis seen with verrucous hyperplasia of the skin. Such presentation must be managed carefully due to possible long-term consequences; there is a clear need for better recognition and treatment in the temperate urban setting.

As shown in our proposed methodology for staging puffy foot syndrome in Table 1, the initial stages of puffy foot syndrome are unremarkable, with lymphedema observed without secondary complications. However, this stage progresses to repeated episodes of cellulitis, lymphangitis, and inflammation, often manifesting in an appearance similar to that seen in Figure 1. If this stage progresses further, it can lead to a massive proliferation of tissue and fibrogenesis which would consist of stage 3 puffy foot syndrome. This fibrogenesis likely occurs due to the leaking of fluid into interstitial spaces; importantly, fibrosis is both a common cause of end-organ failure in many organ systems and a key player in the pathophysiology of disease [10]. This suggests a reinforcing feedback cycle which may lead to a rapid decline in clinical presentation from stage 2 to stage 3 of puffy foot syndrome, underscoring the importance of early recognition to avoid end-organ damage.

**DISCUSSION**

The precise etiology as well as the various long-term complications of puffy foot syndrome caused by obesity and diabetes is yet to be described. Many studies have shown that lymphedema represents a significant possible complication that may arise from extreme obesity, most often due to impairment of lymphatic function; in fact, obese patients have been found to develop lymphedema even without prior surgery or injury [11]. The pathology of these conditions is likely due to the accumulation of fat that blocks lymphatic vessels, leading to an increase of weight-tension and lymphostasis which, if continued long enough, can manifest itself as lymphedema [12]. Mouse models show lymphedema in obese mice noted subcutaneous adipose deposition, increased CD4+ cell inflammation, and increased fibrosis; notably, however, lymphatic function is already impaired at baseline and this impairment is further amplified injury [13]. Furthermore, patients suffering from obesity are at significant risk of developing venous disease due to associated venous stasis which is often neglected until it has progressed to a point where it impairs quality of life, indicating irreversible injury [14]. With added pressure on the veins, particularly in the lower extremities, an increasing amount of fluid leaks into the interstitial space and is drained by the lymphatic system. As lymph drainage is overwhelmed by increasing accumulation of protein-rich interstitial fluid (lymph stasis), lymphatic drainage fails leading to lymphedema, and possibly, puffy foot syndrome, highlighting the connection between varicosities, obesity, and lymphedema. Similar connections have also been seen between diabetic dermatopathy and coronary artery disease [15]. Applying this information to a non-tropical context, it explains some of the epidemiology behind why more lymphedema is currently seen in urban populations with higher rates of obesity, underscoring the need to focus on these populations in our management.

**Table 1. Proposed staging mechanism of puffy foot syndrome.**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
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<tbody>
<tr>
<td>Stage 1</td>
<td>Lymphedema without complications.</td>
</tr>
<tr>
<td>Stage 2</td>
<td>Appearance similar to that seen in <strong>Figure 1. Repeated episodes of cellulitis with inflammation and lymphangitis.</strong></td>
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<tr>
<td>Stage 3</td>
<td>Massive proliferation of tissue associated with chronic lymphedema (seen in every type of lymphedema, even filariasis), massive fibrogenesis</td>
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**Figure 1.** An obese, diabetic, elderly woman with cellulitis, ulcers, and severe diabetic neuropathy diagnosed with puffy foot syndrome.
Data detailing the co-morbidity of diabetes and lymphedema should be evaluated, a combination of the two pathologies which places individuals at risk of damage to the legs and the possibility of complete loss of function [16]. Uncontrolled diabetes may lead to cellulitis and cutaneous ulcers, frequently occurring on the lower extremities and requiring surgical debridement, especially due to the possibility of later-stage necrotizing fasciitis, requiring amputation [17]. This type of recurrent cellulitis may be a cause and complication of secondary lymphedema; cellulitis may destroy lymphatic vessels leading to lymphedema and the accumulating lymph from lymphedema may lead to bacterial proliferation that can give rise to cellulitis [18]. Chronic lymphedema is often evaluated utilizing the Kaposi-Stemmer sign, a valuable clinically finding [19]. Patients with either obesity or diabetes that have progressed to a chronic state likely have significant chance of cosmetic consequences, limb disutility, or amputation required as a result of chronic lymphedema seen in puffy foot syndrome.

Certain congenital conditions can also predispose certain individuals in developing the sequelae observed in puffy foot syndrome and amplify or speed up the effects of obesity and diabetes on these patients, possibly producing Ruocco’s immunocompromised cutaneous district [20]. Therefore, individuals with familial or hereditary lymphedema may be at increased risk, an important distinction to make in the discussion of puffy foot syndrome.

Chronic lymphedema, such as that seen in puffy foot syndrome associated with obesity and diabetes, may give rise to specific malignancies. Massive localized lymphedema has been associated with otherwise rare patterns simulating liposarcomas [21]. Furthermore, this condition represents an immunologically vulnerable site for development of a variety of neoplasms, including malignant vascular ones [22-26]. It is important to note that as a disease of neglect, patients suffering from puffy foot syndrome are at risk for a variety of conditions ranging from irreversible end-organ damage to these aforementioned malignancies. Therefore, there are irreversible risks and consequences both when physicians fail to treat chronic lymphedema associated with puffy foot syndrome.

CONCLUSION

The puffy foot syndrome/lymphedema of the lower extremities is often unrecognized, especially in its early stages. However, as reflected in our clinical practice in an urban academic medical center, several epidemiologic factors may account for an increase in the prevalence of puffy foot syndrome. Obesity and diabetes seem to be leading risk-factors for puffy foot syndrome. Given the differing etiologies and management considerations of non-tropical puffy foot syndrome compared better known tropical lymphedema of the lower extremities, we have highlighted some unique aspects of puffy foot syndrome in a non-tropical context emphasizing obesity and diabetes. Future research work should investigate similar causes of secondary lymphedema with chronic changes that could make also contribute to puffy foot syndrome, such as how intravenous drug use is relevant to the hand [27]. As discussed, puffy foot syndrome is often a disease of neglect. Therefore, considerable effort should be directed at predisposing factors.

References:


