Case report

Elephantiasis *nostras verrucosa* in the setting of lymphoedema *tarda* and neurofibromatosis type 1Joana Calvão ¹, Luís Santiago,¹ Maria Manuel Brites,¹ Américo Figueiredo^{1,2}

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SUMMARY

Elephantiasis *nostras verrucosa* (ENV) comprises an uncommon skin disease characterised by dermal fibrosis with hyperkeratotic, verrucous and papillomatous lesions that usually occur after chronic lymphoedema. We describe the case of a 56-year-old-man with neurofibromatosis type 1, no known surgical history, no chronic medication and no travel history, presenting with worsening non-pitting oedema and impressive foul-smelling mossy plaques and cobblestone-like nodules in both legs and feet, especially on the right, compatible with the diagnosis of ENV.

BACKGROUND

Elephantiasis *nostras verrucosa* (ENV) is a complication of chronic non-filarial lymphoedema that most commonly affects the feet and distal lower extremities. In addition to profound non-pitting oedema and progressive fibrosis of the dermis and subcutaneous tissue, there are verrucous changes with papillomatosis and hyperkeratosis. The resulting cutaneous changes become grossly disfiguring and are difficult to treat.¹

We present a case of an exuberant ENV in a relatively young man with neurofibromatosis type 1.

CASE PRESENTATION

A 56-year-old-man, ex-merchant, with neurofibromatosis type 1 and mild chronic venous insufficiency, but unremarkable surgical history and no chronic medication, presented with worsening oedema and verrucous plaques on his legs of 10 years' duration. Physical examination showed non-pitting oedema and impressive foul-smelling mossy plaques and cobblestone-like nodules in both legs and feet, especially on the right, with a positive Stemmer's sign indicative of lymphoedema (figure 1). Also, numerous café au lait patches and cutaneous neurofibromas were found, mainly on the trunk (figure 2). Palpable bilateral inguinal adenopathies were noted, as well as an enlargement of the right testicle. The patient had a normal body mass index (24.6 kg/m²) and reported no travel history.

INVESTIGATIONS

Laboratory evaluation revealed normal results for the complete blood count, including eosinophil count, renal and liver function tests. Glucose and C reactive protein levels were also in the normal range. Ultrasound evaluation of inguinoscrotal area showed a right inguinal hernia with a large

homolateral hydrocele, without compromise of testicular arterial vascularisation. Due to substantial asymmetry of the legs, venous Doppler studies were performed, with no evidence of deep vein thrombosis, although displayed bilateral valvular insufficiency of common femoral, superficial femoral and popliteal veins, as well as of the internal and external saphenous veins with varicose collaterals. An X-ray of the lower members was also done, but revealed no changes besides the asymmetry of the legs (figure 3). An abdominopelvic CT scan confirmed the existence of a bilateral inguinal hernia, considerably larger on the right but not causing lymphatic or venous compression, without further changes (figure 4).

Figure 1 Elephantiasis *nostras verrucosa*: exuberant mossy plaques in the right leg.

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Figure 2 Multiple cutaneous neurofibromas and café au lait patches in the trunk.

Based on clinical history, physical examination and these findings, the diagnosis of ENV was made.

TREATMENT

The patient started leg elevation and treatment with compression, potassium permanganate soaks, topical keratolytics (10% salicylic acid ointment) and topical activated charcoal, with great improvement within a few days, particularly in what regards the hyperkeratotic and verrucous appearance and the bad odour.

OUTCOME AND FOLLOW-UP

Several months later, he maintains the follow-up in our dermatology department, doing topical treatment with 5% salicylic acid ointment and honey-based dressings with stabilisation of the clinical picture (figure 5) and he is waiting for surgical repair of the inguinal hernia.

Figure 3 X-ray of both legs highlights their asymmetry.

Figure 4 Abdominopelvic CT scan demonstrating the existence of a bilateral inguinal hernia, much larger on the right.

DISCUSSION

ENV comprises an uncommon skin disease characterised by dermal fibrosis, with hyperkeratotic, verrucous and papillomatous lesions that usually occur after chronic lymphoedema.² The pathogenesis underlying ENV remains unknown: it has been previously reported that the CD4+ cell response in lymphoedema was characterised by a mixed Th1/Th2 cell; however, a

Figure 5 Elephantiasis *nostras verrucosa* of the right leg after 2 months of treatment with elastic compression stockings and topical treatment with keratolytics and honey-based dressings.

recent case report suggested that ENV-associated epidermal hyperplasia may be attributed to an enhanced Th17 response.³

Lymphoedema can be either primary or secondary.⁴ Primary lymphoedema is a rare condition arising from a developmental abnormality of the lymphatic system, and can be classified by the age at the time of onset as congenital (manifesting at birth or up to age 1 year), *praecox* (the most common form of primary lymphoedema, that generally becomes clinically evident during puberty) or *tarda* (late-onset lymphoedema, usually manifesting after age 35 years). It most commonly affects one lower extremity, although cases affecting upper extremities have also been described.⁵ Regarding secondary lymphoedema, several causes may be involved, such as surgical damage to the lymphatic system (one of the most common causes in industrialised countries, especially related to tumorous treatment—namely breast cancer and melanoma, but also other gynaecological and genitourinary cancers), radiotherapy, infections such as filariasis (the most common cause of secondary lymphoedema worldwide, frequently occurring in developing countries) or recurrent bacterial infections (specifically cellulitis), inflammatory conditions causing permanently damage the lymphatic system, morbid obesity, trauma, congestive heart failure, portal hypertension and, rarely, pretibial myxoedema.^{2,6} Venous diseases, such as varicose veins or deep vein thrombosis can also lead to lymphoedema, as damaged veins can cause fluid to overflow from the veins into the tissue spaces. On the other hand, causes of chronic unilateral leg swelling include common diseases such as venous insufficiency and deep vein thrombosis, and less commonly are secondary lymphoedema (tumour, radiation and surgery—as discussed previously), pelvic tumours or lymphoma causing pressure on the veins, and rarely congenital venous malformation, pregnancy and iliac vein compression syndrome.⁷ In this particular case, the late onset (after 35 years old) and the unilateral involvement with no other identifiable secondary causes, points to a primary lymphoedema *tarda*, which is the rarest form of primary lymphoedema, accounting for only 10% of cases. Moreover, primary lymphoedema is seen in association with various cutaneous and genetic disorders, such as neurofibromatosis type 1, as in the case described.

Diagnosis of ENV can be made on clinical grounds alone, however, physicians should investigate and, if possible, treat the underlying causes of lymphatic obstruction.⁸

Currently, there is no universal practice in the management of ENV. Although it is difficult to handle with, early recognition and treatment of this unusual entity is the key to achieve a satisfactory result.⁹ The main target of any therapy should be the reduction of the lymphoedema and exudation. Compression with elastic bandages or stockings have been described

to be beneficial. Identification and correction of the cause of the lymphoedema, such as weight reduction, may also help to achieve a better and faster improvement.² Topical keratolytics or humectants, such as salicylic acid and urea, may improve the hyperkeratosis, as well as topical or oral retinoids. For refractory cases, carbon dioxide laser or surgical intervention may be attempted.¹ A recent case report combined obesity management with treatment with tolcapant, an aquaretic drug that functions as a selective vasopressin receptor 2 antagonist, which was greatly effective.¹⁰

Learning points

- Elephantiasis nostras verrucosa (ENV) is a rare late complication of chronic lymphoedema that most commonly affects the feet and distal lower extremities and should be treated with local treatments and compression therapy.
- Lymphoedema can be primary or secondary: in the case described we face a ENV complicating a primary form of lymphoedema (*tarda*) in association with neurofibromatosis type 1.

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Patient's perspective

This disease causes a high impact on my quality of life, not just because of the appearance but especially due to the foul odour associated. After some weeks of treatment, this has had a great improvement.

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