Elephantiasis Nostras Verrucosa Presenting As Chronic Lymphedema In A Patient With Long Standing Rheumatoid Arthritis: A Case Report

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Abstract

Elephantiasis nostras verrucosa (ENV) is a rare form of chronic lymphedema characterized by progressive cutaneous hypertrophy, papillomatosis, and hyperkeratosis, often affecting gravity-dependent regions such as the lower extremities. This condition can lead to severe deformities and is frequently difficult to manage. This case report details a 32-year-old female with a 10-year history of rheumatoid arthritis (RA) who developed massive swelling of both lower limbs accompanied by ulcerations. She was diagnosed with seropositive RA one year prior and had been undergoing treatment with methotrexate. Clinical examination revealed non-pitting edema, cobblestone-like papulonodules, and ulcerations on the left leg. Laboratory findings included low MCV anemia and elevated inflammatory markers, but venous thrombosis was ruled out. A biopsy showed pseudoepitheliomatous hyperplasia without signs of malignancy. Management included limb elevation, compression therapy, and Tofacitinib for RA. This case highlights the interplay between RA and lymphedema, emphasizing the need for comprehensive care to address both conditions and associated complications. A multidisciplinary approach is essential for optimal management and to ensure continuous improvement.

Keywords: Rheumatoid Arthritis, Lymphedema, Elephantiasis Nostras Verrucosa.

Introduction

One rare form of chronic lymphoedema that results in increasing cutaneous hypertrophy is elephantiasis nostras verrucosa (ENV). Severe deformity may result in parts of the body whose blood supply is dependent on gravity, particularly the lower extremities.[1] It is characterised by papillomatosis and hyperkeratosis of the epidermis with hyperkeratotic papulonodules overlaid that resemble cobblestones or verrucose. Although ENV management is frequently difficult, several effective medical and surgical therapeutic approaches have been documented.[1] This case report presents a 32-year-old female with a 10-year history of RA who developed massive swelling of both lower limbs and superimposed ulcerations and review of the literature about association of lymphedema and rheumatoid arthritis in conjunction with ENV.

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Case Notes

A 32 year-old female presented to us with massive swelling of both lower limbs for 3 months along with superimposed ulcerations for 1 month. She was having long standing Rheumatoid arthritis (RA) with disease onset 10 years back. She was RA factor and Anti CCP antibodies positive with high titers. She was on conventional DMARDS (Methotrexate) since then. Swelling was started from feet involving both legs simultaneously extending upto knees with associated

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non-healing ulcer on left leg. Swelling was not painful and there was no associated fever. Her past medical, surgical, travel, and family histories were unremarkable. She was wheel chair bound for 3 months. Physical examination revealed normal vital signs. Her lower extremities had a discrete non-pitting edema extending from feet upto the knees, with lichenification of the limbs. The skin was indurated and had cobblestone-like papulonodules and crusts and there were left leg ulcers on dorsum of foot and lower leg as shown in Figure 1 (a). She was having swollen and tender multiple joints MCPS, PIPS, wrists and knees with limited range of motion both hips. There was no adjacent inguinal lymphadenopathy. Palpation of the lower limb pulses was impossible because of skin induration. Complete blood count revealed Low MCV Anemia Hb 10.8g/L, MCV 72.ESR 60mm/hr, CRP 24mg/L. Blood sugar levels, and liver and renal function tests were within the normal range. Lower extremity venous ultrasound ruled out the presence of deep and superficial veins thrombosis.

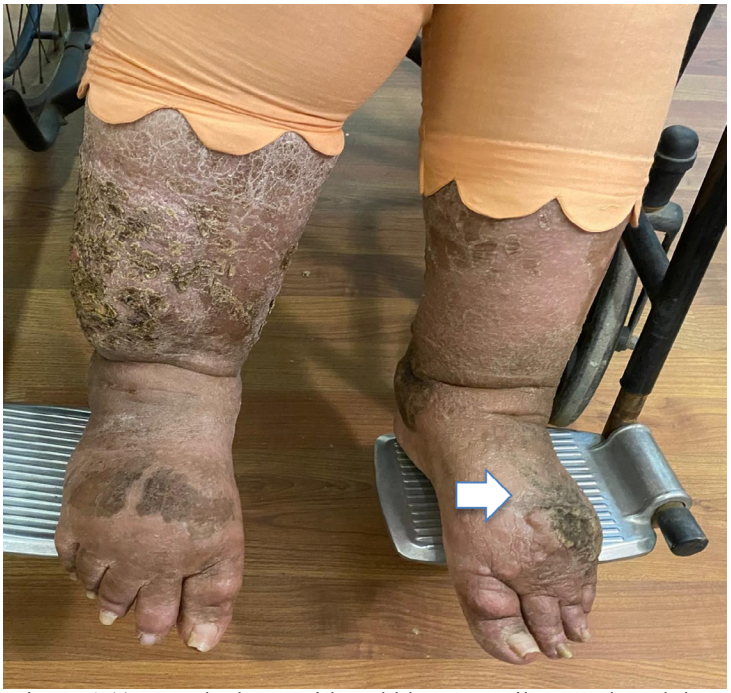

Figure 1:(a) Lymphedema with Cobble-stone Like Papulonodules.

In September 2023, skin ulcers biopsy Figure 2: (a),(b) revealed pseudoepitheliomatous hyperplasia with moderate mixed dermal inflammation and edema of papillary dermis with spongiotic change in epidermis on skin biopsy, biopsy fungal stain negative. No evidence of vasculitis or malignancy.

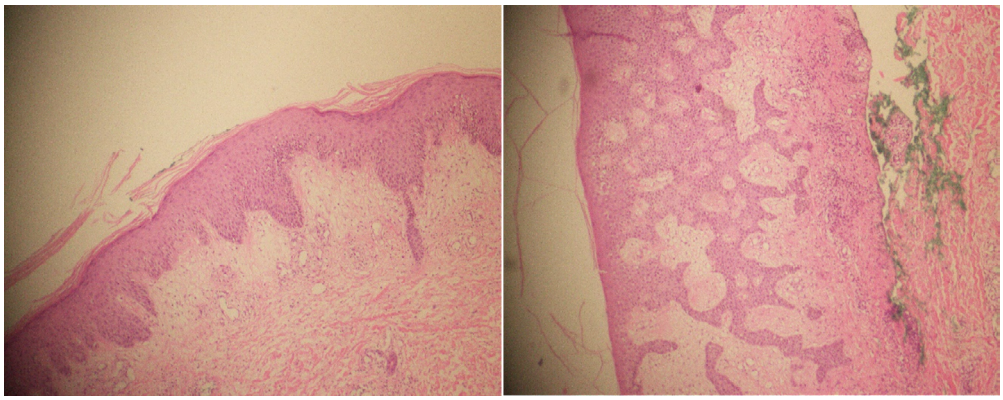

Figure 2: (a), (b) Fragments of Epidermis and Dermis Showing Pseudo-epitheliomatous Hyperplasia and Hyperkeratosis and Mild Chronic Dermal based Inflammation.

The patient was managed with limb elevation, compression therapy and a sterile dressing for her ulcer and her underlying disease. For her active RA, she was started on Tofacitinib after normal preliminary work up. Anti TNF could not be started due to financial constraints. In addition, we educated her and encouraged her to increase

ambulation, elevate her legs, and reduce her body weight. Her lymphedema is subsiding very gradually, most recent picture attached after 3 months of Tofacitnib is attached figure.[2] Her next follow up is due after 2 months.

Figure 3: Image Taken after 3 Months of Starting Tofacitinib and Conservative Management For Lymphedema.

Discussion

Lymphedema is a chronic, progressive illness that affects joint movement and mobility. As the swollen regions get bigger and heavier, it frequently leads to posture changes and discomfort. It ultimately results in a decline in self-esteem, a change in physical and psychosocial functioning, and an overall reduction in quality of life.[2] The most frequent inflammatory rheumatological disease that accompanies lymphedema is reported to be rheumatoid arthritis (RA).[3] Rheumatoid arthritis (RA) is a chronic polyarthritis with an unknown cause that affects around 1% of people worldwide.

Individuals suffering from RA lymphedema may have severe, dispersed, and persistent swelling in their limbs. Reduced lymphatic outflow results in the uncommon but extremely incapacitating illness known as rheumatoid lymphedema.[4] This case underscores the severe impact RA can have when associated with complications like chronic lymphedema and ulcerations. The patient's long-standing RA, managed with Methotrexate, eventually led to significant lower limb swelling and skin ulcerations, highlighting the challenges in controlling the disease's progression.

First reported by Kalliomaki and Vastamaki in 1968, lymphedema linked to RA seems to be a somewhat rare manifestation of the disease. Many data suggest that lymphedema is not just a consequence of seropositive arthritis but also of other types of inflammatory arthropathy.[5-7] Although a number of theories have been put up to explain the potential cause of capillary filtration anomaly and edema, none of them satisfactorily explains the etiology of this feature in RA. The serum's colloid osmotic pressure cannot be lowered by lowering serum proteins or changing the albumin-globulin ratio. Therefore, edema is not caused by osmotic phenomena. Salicylates, phenylbutazone, corticosteroids, and other NSAIDs are frequently prescribed as treatment in RA. However, although edema can occasionally occur before to their treatment, the salt and water retention linked to their usage is not the primary cause of lymphedema.[8]

In patients suffering from inflammatory rheumatological diseases, a number of theories have been put forth regarding its pathogenesis. These include lymphangitis, fibrin-induced lymphatic obstruction, increased capillary permeability, fluid retention linked to immobilization, venous obstruction, lymphatic vessel obstruction, abnormal fibrinolysis, and possible fibrosis of the superficial lymph vessels.[6,9] In several cases, hypoalbuminemia or an increase in plasma fibrinogen breakdown products were seen.[5] It is believed that edema and chronic lymphangitis may be brought on by the diffusion of inflammatory processes into lymphatic channels.[10]

The diagnosis is made clinically since there has been painless swelling along with skin changes noticed in one or more limbs; the diagnosis is confirmed by ultrasonography, Doppler ultrasonography, magnetic resonance imaging (MRI), lymphoscintigraphy, and histological analysis.[11] Clinically notable features of ENV include mossy papules, plaques, and cobblestone-like nodules. Biopsy results show pseudoepitheliomatous hyperplasia, dilated lymphatic spaces, fibrous tissue hyperplasia, chronic inflammation as shown in our case. No indication of malignancy should be present at all. Venous stasis may be the cause of the cutaneous fibrotic changes of the lesions.[12]

A histologic reaction pattern known as pseudoepitheliomatous hyperplasia is characterized by irregular hyperplasia of the epidermis that includes thick, longitudinal downward projections of the epidermis that often have a sharp tip at the base and jagged margins on histopathology. It can result from a multitude of stressors, including trauma, cryotherapy, chronic lymphedema, and persistent irritation around the urostomy and colostomy sites.[10] It

might be particularly challenging to differentiate a PEH from an SCC.[13] The non-healing ulcers on the patient's left leg represent another layer of complexity. Chronic lymphedema predisposes patients to skin breakdown and ulceration due to poor skin perfusion and lymphatic drainage. The biopsy findings of pseudoepitheliomatous hyperplasia with moderate mixed dermal inflammation and spongiotic changes are consistent with chronic inflammatory processes. The negative fungal stain and absence of vasculitis or malignancy ruled out other potential causes, confirming that the ulcerations were secondary to the chronic lymphedema and RA.

The introduction of disease-modifying medications often has little effect on edema in instances of RA or PsA. There are papers in the literature suggesting that medications that block tumour necrosis factor (TNF)-α, which are often used to treat rheumatological illnesses, may also be useful in treating lymphedema.[11,14] Ostrov[14] reported that etanercept significantly decreases the lymphedema in a patient with RA. On the other hand, the temporal relationship suggested a link between the initiation of TNF-α inhibitors and the development of lymphedema. Noticeable treatments for ENV include Comprehensive decongestive therapy (also known as CDT) as the cornerstone for all patients with lymphedema linked to inflammatory rheumatic disorders. It consists of four basic components: skin care, manual lymph drainage, compression, and exercise. Medical management of edema by diuretics, and prevention of recurrent infections and treating underlying condition. Oral retinoids may be effective, but the sustainability of these results appears variable. Rarely, surgical debridement or amputation is performed in recalcitrant cases.[3,12]

In our case, the financial constraints faced by the patient highlight an important issue in chronic disease management. Access to biologic therapies such as Anti-TNF agents can significantly alter the course of RA and prevent complications. Exploring patient assistance programs, insurance coverage options, and alternative funding sources could be pivotal in providing comprehensive care. Regular follow-up is essential to monitor the patient's response to Tofacitinib and adjust the treatment plan as needed. The gradual improvement in her lymphedema indicates a positive response, but continuous assessment is necessary to ensure sustained progress and to address any new complications promptly. A multidisciplinary approach involving rheumatologists, dermatologists, and wound care specialists is recommended to address the various aspects of her condition comprehensively.

Conclusion

In conclusion, this case highlights the considerable difficulties in treating individuals with rheumatoid arthritis RA who have ENV. The patient experienced severe lower limb swelling and ulcerations, complicating her RA management. This emphasizes the significance of tailored treatment regimens and a multidisciplinary approach in managing the underlying cause of RA as well as its side effects. Moreover, noteworthy point is how important it is for healthcare systems to offer chronic disease patients inexpensive access to cutting-edge treatments. Regular follow-up and collaboration between specialists are essential for optimizing patient outcomes and ensuring long-term management of ENV and RA-related complications.

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