CASE REPORT

Lymphedema secondary to limited cutaneous systemic sclerosis

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SUMMARY

Systemic sclerosis (SSc) is an autoimmune connective tissue disease characterised by vascular abnormalities, immune system activation and fibrosis. Lymphatic involvement in SSc was described more recently and starts in early stages. This report describes a 46-year-old patient who developed over the last 2 years asymmetric lymphedema in lower extremities. Compromise in lymphatic drainage was confirmed by lymphoscintigraphy. She also presented Raynaud's phenomenon, a scleroderma pattern in nailfold capillaroscopy, cutaneous thickening and antientromere antibodies, which together resulted in a new diagnosis of limited cutaneous SSc. Treatment with methotrexate, prednisolone and lymphatic drainage resulted in lymphedema improvement. To our knowledge, this is the first case of grade 2 lymphedema in the setting of antientromere-positive limited cutaneous SSc. We highlight the importance of considering rheumatic diseases in the differential diagnosis of lymphedema.

BACKGROUND

Systemic sclerosis (SSc) is an autoimmune connective tissue disease of unknown aetiology resulting in a complex interplay of vasculopathy, inflammation and fibrosis.¹ More recently, lymphatic microangiopathy was also described.^{2,3} Lymphatic vessel

involvement seems to start earlier and more consistently than its blood counterpart and progresses to a significant loss of lymphatic capillaries in later stages of SSc.^{3,4} This lymphatic microangiopathy in addition to increased vascular permeability may underlie the pathophysiology of the early edematous phase frequently observed in SSc.^{3,4} In patients with diffuse cutaneous SSc, lymphatic involvement might be extensive and severe cases of lymphedema have been observed.⁵ The unusual feature of this case is the presence of severe lymphedema in a patient with limited cutaneous SSc.

CASE PRESENTATION

We report a case of a 46-year-old Caucasian woman with persisting and asymmetric oedema in lower limbs and a feeling of heaviness starting to 2 years ago. She also described Raynaud's phenomenon in hands and feet, lasting for more than 15 years. Digital ulceration and cardiorespiratory, genitourinary or gastrointestinal symptoms were denied. No histories of trauma, travel outside Europe, recurrent infections or malignancy were reported. Family history was negative for autoimmune or neoplastic diseases.

On physical examination, we observed cutaneous thickening in upper limbs, extending from the extremities of the fingers to the proximal

Figure 1 Lower extremities presenting with asymmetric lymphedema (A), hypopigmented and hyperpigmented areas and an atrophic lesion (B).

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Figure 2 Lymphoscintigraphy with compromised lymphatic drainage in lower right extremity and, although more discreetly, in the lower left extremity.

metacarpophalangeal joints. Her Modified Rodnan Skin Score (mRSS) was 13 out of 51. Sclerodactyly, telangiectasia or pitting scars were not noticed. Right and left lower limbs had oedema that resisted pitting, a positive Stemmer's sign, hyperpigmented and hypopigmented areas and atrophic skin patches (figure 1A,B). This oedema was asymmetric, involving more aggressively the right lower limb.

INVESTIGATIONS

High titres of anticentromere antibodies (ACA) were detected (titre of 1:1280). Liver and kidney function, thyroid hormones and electrolytes were normal. No serological evidence for filariasis infection or venereal diseases was found. Nailfold capillaroscopy revealed a reduced number of capillaries, some megacapillaries and spontaneous haemorrhages, features typical of active SSc. Arterial and venous Doppler ultrasonography of the limbs excluded compression and thrombosis. Lymphoscintigraphy showed a compromise in lymphatic drainage of the right lower extremity with a starting point in the upper two-thirds of the thigh and a tortuous lymphatic path with slowed flux (figure 2). Lymphatic drainage in the left lower extremity also occurred with some difficulty but to a lower extent. These findings suggested lymphatic impairment. Abdominal and pelvic CT excluded injuries with compressive effect in the emergence of the lymphatic system of lower limbs. Echocardiogram, pulmonary function tests and high-resolution thorax CT excluded heart and pulmonary involvement.

OUTCOME AND FOLLOW-UP

According to the ACR-EULAR criteria (skin thickening of the fingers of hands, abnormal nailfold capillaries, Raynaud's phenomenon and SSc-related autoantibodies), our patient was classified as definite SSc. The distribution of cutaneous sclerosis and the presence of ACA are in accordance with limited cutaneous SSc. The patient was treated with oral methotrexate (10 mg/week), folic acid (5 mg/week) and prednisolone (10 mg/day). Additionally, lymphatic drainage was performed 3 times per week. Over the following 12 months, she experienced a reduction in oedema and an improvement in SF-36. There were no changes in mRSS.

DISCUSSION

To our knowledge, this is the first case report of grade 2 lymphedema described in an ACA-positive limited cutaneous SSc. Other possible causes of lymphedema were excluded, including trauma, recurrent infection, malignancy, infection with the parasitic nematode *Wuchereria bancrofti* (also known as filariasis), venereal and venous diseases. A case of elephantiasis nostras verrucosa secondary to SSc was described in a 56-year-old man with SSc with pulmonary hypertension and ACA-negative.⁵ Moreover, unilateral lymphedema was reported in two patients with morphea as a result of lymphatic compression by Sclerotic Patches.^{6,7} Lymphatic involvement in SSc has been described at least since 1999; however, evaluation of microscopical changes of lymphatic vessels was only possible along the last decade. It was shown that the number of lymphatic vessels is significantly reduced in the skin of patients with SSc and that they correlated inversely with the number of fingertip ulcers.^{3,4,8} The loss of cutaneous lymphatic vessels starts early in the reticular dermis, extends afterward to the papillary dermis and progresses to a significant loss of lymphatic capillaries.^{2,3} An increase in the inner luminal area (implying dilation) of the remaining lymphatic vessel number was also observed in the reticular dermis of patients with SSc.⁴ This lymphatic microangiopathy leads to accumulation of macromolecules and an increase in tissue oncotic and hydrostatic pressure, resulting in impaired tissue perfusion. This may initiate a persistent inflammatory response leading to impaired immune responses, tissue dystrophic changes and fibrosis.^{4,9,10}

Our patient performed regularly lymphatic drainage of lower limbs, resulting in reduced self-perceived pain and better daily activities performance. The importance of lymphatic drainage was showed in a study published by Bongi *et al*, where patients with SSc with edematous hands submitted to lymphatic drainage reduced hand volume and improved hand function, self-perceived oedema and pain.¹¹ These results were explained through stimulation of lymphatic system circulation, increase in lymph vessel suction, oedema mobilisation and excess interstitial fluid removal. A possible role on the peripheral nervous vegetative system was also proposed by decreased sympathetic responses and increased parasympathetic tone, thus inducing a sympatholytic effect and reducing the chronic inflammatory processes.^{11,12}

In conclusion, after exclusion of more frequent secondary causes of lymphedema, our clinical and analytical data supported the hypothesis of grade 2 lymphedema secondary to limited cutaneous SSc. This case highlights the importance of considering rheumatic diseases in the differential diagnosis of lymphedema.

Learning points

- ▶ Rheumatic diseases should be considered in the differential diagnosis of lymphedema.
- ▶ Limited cutaneous systemic sclerosis (SSc) can be a secondary cause of severe lymphedema.
- ▶ Involvement of lymphatic microcirculation in SSc occurs in early phases of the disease and should be promptly addressed.
- ▶ Lymphatic drainage reduces self-perceived oedema and pain, thereby improving function.

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