

Lymphedema Induced by Recurrent Myxedema

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Lymphedema is a pathologic condition that is characterized by the accumulation of excessive, protein-rich fluid in regional interstitial tissue, which results in chronic, progressive swelling. We report the case of a female patient who presented with recurrent myxedema who was eventually diagnosed with lymphedema. Generally, the common cause of lymphedema include surgery, radiation, trauma, infection and malignant tumors. However, in this cases, the lymphedema may be related to recurrent myxedema. This case report emphasizes the necessity of evaluating the lymphatic system in patients with hypothyroidism and persistent swelling.

Key Words: Lymphedema • Recurrent myxedema • Hypothyroidism

INTRODUCTION

Lymphedema is a pathologic condition that is characterized by the accumulation of excessive, protein-rich fluid in regional interstitial tissue, which results in chronic, progressive swelling [1,2]. Lymphedema is classified as primary or secondary depending upon the cause. Primary lymphedema is a developmental abnormality of the lymphatic system that is either congenital or hereditary. Secondary lymphedema develops after disruption of the lymphatic pathways. Common causes for secondary lymphedema include surgery, radiation, trauma, infection, malignant tumors, immobility, and chronic venous insufficiency [2].

Myxedema is a rare cause of lymphedema and it is often difficult to differentiate the two conditions in patients. We report a rare case of lymphedema induced by recurrent myxedema.

CASE REPORT

A 30-year-old female patient presented with a chief

complaint of swelling in the right arm and leg. She had undergone a total thyroidectomy for papillary thyroid carcinoma 2 years ago. She has no history of any additional operations (such as lymph node dissection), trauma, or infection. Before surgery, she had no history of swelling or edema. Since the surgery, she has been taking levothyroxine sodium, which is the medical treatment for hypothyroidism.

Edema was observed in both extremities and the periorbital area 1 year after the surgery. She took 200 µg of levothyroxine sodium, regularly. She was hospitalized in the Department of Endocrinology twice for treatment. Her TSH level was 17.31 µIU/mL (0.55-4.78 µIU/mL) during the first admission and she was diagnosed with hypothyroidism. At the worst, her TSH, T3 and fT4 level was 123.79 µIU/mL, 12.87 ng/dL (65-150 ng/DL) and 0.41 ng/DL (0.78-1.54 ng/DL), respectively. Edema in both extremities and the periorbital areas was improved after the dose of levothyroxine sodium was adjusted to a therapeutic level.

At the most recent presentation, she was experiencing swelling of the face, eyelids, forehead, and extremities (right worse than left), and dry, cool, pale skin. Her hair had thinned, and the skin on her elbows, knees, and soles of the feet was rough. The circumference of her right leg increased 3.5 cm proximally and 4-5.5 cm distally compared to the left leg (Fig. 1). Physical examination did not reveal any signs of muscle weakness or sensory loss in either leg but Stemmer's sign and non-pitting edema were observed in her right leg.

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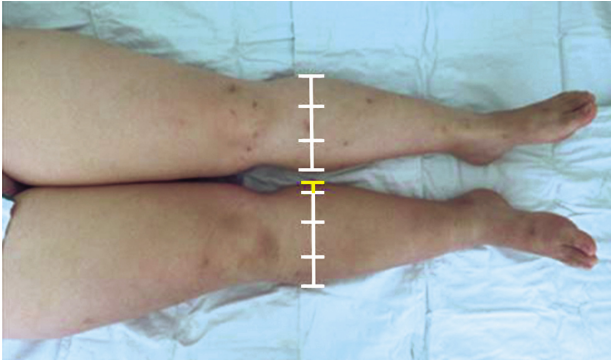


Fig. 1. Clinical appearance of lymphedema with myxedema in the bilateral lower extremities (right worse than left).

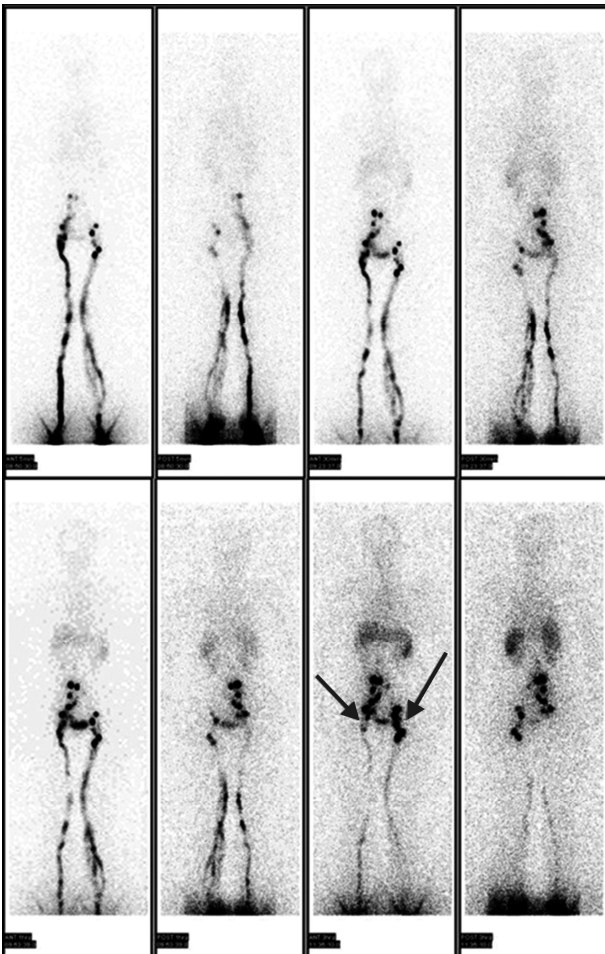


Fig. 2. Lymphoscintigraphy of the lower extremities after injection of 100 uCi/0.02 mL of filtered ^{99m}Tc phytate. There is decreased lymph node activity in the right inguinal region (black arrows).

Swelling was worse in the right leg; however, the severity fluctuated. On peripheral vessel ultrasonography (USG), the deep veins of both lower extremities from the common femoral to the popliteal veins showed a patent lumen with no thrombosis or other gross abnormalities. On 3D CT angiography of the lower extremities, there was no stenosis or occlusion from the com-

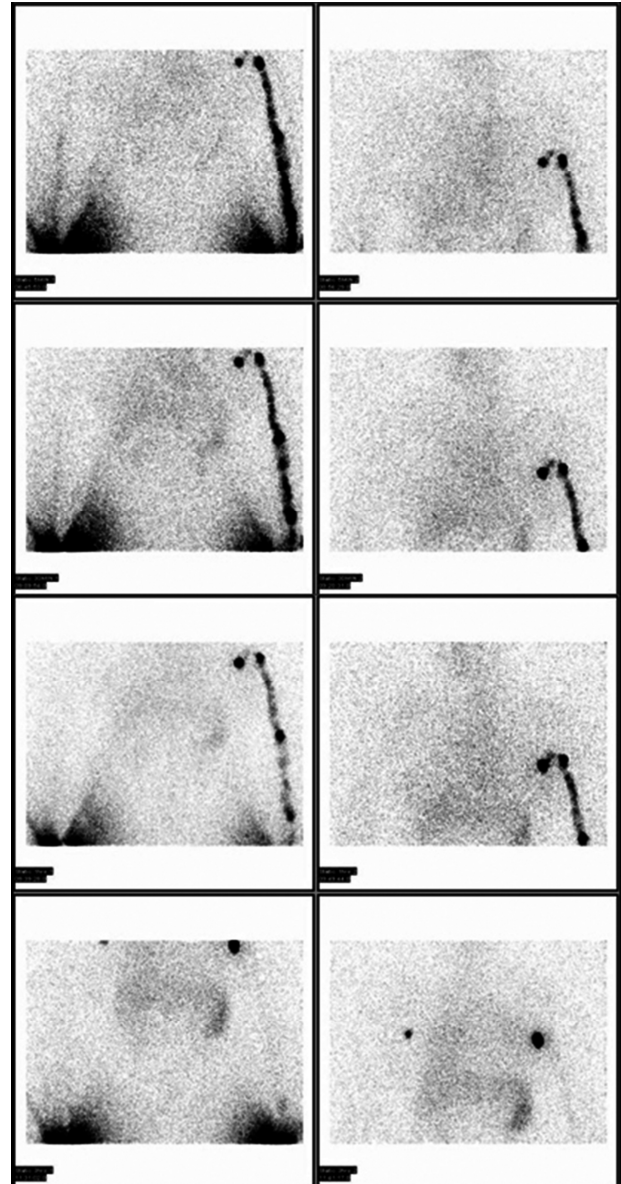


Fig. 3. Lymphoscintigraphy of the upper extremities after injection of 100 uCi/0.02 mL of filtered ^{99m}Tc phytate. There is decreased lymph node activity in the right axillary region.

mon iliac to the foot artery in either lower extremity. Laboratory studies including complete blood count, serum electrolytes, liver function, and kidney function were normal except for an increase of her TSH level to 150.00 μ IU/mL (0.55-4.78 μ IU/mL).

Although she had edema of all extremities, the unilateral increase in the right arm and leg compared to the left is characteristic of lymphedema. Therefore, we conducted a lymphoscintigraphy to test for lymphedema. The results showed that the activity in the right inguinal and axillary lymph nodes was reduced compared to the left (Figs. 2, 3). Thus we diagnosed the patient with lymphedema of the right arm and leg. We prescribed micronized flavonoids (Venitol® Gwangdong Pharm, Korea) and conducted a complete decongestant therapy (CDT program). The circumference of her right leg was reduced to 2 cm proximally and 2.5-3.5 cm distally after 2 weeks of treatment with multilayered bandages, manual lymphatic drainage, and air pressure pneumatic compression. The dose of levothyroxine sodium was increased and she was also prescribed diuretics.

DISCUSSION

Myxedema is a common symptom of hypothyroidism and autoimmune hyperthyroidism. This specific form of edema is caused by fluid and proteoglycan accumulation in the interstitium between the fibers of the subepidermal papillary and reticular dermis [3,4].

Our patient experienced diffuse myxedema associated with hypothyroidism, which was identified by both clinical and laboratory findings. However, the lymphoscintigraphy of her extremities showed that the activity of the right inguinal and axillary lymph nodes was reduced compared to the left side. Therefore, it is possible that lymphedema developed with recurrent hypothyroidism and myxedema.

Lymphedema caused by a reduction in lymphatic transport is a pathologic condition that results in excessive, regional accumulation of protein-rich fluid in the interstitial space. The primary cause of lymphedema is anatomic abnormalities in lymphatic development leading to lymphatic stasis. Secondary lymphedema is commonly caused as a consequence of any traumatic, inflammatory, surgical, or neoplastic obstruction of lymphatic pathways [2]. However, myxedema has not been considered as a cause of secondary lymphedema.

Diffuse myxedema associated with hypothyroidism is initially experienced as skin tension. Other symptoms

of hypothyroidism such as fatigue, alterations in hair texture, increased sensitivity to cold, poor concentration, muscle spasms, menorrhagia, unexplained weight gain, and signs of sleep apnea can be observed [5].

Myxedema primarily consists of a deposition of mucinoid substances in the reticular dermis [6]. With the thyrogenic form, glycosaminoglycans with hyaluronic acid [7] and small amounts of chondroitin sulfate are produced in fibroblasts of the dermis. These star-shaped fibroblasts are called mucinoblasts. With progressive myxedema, increased proteoglycans in the interstitial space splice and displace the bundles of collagen and elastic fibers [4]. Thus, the accumulation of water-binding substances between the fibers of the elastic and collagen bundles can compress the lymphatic networks and lead to lymphedema.

In our case, diffuse myxedema associated with hypothyroidism was treated using L-thyroxine to substitute depleted iodine hormones. Lymphedema-induced progressive myxedema was improved after using micronized flavonoids, lymphatic massages, multilayered bandages, manual lymphatic drainage, and air pressure pneumatic compression. It is important to prevent the onset and aggravation of edema, infection, and trauma.

As shown with this case, lymphedema can be considered when diagnosing patients with myxedema. Also, when myxedema is observed, early diagnosis and aggressive treatment can prevent the occurrence of secondary lymphedema.

There was a similar report in the past, but it was limited to the pretibial area [8]. Our patient had diffuse myxedema in whole extremities and it is a rare case of lymphedema induced by recurrent myxedema. The deposition of the connective tissue components such as mucopolysaccharide caused by myxedema may have compressed lymphatic flow, resulting in a concurrent lymphedema. As lymphedema may be caused by an underlying myxedema, we should evaluate the lymphatic system in patients with hypothyroidism and persistent swelling.

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