CASE REPORT

Giant and Extensive Localized Xanthoma Associated with Primary Lymphedema

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Abstract
Lymphedema is extravasation of lymphatic fluid into extracellular spaces and may be primary or secondary. Primary lymphedema may be caused by truncular lymphatic malformation. Long-standing lymphedema may result in various complications due to increased porosity of lymphatics, defective valves, and increased lymphatic pressure. There are few reports of normolipidemic xanthoma in association with lymphedema. We report a case of giant xanthoma associated with primary lymphedema.

Key Words: Giant xanthoma, lymphatic malformation, lymphedema

Introduction
The association of lymphedema and xanthoma was first described about five decades ago.[1] Lymphatic malformations (LMs) with leaking of lipoproteins lead to the formation of xanthoma. We present a case of giant and extensive localized xanthoma associated with lymphedema in a 55-year-old female.

Case Report
A 55-year-old female presented to the dermatology department with yellow-colored asymptomatic lesions on the right upper limb and trunk, progressively increasing in size and number for the past 10 years. The patient had a history of swelling of the whole of the right upper limb since 15 year of age, which progressively increased in girth. There was a history of oozey lesions off and on for which she had received multiple courses of antibiotics. There was no significant history of trauma. On examination, there was diffuse, nonpitting, woody hard swelling of the whole of the right upper limb. She had skin-to-yellow-colored, multiple, well-defined plaques ranging in size from approximately 1 cm × 1 cm to 20 cm × 20 cm spreading over the right upper arm, extending anteriorly to the lateral part of the right side of the chest and upper abdomen (upto umbilicus) and posteriorly over the upper half of the right back. There was spilling over of these lesions beyond the midline to the left side both on the front and on the back of the trunk [Figures 1a and b]. There were discrete similar smaller lesions over the anterior chest. She was diagnosed to be having giant localized xanthoma with primary lymphedema. Biopsy from the yellow plaques revealed nodular dense monomorphous granulomatous infiltrate of foamy histiocytes with uniform and sparse scattering of lymphocytes involving the reticular dermis and sparing appendages [Figure 2]. Routine hematological and biochemical reports were unremarkable. There was no lipid abnormality. Thyroid profile was normal. About 10 years back, she got 99mTc phytate lymphoscintigraphy done, which showed normal lymphatic system on the left side, while on the right side, there was no visualization of lymphatics and axillary lymph nodes even after 24 h. The patient did not consent for repeat lymphoscintigraphy. No family history of lymphedema, xanthoma, hyperlipidemia, liver disease, gammopathy, or lymphoproliferative disorder was reported. As the patient had chronic lymphedema which does not respond to medical and surgical therapy or physical modalities, she was advised to keep the part clean and avoid trauma.

Discussion
Xanthomas are yellow-to-skin-colored benign tumors characterized by deposition of lipid-laden histiocytes. Associated dyslipidemia may or may not be seen.
Normocholesteremia is usually seen in xanthoma disseminatum, verruciform, and localized type.

Depending on the phase in which LM occurs during the process of embryogenesis, it may be divided into extratruncular and truncular forms. Extratruncular LM occurs during early fetal development and usually leads to abnormality such as cystic/cavernous lymphangioma. Truncular form occurs late in fetogenesis during the formation of lymphatic trunk and lymph nodes and presents as primary lymphedema. Ours was also a case of truncular LM presenting as lymphedema at 15 year of age. Lymphedema can be broadly classified into primary and secondary forms; primary lymphedema depending on the age of onset is named as congenital, lymphedema praecox (onset till 35 year of age), and tarda onset after 35 year of age. In truncular LM, lymphatics may be aplastic, hypoplastic, hyperplastic, stenosed, dilatated, localized, or diffuse.

Normal evolution of such LM is initially dilatation of the lymphatics at places. Increased pressure, defective valves, and propulsion of lymph lead to extravasation of excess tissue proteins presenting as edema which gradually becomes nonpitting, ultimately leading to chronic inflammation and fibrosis. In long-standing cases, hyperkeratosis and verrucous-like lesions appear. Various complications associated with lymphedema include impaired limb function, recurrent cellulitis, elephantiasis, and malignancies such as lymphangiosarcoma, squamous cell carcinoma, lymphoma, melanoma, and Kaposi’s sarcoma.

Association of lymphedema and xanthoma was first described by Cairns and Coburn in 1963. Since then, there have been few reports of few small xanthomatous lesions in a localized area. As explained earlier because of defective embryogenesis, there is increased leakiness.

An altered pressure gradient between intralymphatic and extralymphatic compartments may occur because of infection, trauma, and invasive procedure. This leads to extravasation of macromolecules such as lipoproteins which are engulfed by histiocytes which, in turn, form foam cells. As there is no relation to lipid metabolism, these patients are normolipidemic. In 1970, Hunter, Peterkin, and Morley proposed that lymphatic incompetence led to lipoprotein leak into interstitium which was ingested by macrophages. In our patient, there was a history of superficial infections off and on which could have led to the inflammation of lymphatic channels, increasing lymphatic fenestration and intraluminal lymphatic pressure, and hence precipitating the formation of xanthoma. The giant xanthoma, especially on the trunk, can be explained on the basis of the association of lymphatic trunks in these areas. The limitation of xanthoma to the upper quadrant of trunk is because of transverse watershed demarcation line at the level of umbilicus inferiorly and infraclavicular superiorly, and vertical watershed in the midline further supports the association of LM and development of xanthoma. The interval between the onset of lymphedema and xanthoma may be three to four decades. In our patient, there was a history of lymphedema for 30 years before xanthomas developed. Periodic lymphoscintigraphy is the gold standard to diagnose LM. Duplex ultrasonography provides more details of lymphatic fluid collections. It is practically difficult to cure lymphedema. Self-care is the mainstay of therapy. Compression stockings, physiotherapy, and massaging the lymphedematous area constitute the treatment, which is usually prescribed in chronic lymphedema. Patients should be advised to keep the skin clean, limb elevation and to avoid trauma, and prevent obesity. Medical treatment such as diuretics has been tried but are not effective in chronic lymphedema.
edema.\textsuperscript{[10]} Resolution of xanthomas has been reported after reduction of lymphedema.\textsuperscript{[1,5]}

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient had given her consent for her images and other clinical information to be reported in the journal. The patient understood that her name and initial would not be published and due efforts would be made to conceal her identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**

There are no conflicts of interest.

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