



CASE REPORT

Morphea-like localized involutinal lipoatrophy—a case report associated with family history

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KEYWORDS

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ABSTRACT

Localized involutinal lipoatrophy is a rare, sporadic disease with female tendency and characterized by focal loss of adipose tissue. We report two sisters, aged 8 years and 6 years, who developed asymptomatic depressive areas on the upper left arm and upper right arm, respectively. Cutaneous sonography showed slight thickening of the dermis and remarkably decreased thickness of the cutaneous fat tissue. Histopathology of a biopsy specimen from the elder sister revealed an increase in homogenized collagen bundles and entrapment of eccrine glands high in the dermis, as well as small to medium-sized lipocytes with a scarcity of inflammatory cells.

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Introduction

Localized involutinal lipoatrophy is a rare presentation with a well-defined depression of the skin and noninflammatory lobule involution as shown by histology. Some cases occur after local injection and the lesions tend to be proximally located. Peters and Winkelmann¹ first reported this condition in 1986 and the involvement of family members has rarely been reported since then.² We present here two Taiwanese siblings with localized involutinal lipoatrophy.

Case report

An 8-year-old girl presented with a 2-month history of an asymptomatic depressive lesion on the lateral side of her upper left arm. Physical examination revealed a 3 cm × 4 cm well-defined, oval, flesh-colored to faintly ivory-colored depression on her upper left arm (Figure 1A). The overlying surface was atrophic with telangiectases. Interestingly, her 6-year-old sister had also had an asymptomatic depressive area on her upper right arm for almost 2 months. Clinical

presentation revealed a 3 cm × 4 cm well-defined, flesh-colored, oval, depressed area on her upper right arm (Figure 1B). There were no inflammatory signs in either lesion. Their mother denied any history of trauma or injection in the past 1–2 years. Both children were otherwise healthy and had no associated medical conditions or drug intake. The family of the two patients did not have any symptoms related to localized lipoatrophy. Cutaneous sonography in both sisters showed a slightly increased thickness of the dermis and remarkably decreased thickness of the subcutaneous fat tissue compared with the skin on the contralateral normal upper arm (Figures 2A and 2B). At the site of the lesion in the elder sister, the thickness of the epidermis and dermis was 1.6 mm and the subcutaneous fat was 2.2 mm. In the healthy skin, the thickness of the epidermis and dermis was 1.3 mm and the subcutaneous fat was 3.6 mm.

Laboratory studies including hematologic tests, erythrocyte sedimentation rate, and autoantibody screening tests for immune disease were within normal limits. We performed a skin biopsy on the elder sister, but her mother refused a biopsy for the younger sister.

Histopathological examination showed mild epidermal atrophy, pandermal fibrosis with loss of the perieccrine fat pad, and entrapment of eccrine glands high in the dermis (Figure 3A). There were diminutive fat lobules with small and atrophic fat cells and a highly prominent vasculature,

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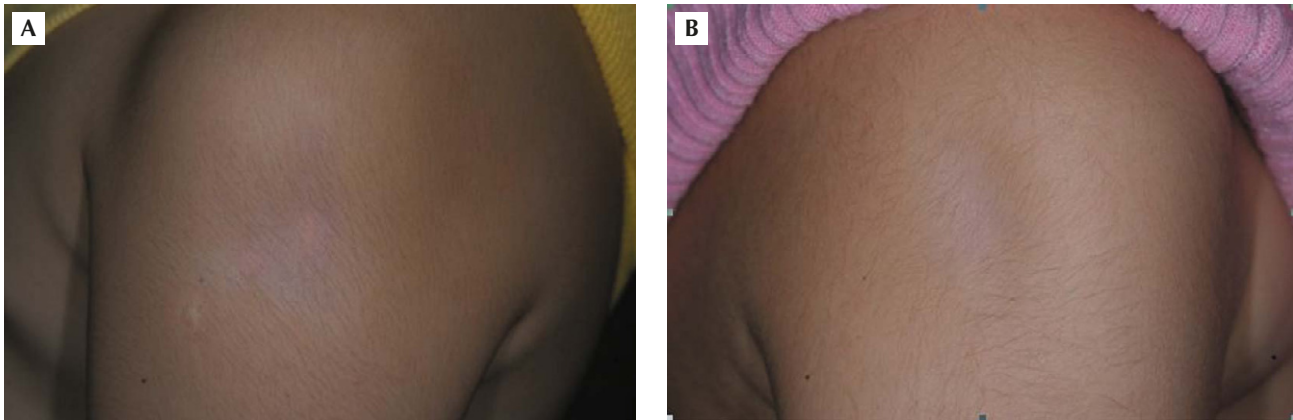


Figure 1 (A) Well-demarcated, noninflamed depression on the elder sister's upper left arm. (B) A depressed, flesh-colored area on the younger sister's upper right arm.

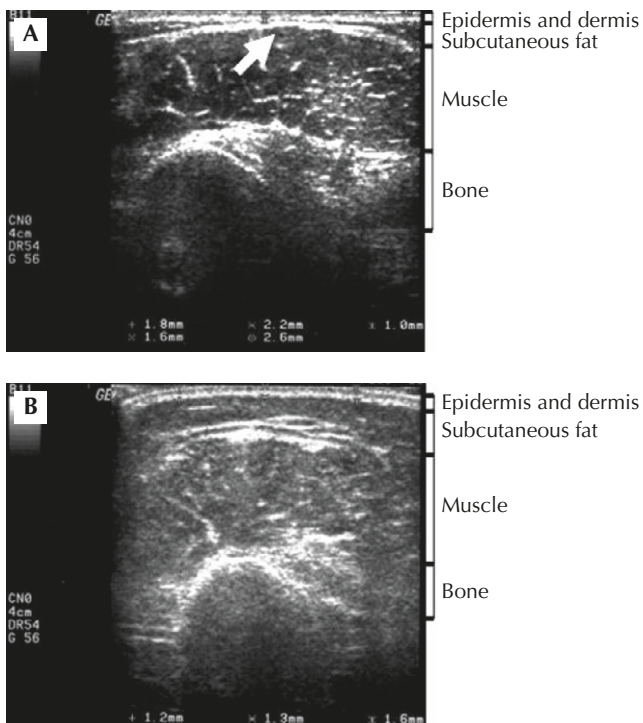


Figure 2 (A) Slightly increased thickness of the dermis and remarkably decreased thickness of the cutaneous fat tissue on cutaneous sonography in the elder sister (arrow). (B) Sonographic appearance of the healthy skin on the upper right arm in the elder sister.

simulating embryonic fat (Figure 3B). There was no significant dermal or subcutaneous inflammation. Immunoreactivity was performed with CD3 (DAKO, Copenhagen, Denmark; dilution titer, 1:100), CD20 (DAKO; dilution titer, 1:100), CD31 (R&D Systems, Minneapolis, MN; dilution titer, 1:100) and CD68 (R&D Systems; dilution titer, 1:100). Scattered CD68+ positive macrophages were infiltrated in close proximity to atrophic lipocytes, and there was negative staining for T-cells and B-cells with CD3 and CD20 markers (Figure 3C). CD31+ endothelial cells in the capillaries also showed a prominent vasculature and angioplasia (Figure 3D). Direct immunofluorescence study results were negative.

The diagnosis was localized involutinal lipatrophy. No resolution of the skin depressions occurred within 3 months.

Discussion

Localized involutinal lipatrophy involves the loss of adipose tissue without preceding clinical or histologic inflammation; however, the exact etiopathogenesis is still unclear. The characteristic subcutaneous histopathologic changes simulate embryonic adipose tissue. In 1986, Peters and Winkelmann¹ first described this entity and more than 30 cases have since been reported. Clinically, localized involutinal lipatrophy is an asymptomatic, localized, non-inflammatory and well-defined depression, mainly on the proximal limbs and buttocks. The clinical differential diagnosis includes morphea, lichen sclerosis, and atrophoderma of Pasini and Pierini. A characteristic feature of localized morphea is that it is well circumscribed and ivory or white. As the lesion subsides, atrophy becomes evident. It is most frequently encountered at a young age. The differential diagnosis must also distinguish it from localized involutinal lipatrophy.

Most reported patients were young females (M:F=2:37) and the average age is 31 years (range, 8–67 years; Table 1^{1–10}). However, the remarkable female predominance in previous reports is difficult to explain. Most cases were not associated with any medical condition. However, some were associated with atopic dermatitis, rheumatoid arthritis, and vitiligo, except for one family with two involved siblings most reported cases have been sporadic.² Our patients were two sisters with no associated medical conditions. Among reported patients, 48.7% had a history of a localized injection at the affected site before the development of the lipatrophy. Although local injection may play a role in the onset of these lesions, more than half of the patients cannot recall any previous injection, as found in our patients. The duration of lesion(s) prior to presentation varies from 2 weeks to 1 year. This finding could be because the lesions have no

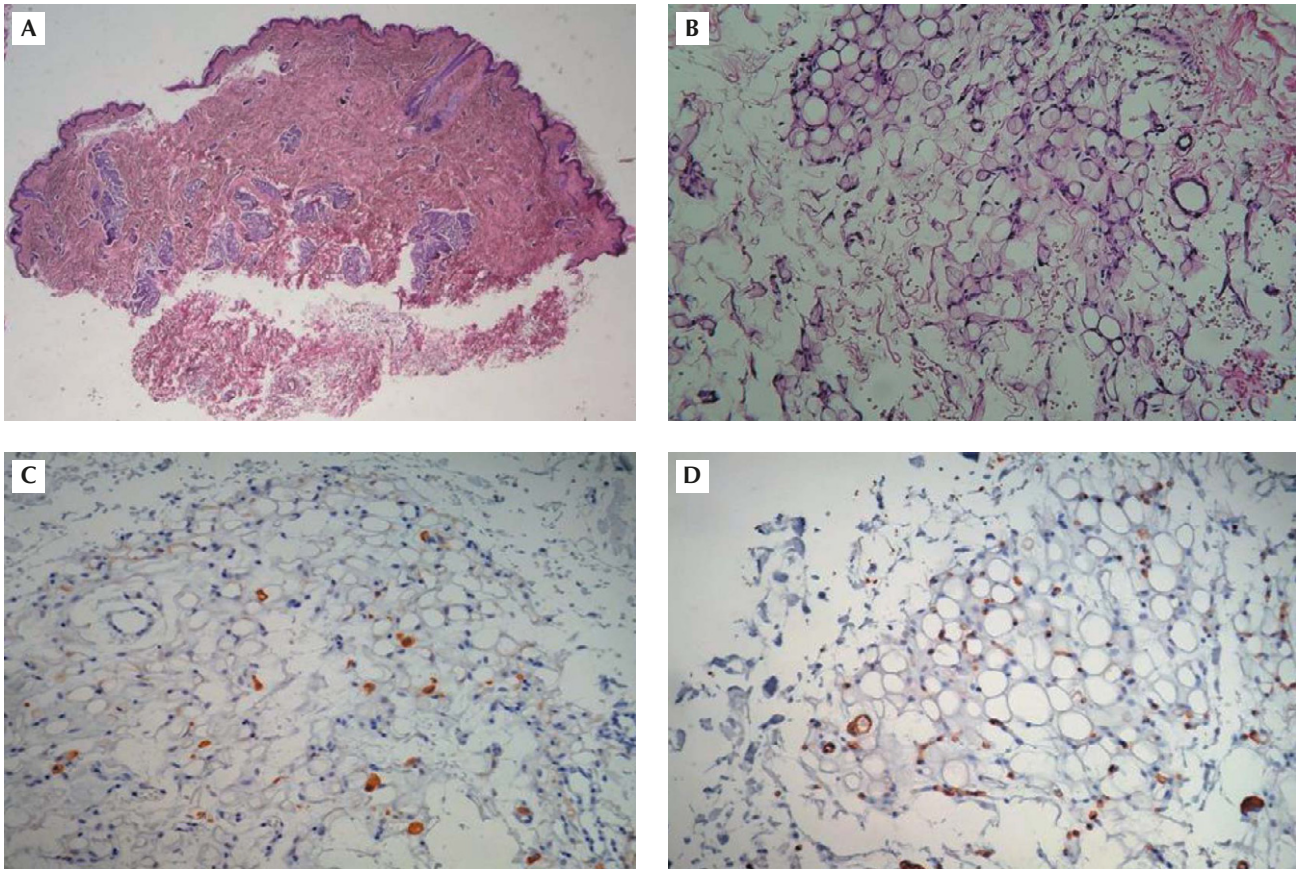


Figure 3 (A) A low power view shows increased collagen bundles and entrapment of the eccrine glands high in the dermis of the elder sister (H&E, original magnification 40 \times). (B) A high power view shows fat lobules composed of small to medium-sized lipocytes with scarcity of inflammatory cells involuted to simulate fetal adipose tissue (H&E, 200 \times). (C) Expression of CD68 positive macrophages in the adipose tissue (CD68, 200 \times). (D) Prominent vasculature in the adipose tissue shown by staining with CD31 marker (CD31, 200 \times).

Table 1 Clinical and histopathologic data from previous cases with localized involutinal lipoatrophy.^{1–10}

Reference	No. of cases	Age (yr)	Sex	Case(s) of prior injection	Duration	Histopathology	Family history
Peters and Winkelmann ¹	6	5–41	5F/1M	1	2 mo–1 yr	Small to medium-sized lipocytes with scarcity of inflammatory cells	No
Lo et al ²	2	8	1F/1M	2	2–7 mo	Atrophic fat cells with prominent vasculature	Yes
Sasaki et al ³	2	30–32	2F	0	2 wk–4 mo	Mucin-phagocytosing histiocytes surrounding shrunken lipocytes	No
Abbas et al ⁴	2	30–43	2F	0	4–6 mo	Diminutive fat lobules, epidermal atrophy and prominent pandermal fibrosis	No
Ahmed ⁵	1	53	1F	1	6 mo	Active macrophages engulfing segments of stromal tissue	No
Zalla et al ⁶	1	47	1F	1	1–5 mo	Small to medium-sized lipocytes with focally prominent blood vessels	No
Dahl et al ⁷	16	13–65	16F	9	N/A	Fat septa fibrosis and acid mucopolysaccharide within fat lobules	No
Yamamoto et al ⁸	6	22–50	6F	4	1–2 mo	Small to medium-sized lipocytes with a number of capillaries	No
Hisamichi et al ⁹	2	23–30	2F	1	1 mo	Numerous small adipocytes in hyaline connective tissue	No
Cendras et al ¹⁰	1	67	1F	0	6 wk	Reduced size of adipocytes with vascular dilatation	No

M=male; F=female; N/A=not available.

symptoms and patients do not pay attention to any early changes in the skin lesion.

Histologically, involuted fat lobules composed of small to atrophic lipocytes are embedded in the prominent vasculature

and hyalinized background, simulating fetal adipose tissue. Increased homogenized collagen bundles in the dermis replacing subcutaneous fat tissue have been reported.^{3,4} Some patients have epidermal changes with hypopigmentation and

atrophy.³⁻⁵ A scarcity of inflammatory cells with CD68+ and mucin-positive macrophages infiltrating involuted lipocytes have also been identified in several reports.⁵⁻⁹ Similar to previous reports, we found that there were definite dermal and subcutaneous pathological findings in the elder sister in addition to mild epidermal atrophy. Immunohistochemical stains of the pauci-inflammatory cell revealed positive results for macrophages and negative results for T-cells and B-cells. It is also important to rule out morphea with secondary fat changes by histological findings of septal thickening and lymphoplasmacytic inflammation.

The pathogenesis of localized involutinal lipoatrophy is still unknown. Local injections of insulin, antibiotics, or steroids inducing immunologic dysregulation are proposed for the development of localized involutinal lipoatrophy. Lysosomally active macrophages composed of clear vacuoles and lipid droplets have been found in close proximity to fat cells under electron microscopy.^{5,7} The activated macrophages are supposed to trigger immunologic disorders by secreting a variety of cytokines such as fibroblast growth factor-2, platelet derived growth factor, interleukin-1, tumor necrosis factor- α , and transforming growth factor- β , resulting in involution of the subcutaneous fat tissue.⁵ We speculate that the dermal changes in our patient may have been mediated by a localized immune response, which can induce cell toxicity and subsequent fibrosis and sclerosis. Among all the cytokines in the pathogenesis of localized involutinal lipoatrophy, transforming growth factor- β is thought to be involved in the development of morphea, and may thus represent a potentially important mediator of the dermal changes in our case.

Ultrasonography has been used for objective and non-invasive monitoring of tumors and chronic skin disease. The subcutaneous fat is a markedly hypoechoic area in comparison to the dermis. Both morphea and scleroderma are characterized by an increment in dermal collagen and the images are characterized by augmentation of echoes, with an echo-rich band zone at the dermis-subcutis border.^{11,12} We used cutaneous sonography in our patients; a slightly increased thickness of the dermis and remarkably decreased thickness of the cutaneous fat tissue were noted. This finding may rule out the possibility of other diseases associated with localized depression.

In summary, the reason for the development of this condition in both sisters at the same time remains unknown. Although their mother does not recall any injection on the lesional site, this may be because of recollection bias. However, half of the reported cases of localized involutinal lipoatrophy were not associated with previous injections. This may indicate that the lipoatrophy in our patients is idiopathic and has an inherited tendency. Further investigation is needed to elucidate the mechanism. A tendency of the skin lesions to resolve without treatment has been reported, but currently, no local regression or spreading has been noted in our patients.

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