

An Ultrastructural Study of Lipodystrophia Centrifugalis Abdominalis Infantilis, with Special Reference to Fibrous Long-Spacing Collagen

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Abstract: Lipodystrophia centrifugalis abdominalis infantilis (LCAI) in a 2.5-year-old Japanese girl is reported. Clinically she had a curved cutaneous depression with a slightly elevated erythematous border on the left abdomen beyond the left groin. The regional lymph node was palpable. Histologic examination showed a decrease of the fat, an inflammatory infiltrate mainly composed of lymphocytes, and septal fibrosis in the subcutaneous tissue. Immunohistochemical analysis found that infiltrating lymphocytes were mainly positive against CD4. Ultrastructurally nuclei in the adipocytes were crescent shaped and located toward the periphery of the cell. Some banded structures with a periodicity of 150 nm, and with intraperiodic bands, referred to as fibrous long-spacing collagen (FLSC), were observed in the septal area of the fatty tissue. These results indicated that FLSC was correlated with the breakdown of fibrillar collagens in LCAI.

Lipodystrophia centrifugalis abdominalis infantilis (LCAI), first reported by Imamura et al. (1), is a benign disorder of subcutaneous fatty tissue. Clinically a large depressed area with a slightly erythematous, swollen edge, which usually begins before the age of 3 years, occurs most commonly on the abdomen (2–5), but non-abdominal sites have also been reported (6). The lesion enlarges in a centrifugal fashion and tends to spontaneously regress after puberty (7). Histologic findings are characterized by a decrease in subcutaneous fat in the depressed area rather than in the surrounding area and an inflammatory infiltrate mainly consisting of lymphocytes and histiocytes (2).

Filamentous aggregates of collagen are distinct structures in the pathologic connective tissue of various organs. The term fibrous long-spacing collagen (FLSC) has been employed to designate collagen fibrils in which the periodicity is greater than the 64 nm periodicity of the common or native collagen fibril, and has been found in a variety of normal and pathologic tissues and organs (8). In studies of the skin, FLSC has been found in various skin disorders, such as inflammation, degeneration, and tumors (9–12).

More than 100 cases of LCAI have been reported. However, thus far no previous studies have reported the electron microscopic findings of this disorder. We herein

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report an interesting case of LCAI with the presence of FLSC, and discuss the relationship of the disorder and the structure.

CASE REPORT

A 2.5-year-old Japanese girl presented with a cutaneous depression on her left lower abdomen beyond the inguinal region. Pregnancy and delivery had been normal, and birthweight was 2998 g. At about 1 year of age, her mother noticed a slightly bluish patch of about 3 cm in diameter in the left inguinal area which gradually depressed and enlarged in a centrifugal distribution. No trauma or injection preceded the appearance of the lesion. There was no consanguinity on examination of the family history.

On examination, the patient's height was 87 cm, weight was 12.5 kg, and psychomotor development was normal. Several pigmented macules, possibly nevus spilus, were observed on the trunk, but there was no evidence for a neurocutaneous syndrome or connective tissue disease, such as morphea. A depressed area with a slightly erythematous border was observed on the left groin and the lower abdomen (Fig. 1). The underlying blood vessels were visible through the skin and regional lymphadenopathy was noted.

Complete blood count showed normal numbers of red blood cells, white blood cells, and platelets. Autoanti-

bodies including antinuclear antibody and anti-DNA antibody were negative. There were no serologic findings suggestive of α_1 -antitrypsin deficiency.

A biopsy specimen was obtained from the border of the lesion including the uninvolved skin, divided into two pieces and used for histologic, immunohistochemical, and ultrastructural studies. Biopsy of the central portion of the lesion was not performed. The tissue samples for histology, immunohistochemistry, and electron microscopy were prepared and investigated using standard techniques.

Histologic examination showed that the epidermis appeared normal, with a mild perivascular infiltrate of lymphocytes in the upper dermis. The skin appendages were well preserved. The most characteristic changes were noted in the subcutaneous fatty tissue. A decrease of fat as well as inflammatory infiltrates mainly composed of lymphocytes and histiocytes were observed. There was a mild degree of fibrosis and thickening of the fat septa. Slight endothelial swelling was observed, but vasculitis was not present. Immunohistochemistry showed that infiltrating mononuclear cells were predominantly positive for reactivity with CD4, whereas CD8 was expressed in a small number of lymphocytes.

Ultrastructurally the nuclei in adipocytes were crescent shaped and placed toward the periphery of the cell. Lipid droplets of various sizes were observed in the cytoplasm. Cell organelles, such as Golgi complex and mitochondria, were well developed. A large number of banded structures, which were occasionally closely associated with normal collagen fibers, were observed in the septal area of fatty tissue. The length of these structures ranged from 5 to 20 μm , and the width from 1 to 2 μm (Fig. 2). The structures were spindle shaped and showed cross-bands (50 nm in width) that were repeated at approximately 150-nm-wide intervals. Fine intraperiodic bands were also observed in these banded structures. The presence of proteoglycans in FLSC was looked for as described previously (13), but none were found. In the follow-up study, resolution was noted about 10 years after the onset of the lesion.

DISCUSSION

In the present study we document FLSC in the fatty tissue in LCAI for the first time. LCAI is characterized by a unique cutaneous eruption and by inflammatory reaction in the fatty tissue, which spontaneously remit in some instances, as observed in our patient. As far as we know, no previous studies have addressed the electron microscopic findings of LCAI.

FLSC in vivo has been observed in various physiologic and pathologic conditions. Dingemans and Teel-

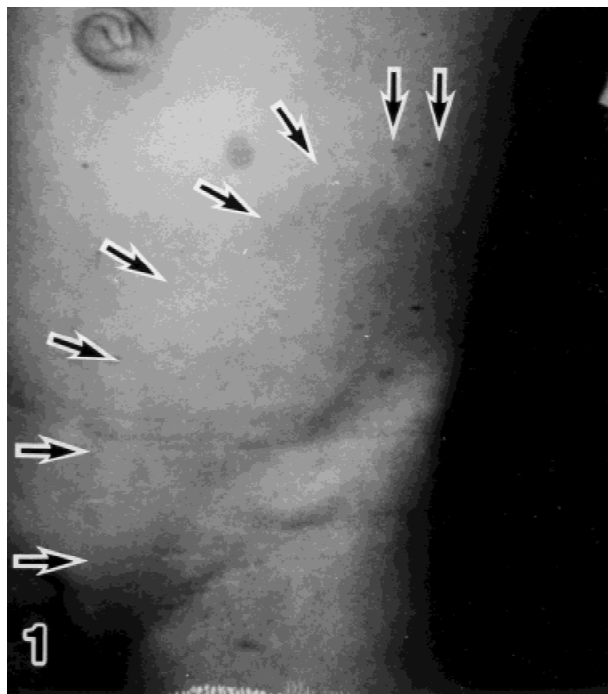


Figure 1. A well-defined, depressed lesion, surrounded by slight erythema in the left groin (arrows).

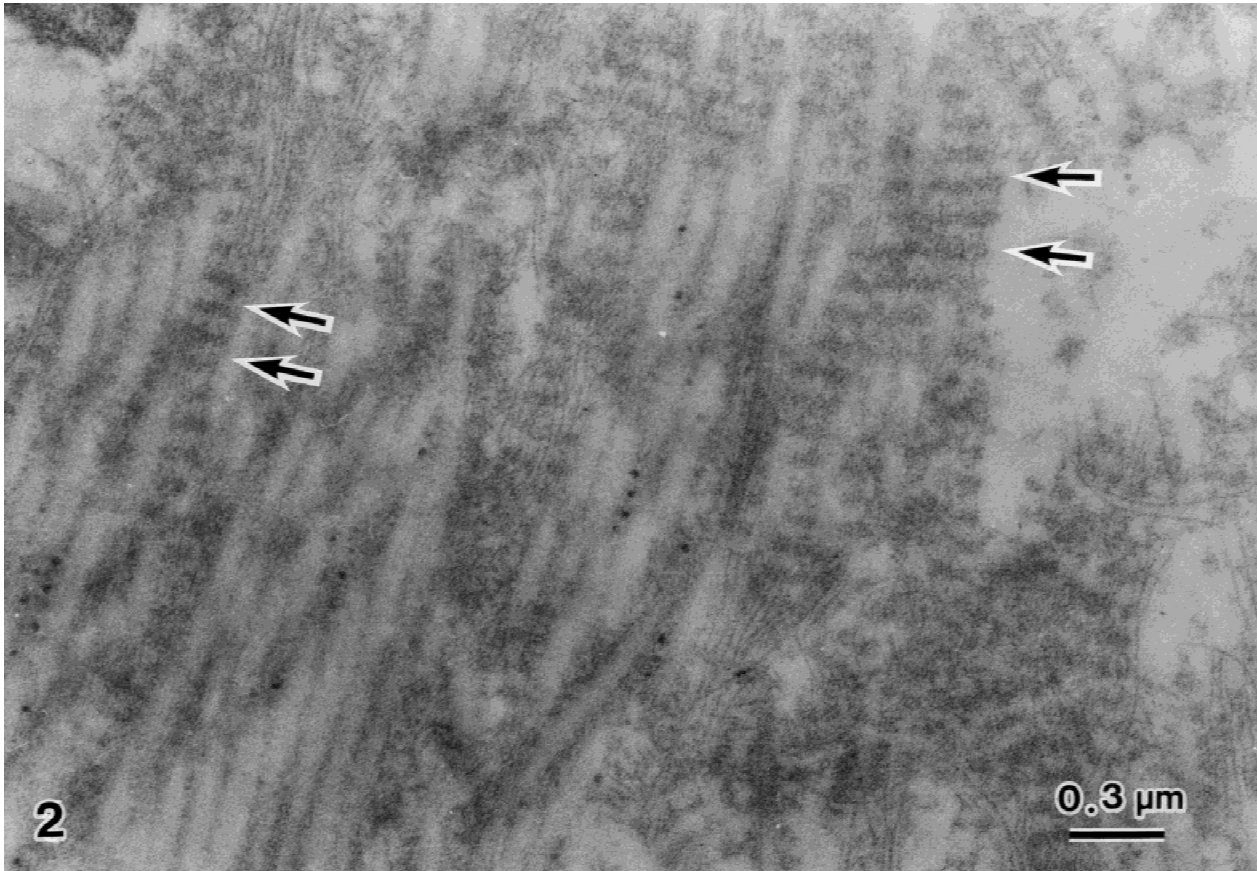


Figure 2. Ultrastructural findings. The banded structure is spindle shaped and shows cross-bands that are repeated at approximately 150-nm-wide intervals (arrows) (magnification 45,000 \times).

ing (13) showed that two forms of FLSC could be distinguished by whether they contained proteoglycans or not. A compact form of FLSC contains proteoglycans, whereas a dispersed form of FLSC does not. The conditions under which the compact or dispersed forms of FLSC occur in tissues suggest a completely different physiologic significance. As shown in our results, which demonstrated no deposition of proteoglycans, FLSC in LCAI may be identified with the dispersed type. The compact type of FLSC has been observed in various mesenchymal tumors (14,15). On the other hand, the dispersed type has been found in granulation tissue and in normal human skin treated with bacterial collagenase (13,16).

At present the biological significance of the dispersed type of FLSC has not been extensively defined. Some investigators have demonstrated that collagenase activity was of substantial importance in the formation of FLSC (13,17). So the FLSC observed in our case may represent an intermediate stage in the breakdown of fibrillar collagens. Although the etiology of LCAI is still unknown, two possibilities may be proposed about the initial patho-

logic change. One is that the changes occur in the adipocytes themselves and the other is that the septal area of fatty tissue is the primary location. In the former view, FLSC may be correlated with secondary fibrotic change after inflammatory reaction. However, in the latter view FLSC may result from the degradation of septal areas and may contribute to the advancement of the study of the pathogenesis of LCAI. Further investigations into the pathogenesis of LCAI should be interesting and informative.

REFERENCES

1. Imamura S, Yamada M, Ikeda T. Lipodystrophia centrifugalis abdominalis infantilis. *Arch Dermatol* 1971;104:291–298.
2. Imamura S, Yamada M, Yamamoto K. Lipodystrophia centrifugalis abdominalis infantilis: a follow-up study. *J Am Acad Dermatol* 1984;11:203–209.
3. Gian YG, Rajan VS, Hock OB. Lipodystrophia centrifugalis abdominalis infantilis. *Br J Dermatol* 1982;106:461–464.
4. Lee S, Houh W, Kim YK, Chun SI, Cho BK. Lipodystro-

- phia centrifugalis abdominalis juvenilis. *Dermatologica* 1982;164:95-100.
5. Llistosella E, Puig L, Perez F. Lipodystrophia centrifugalis abdominalis infantilis: a case report. *Pediatric Dermatol* 1997;14:216-218.
 6. Caputo R. Lipodystrophia centrifugalis abdominalis infantilis: a 15-year follow-up observation. *Acta Derm Venereol* 1989;69:442-443.
 7. Spraker MK, Garcia-Gonzalez E, Sanchez LT. Sclerosing and atrophying conditions. In: Schachner LA, Hansen RC, eds. *Pediatric dermatology*. New York: Churchill Livingstone, 1995.
 8. Chadially FN. Extracellular matrix (extracellular components). In: Chadially FN, ed. *Ultrastructural pathology of the cell and matrix*. London: Butterworths, 1988.
 9. Hashimoto K, Ohyama H. Cross-banded filamentous aggregation in the human dermis. *J Invest Dermatol* 1974; 62:106-112.
 10. Kobayashi T, Asboe-Hansen G. Ultrastructural changes in the inflammatory zone of localized scleroderma. *Acta Derm Venereol* 1974;54:105-112.
 11. Kobayashi T, Danielsen L, Asboe-Hansen G. Ultrastructure of localized myxedema. *Acta Derm Venereol* 1976; 56:173-185.
 12. Kojimahara M, Yamazaki K, Ooneda G. Ultrastructural study of hemangiomas: capillary hemangioma of the skin. *Acta Pathol Jpn* 1981;31:105-115.
 13. Dingemans KP, Teeling P. Long-spacing collagen and proteoglycans in pathologic tissue. *Ultrastruct Pathol* 1994;18: 539-547.
 14. Park P, Ohno T. Ultrastructural study of long spacing collagen fibers and basal lamina in malignant schwannoma. *Tissue Cell* 1985;17:699-707.
 15. Navas-Palacios JJ. The fibromatoses: an ultrastructural study of 31 cases. *Pathol Res Pract* 1983;176:158-175.
 16. Sawada H, Furthmayr H, Konomi H, Nagai Y. Immunoelectron-microscopic localization of extracellular matrix components produced by bovine corneal endothelial cells in vitro. *Exp Cell Res* 1987;171:94-109.
 17. Kajikawa K, Nakanishi I, Yamamura T. The effect of collagenase on the formation of fibrous long spacing collagen aggregates. *Lab Invest* 1980;43:410-417.