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*Editorial*

# Degenerative change of adipose tissue; the so-called membranous lipodystrophy

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Membranous lipodystrophy is the name given by Nasu et al. of Japan in 1973 to a rare disease in which cyst-like lesions of fat occur in subcutaneous and other sites (including within long bones) together with sudanophilic leukoencephalopathy. The same disease was reported earlier by Finnish doctors (Järvi et al. 1968; Hakola et al. 1970; Järvi 1970; Sourander 1970; Hakola 1972) and described under the title of "osteodysplasia polycystica hereditaria combined with sclerosing leukoencephalopathy", or "new hereditary disease charcterized by progressive dementia and lipomembranous polycystic osteodysplasia. Since then approximately 60 cases have been reported in Japan (Inoue et al. 1975; Yagishita et al. 1976; Akai et al. 1977; Tanaka 1980; Kitajima et al. 1988), 10 cases in Finland (Laasonen 1975; Hakola and Partanen 1983), and 5 cases in USA (Wood 1978; Bird et al. 1983).

The cyst-like lesions of limb bones which occur in this rare disease progress in early adult life. The lesions cause local pain, tenderness and pathological fractures, usually followed by neurological disorders including convulsions and presenile dementia. Most of the patients die in the thirties or early forties from bronchopneumonia. Histopathological diagnosis is possible by biopsy of the bone marrow or synovial tissue (Akai et al. 1977; Wood 1978). The fat cells of the bone marrow, synovial membrane and other sites are replaced by a convoluted, hyaline, eosinophilic membrane of variable thickness that surrounds a large space. The membrane is PAS positive but negative by resorcinol fuchsin, staining for elastic tissue. Masson's trichrome and Azan-Mallory stainings of the membrane are blue or red. In frozen sections, the membranes and the content of the cyst-like space are Sudan III positive. The membrane is also clearly stained blue by luxol fast blue (Nasu et al. 1973; Wood 1978).

Ultrastructurally the convoluted membrane was found to be 1 or 2 micron in thickness and was a highly complex substance of perpendicularly projecting microvilli that alternated with more or less focally dilated tubular crypts, which resembled smooth endoplasmic reticulum. The inner aspects of the microvillous complex were well demarcated and it enclosed amorphous highly osmiophilic material. Higher magnification did not show any definite trilaminar structure of the unit membrane that composed of the microvilli or crypts. The outer surface of the membrane was poorly defined showing direct contact with amorphous intercellular substance (Nasu et al. 1973; Wood 1978). Membranocystic lesions with thinner membranes without tubular structures were also found (Kitajima et al. 1988).

Neuropsychiatrically, progressive presenile dementia resembling Pick's disease and impaired function of the pyramidal tracts were found. Pneumoenceophalography showed central atrophy and EEG pointed to deep subcortical lesions. Abnormal behaviour, epileptic seizures and urinary incontinence were also found (Sourander 1970; Hakola 1972, 1983; Nasu et al. 1973). Post mortem examination of the brain revealed cerebral atrophy with marked symmetrical dilatation of the ventricles and diminuition of the white matter. Microscopically, atrophy of the subcortical white matter of the frontal and temporal lobes with marked astrocytosis and fibrillary gliosis and slight or moderate degeneration of myelin sheaths were the most prominent changes. The cortical grey matter was generally well preserved.

Extensive genetic study by Hakola (1972) has revealed that an autosomal recessive gene responsible for the inheritance of the disease complex would explain both its sporadic and familial occurrence. Although the analysis of bone marrow lipids showed no departure from the normal preponderance of triglycerides and fatty acids, the membranous change of the fatty tissues has been considered to be the result of metabolic disorder (Nasu et al. 1973; Wood 1978).

I have found exactly the same membranocystic changes in subcutaneous fat tissue in 53 percent of patients with ischaemic necrosis of the extremities (Machinami 1983, 1984). It has been shown that the membranous lipodystrophy-like changes can be produced by

several forms of circulatory disturbance and that they are one of the non-specific changes of adipose tissue. Membranocystic lesions in fat similar to those of membranous lipodystrophy have been reported in several conditions other than membranous lipodystrophy, such as lupus erythematosus profundus, fat tissue granuloma, experimental ischaemic change of bone marrow, experimental induction of myelofibrosis by saponin, atherosclerotic plaques and degenerating fibrocartilage (Abrikossoff 1929; Horie 1954; Arnold 1956; Rutishauser et al. 1960; Shimamine 1976; Nasu 1978; Machinami 1988). It is thus very interesting to note, that circulatory disturbance due to arteriolar and capillary necrosis was originally considered to be responsible for the membranocystic lesions of membranous lipodystrophy (Järvi 1968; Hakola 1972). I have proposed, following electron microscopic studies, that free fat droplets released from degenerated fat cells are processed by macrophages to produce membranocystic lesions (Machinami 1983). However, no experimental data have yet been obtained to support this idea. The membrane of the membranocystic lesions has been reported to be autofluorescent and composed of carbohydrate and lipid including phospholipid, by conventional histochemistry (Nasu 1978; Fujiwara 1979; Wolman 1980). Although recent histopathological and electron microscopic studies using lectin histochemistry have demonstrated the presence of alpha D galactose residues in the membranocystic lesions (Kitajima et al. 1988), the aetiology and pathogenesis of this disease is still unknown.

## References


Abrikossoff A (1929) Über das Schicksal der spontan auftretenden Fettgranulome (lipophagen Granulome). Verh Dtsch Ges Pathol 24:57–64

Akai M, Tateishi A, Cheng CH, Morii K, Abe M, Ohno T, Ben M (1977) Membranous lipodystrophy. A clinicopathological study of six cases. J Bone Joint Surg 59 (Am):802–809

Arnold HL (1956) Lupus erythematosus profundus. AMA Arch Dermatol 73:15–32

Bird TD, Koerker RM, Leaird BJ, Vluk BW, Thorning DR (1983) Lipomembranous polycystic osteodysplasia (brain, bone and fat disease): A genetic cause of presenile dementia. Neurology 33:81–86

Fujiwara M (1979) Histopathological and histochemical studies of membranocystic lesion (Nasu). Shinshu Med J (in Japanese) 27:78–100

Hakola HPA, Järvi OH, Sourander P (1970) Osteodysplasia polycystica hereditaria combined with sclerosing leukoencephalopathy. Acta Neurol Scand (Suppl) 43:79–80

Hakola HPA (1972) Neuropsychiatric and genetic aspects of a new hereditary disease characterized by progressive dementia and lipomembranous polycystic osteodysplasia. Acta Neuropsych Scand (Suppl) 232:1–175

Hakola HPA, Partanen VSJ (1983) Neurophysiological findings in the hereditary presenile dementia characterised by polycystic lipomembranous osteodysplasia and sclerosing leukoencephalopathy. J Neurol Neurosurg Psychiatry 46:515–520

Horie K (1954) Histologic studies on lipogranuloma. Keio J Med 3:215–225

Inoue K, Funayama M, Suda A, Higuchi I (1975) Intraosseous lipomatosis. Report of a case. J Jpn Orthop Ass 49:223–230

Järvi OH, Hakola HPA, Lauttamus LL (1968) Cystic capillary-necrotic osteodysplasia: A systemic bone disease probably caused by arteriolar and capillary necrosis: Relation to brain affections. Abstr. VII International Congress of International Academy of Pathology. Milan, pp 291–292

Järvi OH (1970) A new entity of phacomatosis: A. Bone lesions (hereditary polycystic osteodysplasia). Acta Pathol Microbiol Scand (Suppl) 215:27

Kitajima I, Suganuma T, Murata F, Nagamatsu K (1988) Ultrastructural demonstration of Maclura pomifera agglutinin binding sites in the membranocystic lesions of membranous lipodystrophy (Nasu-Hakola disease). Virchows Archiv [A] 413:475–483

Laasonen von EM (1975) Das Syndrom der Polyzystischen Osteodysplasie mit progressiver Demenz. Fortschr Röntgenstr 122:313–316

Machinami R (1983) Membranous lipodystrophy-like changes in ischemic necrosis of the legs. Virchows Archiv [A] 399:191–205

Machinami R (1984) Incidence of membranous lipodystrophylike change among patients with limb necrosis caused by chronic arterial obstruction. Arch Pathol Lab Med 108:823–826

Machinami R (1988) Membranous lipodystrophy like lesions in the fibrocartilage. Abstr. XVII International Congress of International Academy of Pathology. Dublin, p 37

Nasu T, Tsukahara Y, Terayama K (1973) A lipid metabolic disease – "membranous lipodystrophy" – An autopsy case demonstrating numerous peculiar membrane structures composed of compound lipid in bone marrow and various adipose tissues. Acta Pathol Jpn 23:539–558

Nasu T (1978) Pathology of membranous lipodystrophy (in Japanese). Tr Soc Pathol Jpn 67:57–98

Rutishauser E, Rohner A, Held D (1960) Experimentelle Untersuchungen über die Wirkung der Ischämie auf den Knochen und das Mark. Virchows Arch [A] 333:101–118

Shinamine T (1976) Chronic bone marrow failure (in Japanese). Tr Soc Pathol Jpn 65:27–60

Sourander P (1970) A new entity of phacomatosis: B. Brain lesions (sclerosing leucoencephalopathy). Acta Pathol Microbiol Scand (Suppl) 215:44

Tanaka J (1980) Leukoencephalopathic alteration in membranous lipodystrophy. Acta Neuropathol 50:193–197

Wolman M (1980) Lipid pigments (Chromolipids): Their origin, nature and significance. Pathobiol Annual 10:253–267

Wood C (1978) Membranous lipodystrophy of bone. Arch Pathol Lab Med 102:22–27

Yagishita S, Ito Y, Ikezaki R (1976) Lipomembranous polycystic osteodysplasia. Virchows Archiv [A] 372:245–251