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FAMILIAL MULTIPLE LIPOMATOSIS

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Abstract. A family genealogy, comprising four cases of familial multiple lipomatosis, making their appearance one after the other in three generations is reported. Two cases with impressive clinical features are presented in detail. This report contributes to the opion that the disease is transmitted by the autosomal dominant route of inheritance.

Key words: Lipomatosis; Hereditary disease; Dominat inheritance

Familial multiple lipomatosis (FML) is rarely a hereditary disease. Cases described with an autosomal dominant and, rarely, recessive inheritance (2, 4, 7) appearing in two and three generations can be found in literature. Recently, Italian authors reported cases of FML in two families, with autosomal recessive inheritance in four, and dominant in two generations (5).

Our paper deals with a familial genealogy (Fig. 1) including four cases of FML. The disease was determined in 3 of 6 surviving members of the family and anamnestic data showed the same changes in mother and grandmother (both deceased).

CASE REPORTS

Case 1. K. I., a 72-year-old farmer from Lak-Martin village, on the island of Krk, SR Croatia, Yugoslavia. Case history No. 10377/1978.

Familial anamnesis: His father, who was born in a neighbouring village died of stomach cancer. His mother had numerous "swellings" on her trunk and arms that had appeared in her twenty-fifth year of life. Her parents were from the same place but they were not related. His brother was killed in the war in his 19th year of life; one sister died from heart trouble when she was fifty. Neither showed similar skin changes. Three sisters are still alive. One is married and has four children. The other two are unmarried and have no issue. All are healthy and without skin changes.

The patient's wife is also healthy. Her parents were from the same place, and were not related. A daughter is 47 years old. She is not married and has "such swellings" all over her body. The son is 45 years old, married and childless, and has had the same swellings on trunk and arms since his 23rd year, though much smaller in size.

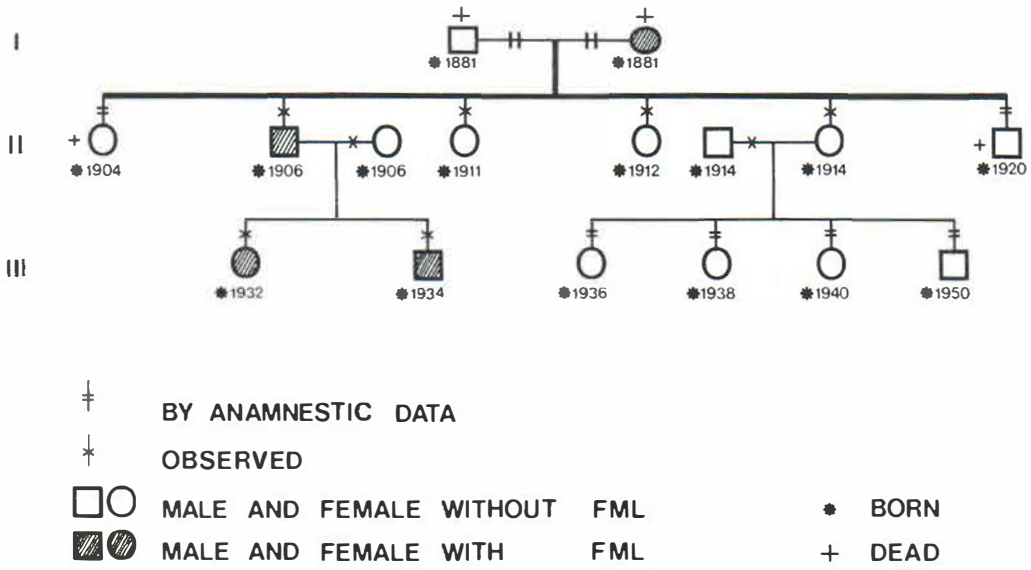

Fig. 1. The genealogical tree of family K.

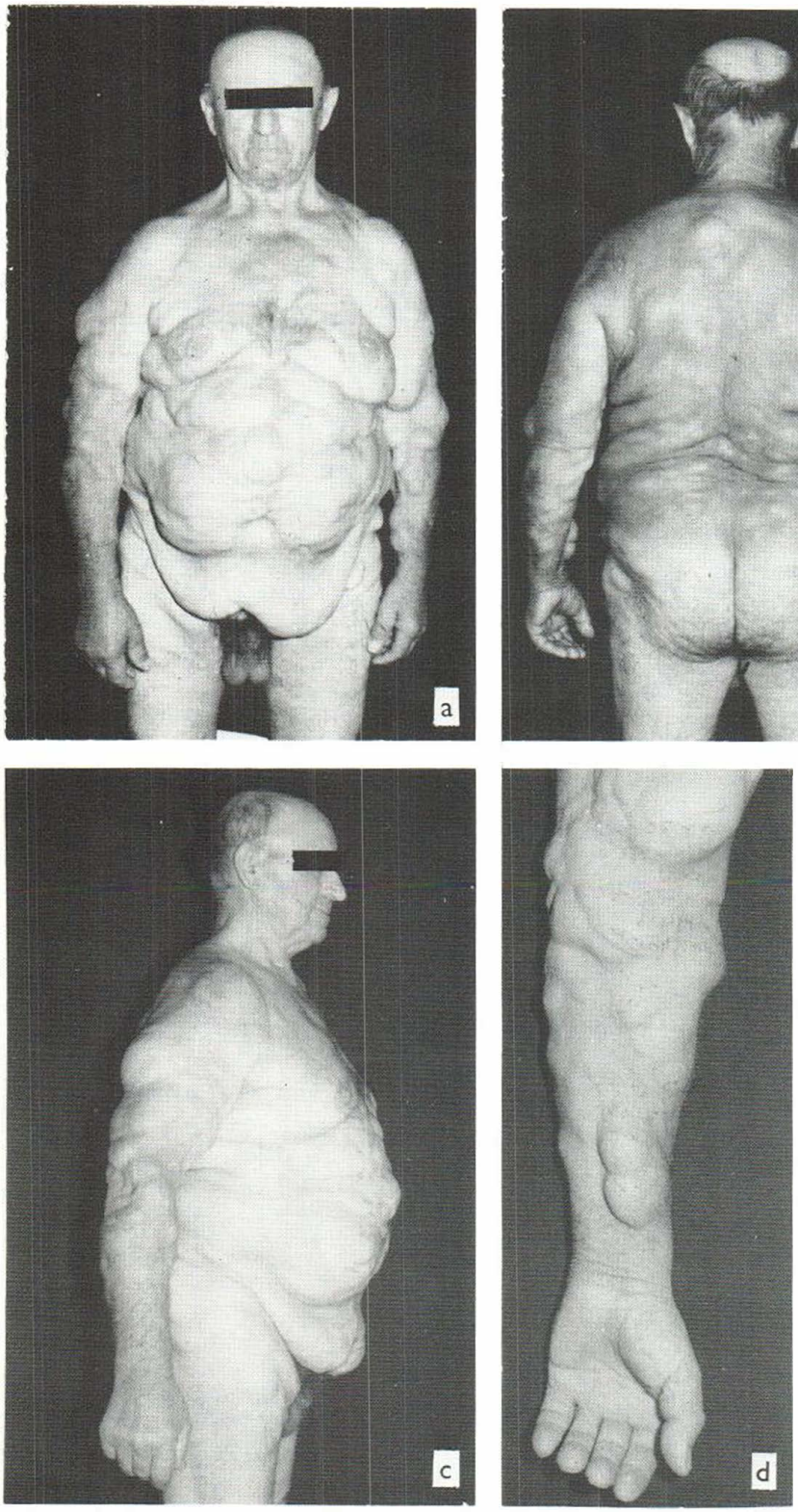

Fig. 2. Case 1. (*a*) Anterior aspect; (*b*) posterior; (*c*) lateral. (*d*) Detail of volar side of left forearm.

Personal anamnesis: The patient has never been seriously ill. The first growth he noticed on the skin of the right forearm when he was twenty. Similar growths appeared and gradually enlarged on the trunk, arms and legs up to the knees in the course of hard work on the farm.

Clinical features: Numerous tumorous growths ranging in size from that of a hazel nut to that of a hen's egg and even larger can be seen on the front and back sides of the trunk, on the arms, and on lower extremities up to the knees. These growths are round, soft, movable in relation to the substratum, smooth, hemispheric and painless on pressure. The skin above the tumours is movable. On the limbs the tumours are predominantly single, while those on the trunk and belly wall are numerous and grouped, forming in some places uneven plaques of varying size and form. Symmetric occurrence has been observed. The tumours on the lower part of the belly are so large that, by their own weight, in the standing position especially, they form two hanging, sack-like growths covering both groins (Fig. 2*a, b, c, d*).

General status: Height 169 cm, body weight 95 kg, skin colour yellowish. Visible mucous membranes are unchanged. Internal (EKG), ocular, neuropsychiatric (EMG, EECG), otorhinolaryngological and stomatological clinical findings are in the range of normality or else correspond to the patient's age. RR: 160/90. He does not smoke, but drinks about 1–2 litres of fortified wine every day. Roentgenologic photo of lungs: standard photos of thoracic organs do not reveal signs of active intrapulmonary changes. The heart shadow is of a hypertrophic configuration. Retrosternal and retrocardiac spaces are normal. No pathological chages have been noted in bones in roentgenologic photos of skeleton.

Laboratory findings: Seroreactions to syphilis were non-reactive; sedimentation 11/30; blood sugar 45 mg%; leukocytes 4700; red and differential white counts were normal. Complete urinary status was normal; NPN in blood 31.46 mg%. Liver tests were normal; acidum uricum 4.4 mg%; total lipids 1170 mg%; cholesterol 260 mg%; triglycerides 65 mg%. Lipidogram: alpha 28%; prebeta 4%; beta 68%; 17-ketosteroids from the urine 11.2 mg/24^{h}; 17-hydroxycorticoids from the urine 4.4 mg/24^{h}. All the other laboratory investigation findings were in the normal range.

Pathohistologic diagnosis: Lipoma (excised tumour from the right forearm). Large fat cells, peripherally surrounded by thin fibrous capsule containing some enlarged blood vessels, could be seen in the preparation. Nuclei were without atypical forms and mitoses. There were no signs of any other proliferation or inflammation (Fig. 3).

Karyogram: The analysis of chromosomes showed the male karyotype 46 XY. Aberrations of chromosomes have not been noted according to the method applied to peripheral blood (Institute for General Biology, Medical Faculty, University of Rijeka).

Case 2. K. M., a 47-year-old, unmarried childless worker who lives in the same place on the island of Krk, as patient no. 1.

Personal anamnesis: Some soft growths appeared on the skin of the arms when she was 27. The same changes later occurred on other parts of the body, spreading gradually in the course of her lifetime. During recent years the growths began to spread more rapidly. Some parts of her body also became enlarged. She is no longer troubled by the disease and is not suffering pain, but she feels tired.

Clinical features: Numerous single tumorous, ball-like, smooth growths, movable towards the substratum up to hen's egg size and larger, were visible and palpable under the skin on her trunk and extremities. Long thick folds of fat tissue have been formed on lateral sides of the thorax. A "lardy hanging belly" was markedly visible. The buttocks are large and soft, with numerous, single, densely situated smaller and larger tumours. A large tumorous growth, the size of an orange, could be seen on the outer side of the right thigh (Fig. 4*a, b*).

General status: Height 172 cm, body weight 93 kg. She neither smokes nor drinks. Menstruations are irregular. RR 150/100. The same clinical and laboratory investigations were carried out as in the previous subject. The values for total lipids, cholesterol, triglycerides and lipidograms were slightly below normal. Other findings were in the normal range.

Karyogram: showed female karyotype 46 XY. Aberrations of chromosomes were not noted according to the same method applied in the previous case.

Pathohistologic diagnosis: also revealed an encapsulated lipoma.

DISCUSSION AND CONCLUSION

The incidence of FML and certain other lipomatoses is attributed to endocrine disorders, traumas, hypercholesterolemia, neurotrophic lesions, and some chronic infections (tuberculosis and syphilis). Constitutional factors with metabolism disorders of lipids and trophoneurotic troubles in particular have been mentioned. Heredity must play the main role in the origin of FML, and other exogenous or endogenous factors appear to be of secondary importance. Consequently, some authors speak of "conatal appearance on disembryonal substratum being influenced by inheritance, trauma or neurogenic troubles" (2, 8). All clinical and laboratory investigations carried out in our patients gave values in the normal range.

Lipomas are most frequent in the third decade and less frequent in the fourth and the fifth decade of life in FML. First tumours made their appearance in all our diseased subjects in the third decade of life.

The incidence and growth of tumours in FML is asymptomatic, i.e. the sick do not suffer pain (lipomatosis indolens). Although the clinical features in our two reported cases were markedly expressed, the patients did not suffer from any particular difficulty in carrying out their everyday physical tasks.

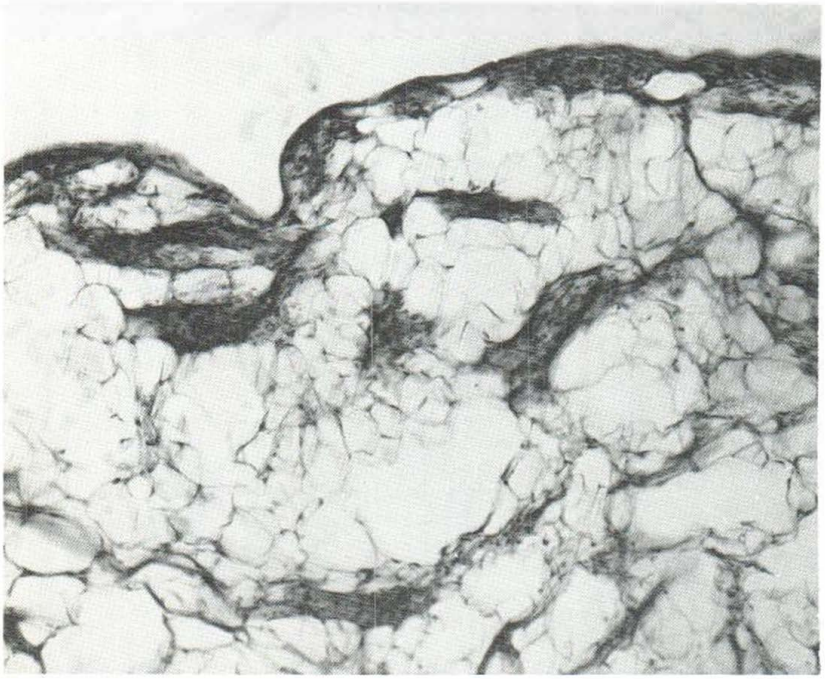

Fig. 3. Large fat cells peripherally, surrounded by a thin fibrous capsule. Nuclei without atypical forms and mitoses (hematoxylin-eosin, ×125).

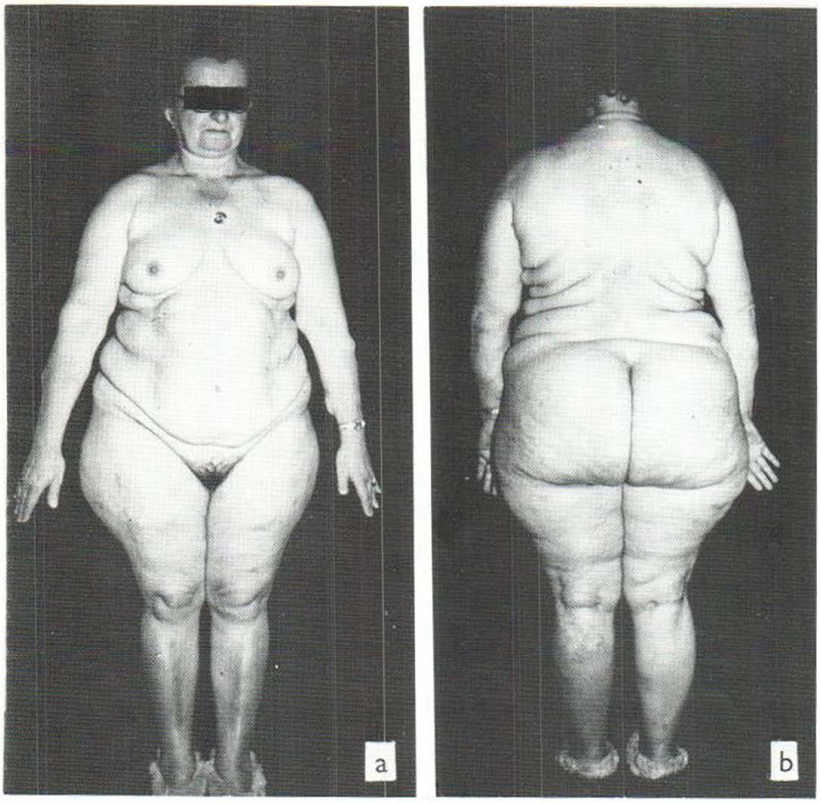

Fig. 4. Case 2. (*a*) Anterior aspect; (*b*) posterior.

It has been observed that the disease occurs more frequently with autosomal dominant inheritance in two, three and more generations and is sometimes combined with psychic and physical disorders. Cases with recessive inheritance have only rarely been reported (2). Our 4 subjects with FML in three generations support the theory of a dominant inheritance. If we consider the incidence of the disease in four children of the youngest sister, whose status is unchanged, then we could speak about the possibility of the recessive type of inheritance.

FML has been found twice as often in males as in females. The dominant inheritance was noticed in 32 families of 37 observed, 16 of them showing a significant male prevalence (7). There was no sex prevalence in our cases.

Clinical differential diagnosis included tumorous growths in neurofibromatosis, multiple leiomyomatosis, generalized xanthomatosis and cystic growths in multiple steatocystomatosis. Because of its asymptomatic development and similar tumorous growths, the last-named can cause the most diagnostic troubles (1). Reliable diagnosis is established in doubtful cases by histopathological examination. Histological pictures of tumours in our patients showed circumscribed encapsulated lipomas.

Differential diagnostic FML differs from lipomatosis dolorosa Dercum. This disease sometimes displays a similar clinical picture but it is followed by pain as a dominant symptom. It occurs more frequently in women in menopause and the localization of lipomatous growths is more widespread on the trunk and upper extremities. The familial incidence is very rarely observed (3).

The term FML has often been used for similar lipomatoses such as lipomatosis Launois-Bensaude. This disease has generated a multiplicty of synonyms, being a polyetiologic syndrome with local, demonstrably symmetric, painless accumulation of fat tissue, predominantly in the region of lymphatic tissue. The question of inheritance and the familial hereditary disposition has not been firmly established in spite of some cases reported in the literature which support this opinion. Chronic alcoholism with disordered fat metabolism has often been mentioned as one etiologic factor (6).

It can be concluded, finally, that our cases can be readily excluded from all other lipmatoses and similar diseases on the basis of their genesis, form, painlessness and dominant inheritance of the disease.

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