Familial Multiple Lipomatosis

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Key words: multiple lipomatosis, hereditary disease, surgical excision

Abstract

Background: Familial multiple lipomatosis is an extremely rare disease. The disease usually does not affect the daily life of FML victims, but they may experience difficulty in performing everyday physical tasks if the lipomas are multiple and large. Inheritance is frequently by autosomal dominant transmission, although cases with recessive inheritance have also been reported.

Objectives: To determine the pattern of inheritance of the disease in a family with 83 members spanning three generations.

Methods: A complete family analysis was performed and all surviving members of the family were examined. Laboratory investigations were conducted in those with FML, including serum lipid, cholesterol and glucose levels, white blood cell count, hemoglobin, erythrocyte sedimentation rate, and renal and hepatic function tests.

Results: There were no consanguineous relationships between spouses in the family. The disease was first seen on the neck of the (male) index patient. This patient had 4 sons, 8 daughters and 60 grandchildren. The disease was established in four of his daughters and two of his sons. One of the female grandchildren whose mother has the disease was also affected. The laboratory findings were normal for all patients.

Conclusion: Our findings showed that a) the disease is transmitted by the autosomal dominant route of inheritance; and b) lipomas observed at an early age may be numerous and large, may diffuse, and sometimes have to be excised surgically.

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While lipoma is one of the most common benign soft tissue tumors, familial multiple lipomatosis is extremely rare. In FML, lipomas are usually painless and patients are not troubled by the disease [1,2]. Sometimes however, tumors are excised because they create a problem, as occurred in a member of the family that we investigated. In this patient, multiple lipomas on the right thigh became so enlarged that the patient was unable to wear trousers.

In the majority of cases the disease is reported to occur with autosomal dominant inheritance [1–5], although recessive inheritance has also been reported [4,6]. We investigated an affected family spanning three generations to determine the pattern of inheritance of FML.

Materials and Methods

We investigated an FML-affected family with a total of 83 members. A complete family analysis was performed and all the members of the family were examined. In those affected by FML, laboratory investigations were conducted, including serum lipid, cholesterol and glucose levels, white blood cell count, hemoglobin, erythrocyte sedimentation rate, and renal and hepatic function tests.

FML = familial multiple lipomatosis

Results

The disease was observed first on the neck of a man (the index patient). He had 12 children, 2 of whom died in infancy and another 3 died from other diseases at ages 22, 23 and 45 years. Of his surviving children, four daughters and two sons suffer from FML. These siblings have 60 children. One of his granddaughters, aged 25, has FML, and her mother (the daughter of the index patient) also has the disease. There were no consanguineous relationships between spouses in the family [Figure 1]. All but one family member have small lipomas on their arms, forearms and thighs which appeared in the third and fourth decade of life. However, when the youngest son of the index patient was 14 years old, he noticed a tumor on his right thigh. The tumor slowly enlarged and multipled. Another tumor appeared on his left thigh, both arms and trunk. Recently, a tumor arose on the proximal part of the right leg. Lipomas on the right side were more numerous and larger than the lipomas on the left side. The tumors were movable and painless. Because of his difficulty in wearing trousers this patient asked us to excise some of the tumors on the right thigh [Figure 2]. During surgery under spinal anesthesia, we excised multiple tumors that were localized subcutaneously on the anteromedial and anterolateral part of the right thigh. They resembled a bunch of grapes, were encapsulated and bright yellow in color [Figure 3].

Serum lipid, cholesterol and glucose levels, white blood cell count, hemoglobin, erythrocyte sedimentation rate, and renal and hepatic function tests were within the normal range in all the FML-affected family members.

Discussion

Familial multiple lipomatosis is a very rare benign condition. It is usually transmitted by the autosomal dominant route of inheritance [1–5], although cases with recessive inheritance have also been reported [4,6]. Some authors [7] claim that FML is particularly prevalent in males, but the female-to-male ratio is usually close [1,3,4].

The first patient of the family that we investigated had 4 sons, 8 daughters and 60 grandchildren. Four of his 12 offspring died before the third decade of life from other diseases. There were no consanguineous relationships between spouses in the family. The disease was established in four of the patient's daughters and two of his sons, indicating that approximately half of the siblings were affected. We may presume that his four deceased offspring may also have been affected. One of the female grandchildren whose mother

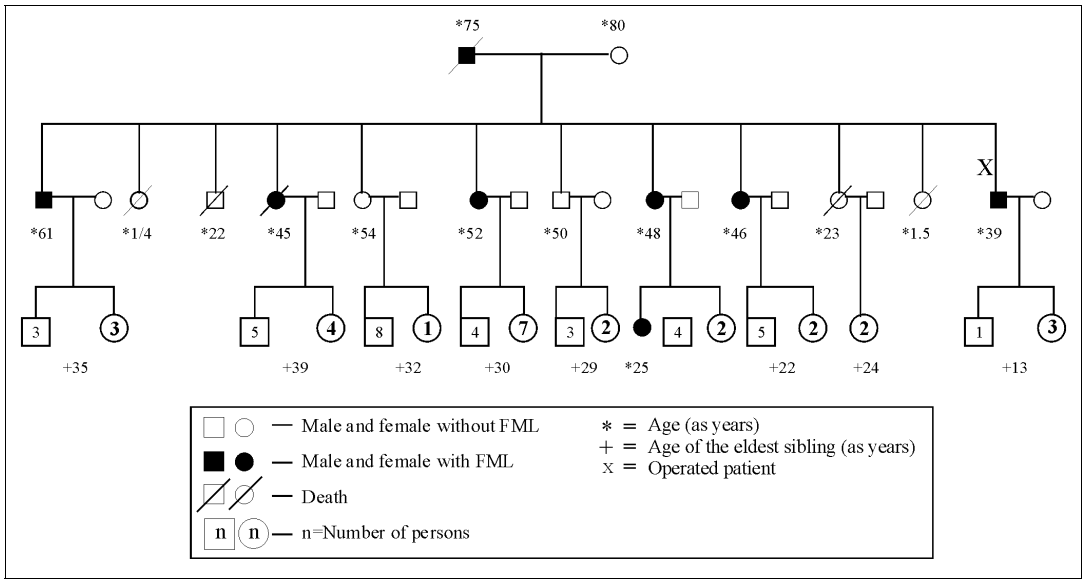

Figure 1. Pedigree of the family.

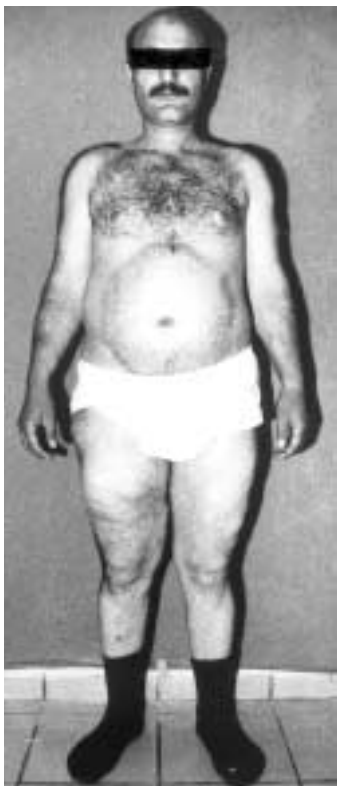

Figure 2. Photograph of the operated patient

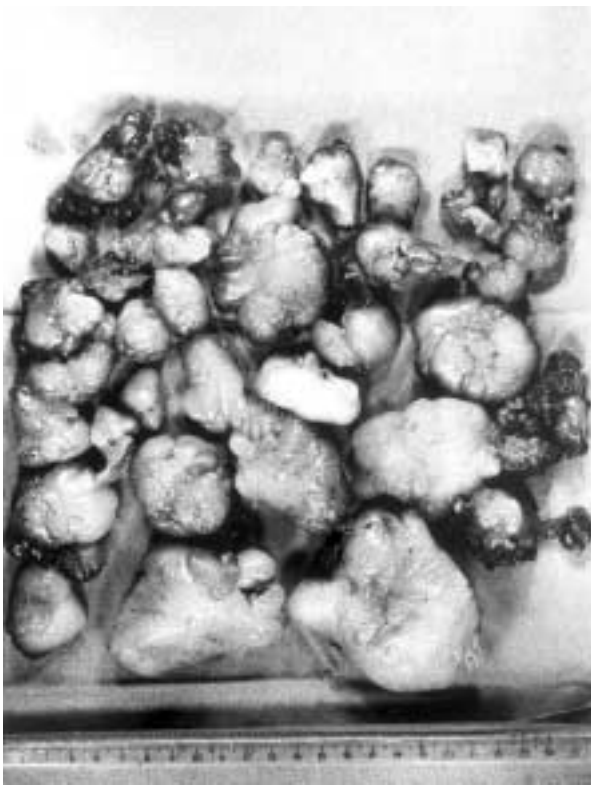

Figure 3. Excised lipomas

was this combination present.

Lipomas are generally painless and do not affect the daily activities of afflicted individuals [3,4]. This was confirmed in the youngest son of our family, who did not have pain related to lipomas. However, because of the multiple lipomas on the right thigh, the diameter of the right thigh enlarged and the patient had difficulty wearing pants. The patient requested that some of the lipomas on the right thigh be excised.

According to the literature, FML lipomas usually appear in the third decade, and rarely in the fourth or fifth decades [3,4]. Leffell and Braverman [9] reported that FML lipomas are seen on the neck, and are movable and solitary. Some authors, however, have reported lipomas on the trunk, arm and thigh [1,3,4].

According to the history of the family described here, the disease had been observed only on the neck of the first patient. In the other family members who were afflicted with FML the lipomas were localized on the trunk, the upper extremities and the thighs. They were few in number and had not caused any problem. In addition, these lipomas had arisen in the third and fourth decades. Unlike in the other affected family members, in the youngest son the first lipoma was noticed when he was 14 years old, i.e., in the second decade. We believe that due to the early onset of the disease, the lipomas were multiple, large and diffuse. Because onset of the lipomas was on the right side, they were more numerous and larger than those on the left side. Thus, contrary to the report of Leffell and Braverman [9], we found that FML lipomas can be diffuse and are not only localized to the neck.

In conclusion, FML is an autosomal dominant inherited disease; the lipomas appear at an early age, they may be multiple, large, diffuse, and sometimes have to be excised surgically.

was affected also has the disease. We believe that as the children grow older the number of affected individuals will increase. Our findings in this family strongly suggest that FML is an autosomal dominant inherited disease. We did not find a gender prevelance.

Some authors have suggested an association between FML and hyperlipidemia [5,8]; the patients in our family had plasma lipid levels in the normal range. Furthermore, FML has been reported to appear with peripheral neuropathy [2,6]; in none of our patients

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Does not every true man feel that he is himself made higher by doing reverence to what is really above him?

Thomas Carlyle, 19th century Scottish essayist and social historian

Capsule

B cell memory for antibody production

What persuades a memory lymphocyte to stick around for years after an infection has been cleared? For B cells, the explanations have been that either antigens persist somehow or that some B cells develop into long-lived antibody-secreting plasma cells that need no stimulation. Bernasconi et al. provide evidence for an intermediate mechanism in which non-specific stimuli – not limited to antigens from any one pathogen – spur B cells into continued antibody production. In culture, human memory, but not naive B cells divided strongly in response to CpG sequences of DNA, which are powerful signals to innate immune cells. The T cell cytokine interleukin-15 evoked the same response and, like CpG, could induce some B cells to become plasma cells. Frequencies of antigen-specific plasma B cells and levels of circulating antibody in individuals more than a decade after vaccination agreed with predictions derived from these experiments.

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Capsule

HIV protease inhibitors and Kaposi sarcoma

Treatment with HIV-1 protease inhibitors (PI) is associated with a reduced incidence or regression of Kaposi sarcoma (KS). Sgadari et al. show that systemic administration of the PIs indinavir or saquinavir to nude mice blocks the development and induces regression of angioproliferative KS-like lesions promoted by primary human KS cells, basic fibroblast growth factor (bFGF), or bFGF and vascular endothelial growth factor (VEGF) combined. These PIs also block bFGF or VEGF-induced angiogenesis in the chorioallantoic membrane assay with a potency similar to paclitaxel (Taxol). These effects are mediated by the inhibition of endothelial- and KS-cell invasion and of matrix metalloproteinase-2 proteolytic activation by PIs at concentrations present in plasma of treated individuals. As PIs also inhibit the *in vivo* growth and invasion of an angiogenic tumor cell line, these data indicate that PIs are potent anti-angiogenic and anti-tumor molecules that might be used in treating non-HIV KS and in other HIV-associated tumors.

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