

Familial Multiple Lipomatosis

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Abstract. Background. Familial multiple lipomatosis (FML) is an extremely rare disease which does not affect the daily life of the patients, but if the lipomas are multiple and large they can affect the function of the affected limbs. The disease is transmitted in an autosomal dominant fashion, but also cases with a recessive inheritance have also been reported. Objectives. This article presents the clinical case of a male with familial multiple lipomatosis in which we want to analyze the clinical particularities, family history and paraclinic values. Methods. In this case we evaluated the clinical localization of nodules and their history of growing, the associated medical history and the family history of the patient, and the laboratory investigation including serum lipid, cholesterol and glucose levels, white blood cell count, hemoglobin, erythrocyte sedimentation rate, and renal and hepatic function tests. Results. The past medical history of the patient showed no diseases, except the 3rd degree obesity and an occasionally alcohol consumption. Similar but less extensive lesions were observed in his grandfather and a cousin. The physical examination revealed multiple, subcutaneous, soft, mobile and non painful nodules located in the bilateral arms, forearms and thighs, abdomen, thorax and perineum. The lesions from the abdomen were the biggest and they deformed the region. The lipomas of the thighs, thorax and abdomen were so large that the patient was unable to wear trousers and appropriate clothing. The lipomas in the right upper limb interfered with elbow flexion. The laboratory findings were normal. Conclusions. The diagnosis of FML was based on the characteristic clinical history, family history and histopathology. Our patient had more than 100 lipomas, some of them large and because of the limitation of limbs flexion they have to be excised surgically.

Key Words: male, lipomas, multiple familial lipomatosis.

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Introduction

Lipoma is one of the most common benign soft tissue tumors, but familial multiple lipomatosis (FML) is extremely rare (0,002%). In 1846 Brodie (Brodie 1846) was the first who reported multiple lipomatosis, but the hereditary aspect of this multiple lipomatosis was reported only in 1891 by Blashko (Toy 2003). In FML the lipomas are usually painless and patients are not troubled by the disease. Sometimes these numerous, large, encapsulated or diffuse fatty tumours have to be surgically excised because they can create a problem (Keskin et al 2002). In our patient the lipomas of the thighs, thorax and abdomen were so large that the patient was unable to wear trousers and appropriate clothing. The lipomas of the forearms and arms in the right upper limb interfered with elbow movement. FML is a rare disorder of lipomas on the thorax, neck, arms, abdomen and thighs and the symptoms were first described in 1937 (Murchinson 1937). It is most likely an autosomal disorder and is met in men and women (Keskin et al 2002). The lipomas consist of fat which is rubbery and cohesive (Herbst). The largest number of lipomas previously reported in a single patient was 160 (Ersek et al 1989).

Materials and Methods

We present the clinical case of a male patient CL, age 49, who came in our department for evaluation and treatment of multiple widespread subcutaneous nodules in his body (Fig.1, 2). We

obtained the patient informed consent to use for publishing his data and photos. The lesions were long standing and some of them began during his childhood. More lesions appeared over time and some of them have been surgically excised. The physical examination revealed multiple, subcutaneous, soft, mobile and non painful nodules which are localized in the arms bilateral, forearms bilateral, thighs bilateral, abdomen, thorax and perineum.

We took laboratory investigation including serum lipid, cholesterol and glucose levels, white blood cell count, hemoglobin, erythrocyte sedimentation rate, and renal and hepatic function tests. We also investigated the presence of FML in his family.

Results

His past medical history showed no diseases, except the obesity grade 3 (IMC=36) and the occasionally alcohol consumption. Similar, but less extensive lesions, were observed in his grandfather and a cousin.

Previously, in his third and fourth decade of life, he underwent two times surgical excision of three lipomas each time. When he was admitted in our unit, in 2009, the lesions from the forearms and arms bilateral were excised under local anesthesia. Through 20 incisions 30 nodules were excised (Fig.3). The lipomas varied in size and they had a rubbery consistence.

After 4 years we excised the lesions from the thorax, abdomen, perineum and thigh under general anesthesia (Fig.4). We performed 75 incisions, and 120 nodules were excised (Fig.5).



Figure 1: Multiple subcutaneous lesions in the thighs



Figure 2: Multiple subcutaneous lesions in the thorax and abdomen



Figure 3: Multiple lipomas on the right arm and forearm.

The lesions from the abdomen were the biggest and they deform the region. In the abdominal region the lipomas on the right side were more numerous and larger than the lipomas on the left side. The nodules were painless and they did not affect the daily activities.

The histopathological examination showed the presence of globules of mature yellow adipose tissue surrounded by thin fibrous capsule.

Serum lipid, cholesterol and glucose levels, white blood cell count, hemoglobin, erythrocyte sedimentation rate, and renal and hepatic function tests were within normal range.

Based on the characteristic clinical history, family history and histopathology the diagnosis of FML was made.

Discussion

Lipomas are the most common benign tumors seen in the soft body parts, being usually solitary lesions (Ronan & Broderick 2000; Rosmaninho et al 2012), with an annual incidence in the general population of 0.21%, comprising approximately 50% of all benign soft tissue tumors (Lefell & Braverman 1986; Wilson & Boland 1994).



Figure 4: Lipoma: intraoperative aspect (through small incisions the lipomas were pulled entirely with force and because of an increased connective tissue they make an audible noise when we cut them).



Figure 5: Excised lipomas

Multiple lipomas, found on the trunk and extremities with a relative sparing of the head and shoulders, appeared mostly in the third decade of life and affecting several members of a family, may be highly suggestive of FML (Lefell & Braverman 1986; Rubinstein et al 1989). Our patient had lipomas mainly on the trunk and extremities, he had other members of his family affected, even if the lipomas appeared earlier. However, the lipomas may occur at any age and have a more diffuse distribution. It seems that the disease is not associated with any abnormalities in lipid metabolism (Rubinstein et al 1989), as it was seen in our patient.

FML is a rare benign hereditary syndrome and an incidence of 0.002% has been reported (Gologorski et al 2007). The lipomas are usually painless and they do not affect the daily activities of afflicted individuals (Rosmaninho et al 2012). Our patient had neither pain because of the tumors, nor the daily activity was affected seriously.

FML is usually transmitted in an autosomal dominant fashion (Gologorski et al 2007; Mohar 1980), but also cases with a recessive inheritance have been reported. A translocation involving

the high-mobility-group protein isoform I-C on chromosome 12 and the lipoma preferred partner gene on chromosome 3 is implicated in the disease genesis (Keskin et al 2002; Rosmaninho et al 2012; Schonmakers et al 1995; Mrozek et al 1993). We did not perform a DNA analysis for our patient. Some authors consider that spontaneous regression and malignant degeneration are rare (Toy 2003). Our patient did not observe spontaneous regression and all the lesions had benign characteristics.

It seems that men are affected twice more commonly than women (Lefell & Braverman 1986). It is important to distinguish FML from other causes associated with subcutaneous lipomas such as Madelung's disease, Dercum's disease, Bannayan-Zonana syndrome and Cowden syndrome (Lefell & Braverman 1986). Madelung's disease is a rare proliferative disorder of the adipose tissue characterized by symmetrical uncapsulated fat deposits, located mainly in the neck and shoulder regions and in 90% of the cases is associated with alcoholism (Gon et al 2005). Other associated metabolic disorders include hyperlipidaemia, hyperthyroidism, hypothyroidism, hypogonadism and diabetes mellitus. The lipomas in Dercum's disease (or adiposis dolorosa) are multiple, very painful and the disease affects mainly postmenopausal women (Wortham & Tomlinson 2005; Hansson et al 2012). Asthenia and mental disturbances are possible associated symptoms (Brodovski et al 1994). Possible etiologies include: nervous system dysfunction, mechanical pressure on nerves, adipose tissue dysfunction and trauma.

In Bannayan-Zonana syndrome the accumulation of fatty tissue is associated with development delay, hypotonia and lipid myopathy usually recognized during the first few years of life (Rosmaninho et al 2012).

Cowden syndrome is characterized by multiple hamartomas and an increased risk of certain forms of cancer. Facial trichilemmomas, papillomatous papules and fibromas are most common from the skin tumors.

The main treatment of FML is the surgical excision of the lesions, which are responsible for cosmetic and functional impairment. In our case the functional impairment was seen in the abduction and adduction of the thigh and in a decreased flexion of the right elbow. Other possible treatment techniques include liposuction (Ersek et al 1989) and injection lipolysis with phosphatidyl choline (Ronan & Broderick 2000; Bechara et al 2006). After surgical removal of the fatty lobules, some of them may recur and in some of these cases they may lead to amputation of extremity due to distortion or loss of function.

Conclusion

FML is an autosomal dominant inherited disease in which multiple, large, diffuse lipomas appear at an early age. Our patient developed in time more than 150 lipomas, some of them impairing the function of his thigh and arms, forcing a surgical excision of a large number of lesions through general anesthesia. We suggest periodical controls for an early diagnose of further lipomas.

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Citation Chirilă D, Gligor D. Familial Multiple Lipomatosis. *HVM Bioflux* 2014;6(2):66-69.

Editor Stefan C. Vesa

Received 27 July 2014

Accepted 3 August 2014

Published Online 4 August 2014

Funding None reported

**Conflicts/
Competing
Interests** None reported