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Multiple Symmetric Lipomatosis Type 2 in Females – Report of Two Cases

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SUMMARY Two patients with features of multiple symmetric lipomatosis type 2 are presented. This particular disorder with a characteristic distribution of fat should be considered on differential diagnosis of obesity. Besides being rare, it may occasionally be unrecognized, especially in females. The etiology remains unknown; however, the association with high alcohol consumption is very strong. Several issues about the possible metabolic role of lipomatous adipose tissue have been discussed. Patients with multiple symmetric lipomatosis should be treated by liposuction or surgery instead of being submitted to diets.

KEY WORDS: multiple symmetric lipomatosis, obesity, adipose tissue, liposuction

INTRODUCTION

A little more than a decade ago, the discovery of adipokines raised a new interest in adipose tissue. It has been even admitted as a new endocrine organ. Changes in fat distribution among different depots of adipose tissue have emerged as an origin of important disorders (1). Visceral adipose tissue accumulation has been considered to promote metabolic diseases like diabetes and atherosclerosis. The increase in subcutaneous adipose tissue mass is a cause of common esthetic concerns; it has been widely extracted by liposuction, but also used as implant in other correction procedures. Finally, adipose tissue has been proven as a rich source of mesenchymal stem cells that can differentiate towards adipogenic, osteogenic, chondrogenic, myogenic and neurogenic lineages. Mesenchymal stem cells have been considered as the reserve for tissue maintenance and repair with the possible future huge clinical implications (2).

In times when an obesity epidemic has been overwhelming the contemporary health care, we present a specific disorder of fat accumulation, multiple symmetric lipomatosis (MSL). A deeper insight into this disease might also bring novel perspectives in the problem of obesity. Brodie was the first to observe MSL in 1848, but Madelung in 1888 and Launois Bensaude in 1889 described the disorder in series of cases, so it is usually referred to as Madelung disease or Launois Bensaude syndrome (3). MSL seems to occur more frequently in Mediterranean countries, although several cases described to date originated from different parts of the world (4).

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Two main forms of MSL are known. In type 1 MSL, lipomatous tissue is accumulating around the neck, upper trunk and arms. This type occurs in men, patients are often underweight and uninvolved subcutaneous tissue is usually reduced or even atrophic. Type 2 MSL affects both men and women. It is characterized by adipose tissue accumulation in the upper back, deltoid regions, upper arms, hips and thigh regions. Similar to an exaggerated female fat distribution producing the so-called pseudo-athletic appearance (3). We have chosen two different cases among our patients with type 2 MSL to describe the main characteristics and discuss several issues in the field.

CASE REPORTS

Case 1

A 61-year-old woman was referred to plastic surgeon because of esthetic disfigurement. She noticed initial appearance of lipoma at the age of 50 in the upper back region and it was surgically removed. However, in the last 3 years she noticed intensive enlargement of fatty deposits in her upper back but also on both arms and hips (Fig. 1). She claimed to have gained about 8 kg during that period. She entered her menopause at age 43. She smoked and admitted only moderate alcohol intake, however, her impaired liver function raised suspicion of that statement. In fact, elevated level of γ-glutamyltransferase (GGT) was the only abnormality revealed on laboratory testing.

Her body weight was 81 kg, height 161 cm and body mass index (BMI) 31.5 kg/m^2. Physical examination revealed no alterations other than lipomatous enlargements on her upper back and proximal limbs. The largest upper back lipoma as the most disfiguring one was surgically removed. Cytologic and additional histologic examination showed only normal adipose tissue.

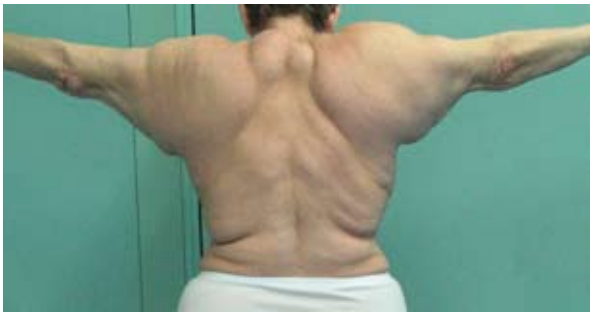
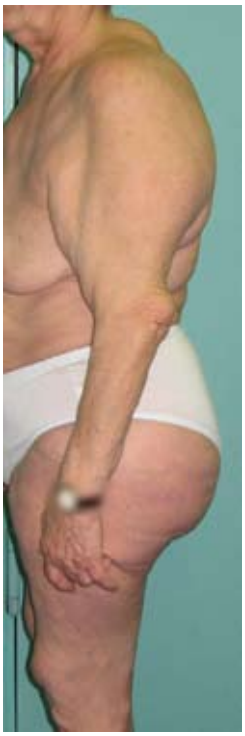


Figure 1. Case No. 1: back view (A); side view (B).

Case 2

A 74-year-old woman was referred to our endocrinology outpatient clinic because of obesity. The characteristic pattern of lipomatosis fat distribution in this generally very obese woman was first revealed during blood pressure measurement by observing disproportionate fat accumulation between her arms and forearms. On direct questioning, she remembered that she had had several lipomas “large as eggs” surgically removed in the regions of posterior knees and elbows from the age of 50. Afterwards, she observed progressive thickening of both her arms and upper legs. Her menopause onset was at the age of 44 and her weight increased from that period by about 25 kg. She admitted having drinking a lot at her younger age. Her right hip was replaced because of osteoarthritis at age 64. For the last four years, she had been treated for arterial hypertension and supraventricular arrhythmia.

Her body weight was 101 kg and height 155 cm, yielding a BMI of 42 kg/m^2. She had evident scars after lipoma excision on her elbows and knees. On palpation, her upper arms were almost completely occupied with diffuse fatty deposits and only some nodular fatty masses could be differentiated close to the right elbow. Diffuse lipomatous masses spread from her thighs to the upper third of her lower legs and ended with a relatively sharp limit. Besides that, she had a few prominent nodular



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masses of 3 to 4 cm in diameter on the back of her knees. Laboratory testing revealed only a slight temporary increase in thyroid-stimulating hormone (TSH), with no other metabolic abnormalities. No therapeutic intervention for her lipomatous tissue was planned.

DISCUSSION

Patients with type 1 MSL present with specific fat collar and due to this striking appearance the diagnosis can usually be confirmed on the first sight. However, the cases of type 2 MSL described here show that occasionally the disease may not be so evident. It is now admitted that the diagnosis of MSL is confirmed by the presence of multiple non-encapsulated lipomas, the recognition that these fat masses are symmetric and that there is persistent uninvolvement of distal parts of the forearms and legs (3,5).

For instance, the largest contemporary series of patients with MSL were recruited in Italy. During the 1974-2000 period, some 60 males and only two female patients with MSL were identified. From that time on, in only two following years, nine more women with MSL were identified (3). All women reported up to now in that cohort and other literature reports had type 2 MSL, indicating that its clinical expression is sex related. In fact, the unawareness and peculiar clinical picture of the disease makes us also wonder whether type 2 MSL may occasionally proceed unrecognized. The particular pathognomonic appearance may be concealed or become less evident when occurring together with simple obesity, especially in women. Our case 2 is instructing. In the beginning, the disorder was treated as simple lipomas and later, when prominent diffuse fat masses predominated, it was almost confused with simple morbid obesity. This could especially happen in elderly individuals with hanging lipomatous fatty deposits because of involution and loss of elasticity of the skin and subcutaneous tissue. Cytologic examination would be the most practical tool for this differential diagnosis but no clear differences have yet been recognized between normal and lipomatous adipose tissue.

We can only emphasize that one of the key elements to suspect the diagnosis of lipomatosis is a history of lipoma occurrence several years before. The nodular aspect of lipomatous masses can only be observed at the disease onset. Subsequently, the lipomatous tissue spreads and occupies the arms and upper parts of the legs. The evolution varies greatly, but our patients confirm that in spite of operative treatment, lipomas have high ability to regenerate (5). This is also a common excuse why liposuction as the most appropriate treatment has not been usually offered to these patients.

The etiology of lipomatosis has been related to defects in adrenergic stimulated lipolysis or proliferation of the brown adipose tissue remnants (6). However, the latest investigations refer to the possible mitochondrial metabolism impairment that leads to triglyceride accumulation in adipocytes (7). Mitochondria are also very important for alcohol metabolism. Actually, higher alcohol consumption was the most common trait in our and most other patients reported; therefore the postulated causal relationship is quite likely. Cases of MSL have also been described in patients with point mutations of mitochondrial DNA (7).

Weight gain in patients with lipomatosis is mostly attributable to the expansion of lipomatous tissue. From the practical point of view, most important is that diets should not be prescribed to lipomatosis patients because this tissue is not sensitive to calorie restriction. Although it is currently admitted that both hypertrophic and hyperplastic expansion of adipocytes exists, it is considered that enhanced adipogenesis *per se* cannot be the cause of obesity (1). Adipogenesis in obesity is claimed to be only the result of imbalance between energy intake and output, i.e. the consequence of excess calories. The accumulation of adipose tissue in lipomatosis could be an example of adipogenesis that is not calorie-dependent. The role of this type of adipocyte growth in other cases of obesity might be intriguing. Adipose tissue has depot specific characteristics. Differences are well known between visceral and subcutaneous fat, but subcutaneous adipocytes from abdominal and femoral region were also proved to have different signaling in adipogenesis (1). This kind of differences might hide the secret of the type of cells that are, under still unknown conditions, prone to proliferation and cause the singular body shape of MSL patients.

The metabolic role of the lipomatous adipose tissue seems to differ from the metabolic burden of simple obesity. Although it cannot be generalized, some results indicate a decreased insulin resistance in MSL patients. The accumulation of subcutaneous fat leads to change in the subcutaneous to visceral fat content ratio, and this may reduce the insulin resistance analogous to the action of antidiabetic drugs like PPARγ agonists, thiazolidinediones. In this way, lipomatosis has been supposed to present a more benign mean of increasing energy stores. An audacious hypoth-

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esis on MSL as a paradigm of metabolically innocent obesity has been proposed (8).

In conclusion, type 2 MSL with its characteristic distribution of fat deposits should first be remembered on the differential diagnosis of obesity. In a wider context, revealing the secret of these symmetric lipomatous deposits would contribute to the expanding knowledge about the diverse roles of adipose tissue.

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