

Multiple Benign Symmetric Lipomatosis - A Differential Diagnosis of Obesity

V. Ardeleanu^{1,2}, S. Chicos¹, C. Georgescu¹, D. Tutunaru¹

¹Emergency Clinical Hospital "Saint Andrew the Apostle" First Surgery Clinic, Galați, Romania

²"Lower Danube" University, Faculty of Medicine and Pharmacy, Galați, Romania

Rezumat

Lipomatoza multiplă benignă simetrică - diagnostic diferențial al obezității

Boala Madelung sau lipomatoza simetrică benignă (BSL), este o afecțiune rară, caracterizată de creșterea difuză, nedureroasă și progresivă de lipoame neîncapsulate simetrice. Etiologia acestei maladii rămâne necunoscută, deși în literatura de specialitate această maladie a fost asociată cu consumul abuziv de alcool și nicotină, cu tulburări metabolice și cu unele tumori maligne. Se presupune că ar exista o predispoziție genetică pentru această maladie. Conduita terapeutică în asemenea cazuri constă în ablația chirurgicală a lipoamelor, de cele mai multe ori în mai multe ședințe, însă frecvent urmat de recidivă. Cu toate acestea, ablația chirurgicală a acestor lipoame poate oferi pacientului o funcționalitate satisfăcătoare și rezultate cosmetice. Diagnosticul diferențial se face cu obezitatea morbidă, sindromul Cushing, angioliomatoză, lipoamele încapsulate, neurofibromatoza, liposarcomul mixoid, limfoame, boli ale glandelor salivare, sindromul Frölich și lipomatoza la pacienții infectați cu HIV. Lucrarea de față prezintă cazul unui bărbat de 55 de ani, care prezenta mai multe mase lipomatoase voluminoase, dispuse simetric pe fața anterioară și dorsală a trunchiului, și câteva lipoame mai mici la nivelul membrelor superioare și inferioare. Tratamentul a constat în rezecția acestor lipoame în mai multe ședințe, fără recidivă la un an după ultima operație.

Cuvinte cheie: lipomatoza simetrică benignă, sindromul Launois-Bensaude, tratament chirurgical, alcoolism

Abstract

Benign symmetrical lipomatosis (BSL), or Madelung's disease, is a rare disease characterized by the progressive growth of diffuse, painless, non-enveloped symmetric lipomas. The etiology of this disease remains unknown, although it was associated in the medical literature with alcohol and nicotine abuse, metabolic disorders and a number of malignancies. It is assumed that there is a genetic predisposition for this affliction. The management in such cases is surgical removal of the lipomas, most times in several sessions, but this is often followed by relapse. However, surgical removal of the lipomas can provide satisfactory patient functionality and cosmetic results. The differential diagnosis is made with morbid obesity, Cushing syndrome, angioliomatosis, encapsulated lipomas, neurofibromatosis, myxoid liposarcoma, lymphoma, salivary gland disease, Frölich and lipomatosis syndrome in patients infected with HIV. The current paper reports the case of a 55 year-old man, who presented with several large lipomatous masses, arranged symmetrically on the front and back of the trunk, and several smaller lipomas in the upper and lower limbs. Treatment consisted of resection of these lipomas in several sessions, without recurrence at one year after the last operation.

Key words: benign symmetric lipomatosis, Launois-Bensaude's syndrome, surgical treatment, alcoholism

Corresponding author:

Georgescu Costinela, MD
Emergency Clinic Hospital "Saint Apostol
Andrei" First Surgery Clinic, Galați
Romania
E-mail: costinelag@gmail.com

Introduction

Madelung disease, also known as benign symmetrical lipomatosis, Launois-Bensaude adenolipomatosis, Brodie syndrome, Buschke disease, multiple symmetrical lipomatosis with cervical prevalence – represents the symmetrical development of various non-enveloped painless lipomas, which can grow to considerable sizes, rendering the life of the patient harder, functionally and cosmetically speaking.

The first records referring to disease were made by B.C. Brodie in 1846 and Otto W. Madelung in 1888, respectively. The classical description of this disease, though, belongs to French doctors P.E. Launois and R. Bensaude who published a case study in 1898 based on 65 patients.

Ulpal and Nemeth (2001) have investigated the international medical literature from 1981 to 2000, thus discovering 190 publications in relation to symmetrical Launois – Bensaude lipomatosis, pointing out the aspect of it being a rare metabolic disease and, unfortunately, little known by many clinicians. The disease has a 1 to 250,000 incidence. (1)

Case report

Patient S.I., 55 years old (patient file no. 3684/24.01.2011), was admitted for various solid and large parietal tumours, which in time have affected the daily activity of the latter. (see Fig. 1,2,3)

Imaging investigations showed liver steatosis (LD/LS = 152/110), while lab results suggested liver cytolysis: TGP-47, TGO-57, GGT-132, FA-300, Chol-164, TG-55. Proteins - 7.4, uric acid - 5.3, creatinine - 0.74, urea - 25.1, glycaemia - 89, bilirubin - 0.63 with 0.18. Blood tests were normal..

From personal pathological records, hypertension, ischaemic cardiopathy and alcoholism were taken into consideration. The anaesthetic risk was evaluated as ASA III.

The patient underwent two surgeries (28/01/2011 and 16/02/2011) 18 days apart from one another, in which the lipomatous masses from the ventral thorax, at first on the right side, then the left side, were removed.

Results

Histopathological exam revealed: 1st fragment: fibrocystic mastopathy with expanded cystic glands, moderately infiltrated, chronically inflammatory disseminated stromal fibrosis, mild epithelial hyperplasia and fibroadenomatoid modifications; 2nd fragment: fragments of adipose tissue with congestive edema and interstitial hemorrhages; lipoma with stasis and recess fibrosis. Mammary gland fragment with fibrous stroma and mild intraductal hyperplasia.

Postoperative evolution was marked by the necrosis of the edges of the first wound due to lack of tissue irrigation, solved by necrectomia of the edges. The patient was discharged after 28 days.

Discussion

Multiple symmetrical lipomatosis is characterized by the presence of large adipose masses, little circumscribed, soft, painless, with progressive development, and usually placed at cervical or limb/extremity levels. Lipomatous masses develop in the subcutaneous cellular tissue and frequently infiltrate the neighbouring layers. The disease occurs generally in men aged between 30 to 60, the men/women ratio varying between 15/1 to 30/1, with the widest spread in the Mediterranean countries. (2). Multiple symmetrical lipomatosis may occur sporadically or it may be transmitted by family descent (dominant autosomal transmittance).

Enzi (3) distinguishes 2 types of lipomatosis. In type I, the lipomas are located primarily in the nuchal region and in the subclavian and deltoid regions, forming the so-called “bull's neck” (Madelung collar), in the other parts of the body, the fat is equally distributed; profound lipomatosis may occur, as in mediastinum invasion with compression of the trachea, followed by a sensation of suffocation of the patient. With type II, the lipomas are not localized in the neck area, but they are extended along the body, appearing as simple obesity. The correct diagnosis is based on symmetrical distribution of the fat mass and on the fact that the arms and legs do not present



Figures 1-4. Represent the patient's preoperative images (front and side incidences). The symmetric distribution of the lipomatous masses can be observed

lipodystrophic areas. Profound lipomatosis is not found in type II (3).

Clinically, the association with alcoholism leads to the distinction of two types of clinical presentations: in patients that do not drink alcohol, manifestations such as ataxia, dysarthria, tremor, dysmetria were recorded, while patients that associated a chronic consumption of alcohol, presented symptoms such as ataxia, pyramid syndrome, Parkinson disease, ophthalmoparesis and impotence (4,5).

Usually, obesity progresses rapidly, especially at the neck and limb levels. 60% of patients are overweight and up to 90% are chronic alcohol consumers (1). Clinical cases were described, where the adipose tissue progressed all the way down to the scrotum (6). The histological aspect is of normal fat tissue, histological studies showing an accumulation of lipids in the brown adipose tissue (BAT). The possibility of malignant transformations is exceptional. Still, Tizian (1983) has noted an intramyxoid sarcoma developed from a benign symmetrical lipomatosis and Durand (1973) published a case of liposarcoma of the same benign adipose origin(7).

Lipomas are considered to be the result of some BAT defects, coming from embryonic residues (8,9). Studies on cellular cultures regarding MSL adipocytes have shown a lipolytic defect as a response to catecholamines, which leads to triglyceride accumulation. MSL adipocytes can synthesize thermogenin (UCP-1) – a selective marker of brown adipocytes, found in BAT mitochondria. This is used to generate non-shivering heat during thermogenesis, this being the main means of heat generation in babies. In MSL adipocytes, the synthesis of UCP-1 cannot be induced by norepinephrine (NA). Furthermore, NA cannot improve the synthesis of nitric oxide, which leads to a decrease of its anti-proliferative effect and, implicitly, of the adipogenic effect (9). The initiation pathway of these modifications is unknown, but these mechanisms, by synergistic and complementary action, determine the progression of obesity. From the histopathological point of view, the adipose cells are somewhat smaller than normal, suggesting hyperplasia. Isolated adipocytes present with an increased activity of lipase lipoprotein and represent a defect of adrenergic lipolysis. The lipolytic response to cyclic AMP is intact, thus suggesting an abnormality at the level of the hormonal receiver/adenylat-cyclase. Biochemical abnormalities are not present in all cases (10).

Recent genetic studies have signalled the presence of some mitochondrial dysfunctions. Thus, dysfunctions of red fibres have been registered in skeletal muscle fibres, and also a decrease in the activity of the cytochrome C oxidase (4,11), while in the respiratory muscle fibres a decrease in the activity of the 3 enzymes of the respiratory mitochondrial chain, complex I (NADH, ubiquinone reductase), complex III (ubiquinol, cytochrome C reductase) and complex IV (cytochrome C oxidase)(12) respectively, was found.

Some authors support the idea that the activity of the disease is correlated with polyneuropathy and not with alcoholism (13). Up to present though, MSL remains a disorder that cannot be treated with drugs. Moreover, clinical studies that induce a stimulation of lipolysis through

adrenergic effect, by administering salbutamol orally, have proved to be inefficient (14).

The co-existence of a folate deficiency, the presence of macrocytic anaemia – with a liver abnormality, are due to alcoholism and not to lipomatosis. Neuropathy, be it sensory, motor or vegetative, may show different clinical forms until the appearance of neuropathic ulcer. Studies were made, in which the sural nerve was biopsied, finding chronic distal atrophy, which suggested that the neuropathy was due entirely to the illness and not to the alcohol, as axonal degeneration and demyelination, characteristic to lesions due to alcohol, were not registered (10). On the other side, some authors have described demyelination lesions.

Associated metabolic disorders can be found: resistance to insulin, hyperuricemia, hypertriglyceridemia, renal tubular acidosis, increase in liver enzymes (cytolysis, cholestasis), disorders of the thyroid function, adrenal glands, pituitary gland. Paradoxically, an increase in high density lipoproteins (HDL) (2,5,10) is registered.

Differential diagnosis is made with Madelung disease and morbid obesity, Cushing syndrome, angiolipomatosis, enveloped lipomas, neurofibromatosis, myxoid liposarcoma, lymphomas, diseases of the salivary glands, Frolich syndrome and lipomatosis in patients with HIV (15,16,17).

From the treatment point of view, different drugs were tried. The most popular method remains the administering of fibrates. Fibrates are the agonists of the alpha activator receptor of peroxisome proliferation (PPAR-alpha) and are very efficient in the treatment of hyperlipidaemia. PPAR-alpha was recently described as a suppressor of the manifestations of the proteins involved in BAT and may function by maintaining BAT in a passive state (18). Fibrates have the advantage that they are well-tolerated and, by lowering the level of triglycerides, they stop the progress of the disease.

Up to the present day, the therapeutic option of choice for this disorder, especially in cases where nerve or vessel compression appears, remains the surgical removal of the lipomas, either by lipectomy or liposuction, noting that its infiltrative diffuse aspect sometimes prevents complete removal, making the cosmetic and functional benefits of the surgery temporary. The treatment for some symptoms such as dyspnoea and dysphagia consists in surgical excision of the fat deposits, the so-called functional dissections of the neck (19). Liposuction seems the best option, although it cannot prevent recurrences (20).

Mesotherapy was also used initially, for the improvement of pain, but it is presently employed for body modelling and adipose tissue reduction. One of the substances used is lecithin, a lipolytic agent that actually stimulates the beta-adrenergic receptors. Although the basic mechanism is not clear, many of the clinical studies conducted have registered promising results by using subcutaneous injections of phosphatidylcholine for the treatment of fat deposits, including lipomas (21,22,23). The prognosis depends mainly on the association of a neuropathy which, according to some studies, may lead to death in 25.8% of cases (1).

Based on the studies conducted, we may conclude that the

most plausible hypothesis regarding the development of this disease considers as main cause either, either an enzyme defect or a modification of membrane receptors, which would determine a decrease in adrenergic lipolysis (24,25,26), or a sympathetic denervation of brown adipocytes, which would lead to the development of hypertrophy (25) and mutations in the mitochondrial DNA (24,26). In this context, alcohol consumption may function as a co-factor, causing a decrease in the number and activity of beta-adrenergic receptors, triggering lipo-genesis.

Conclusions

Benign symmetrical lipomatosis is a rare metabolic disease, characterized by the development of adipose tissue deposits, little enveloped, and with a particular distribution that is also defining for the disease.

Generalized trunk localization, which may comprise the scrotum as well as the cervix, of the lipomatous masses is rarely encountered, in comparison to cervical localization.

The disease is associated often enough with chronic alcoholism, secondary liver lesions, neurological affection and endocrine disorders, depending on which the prognosis of the disease can be made.

The treatment of choice is surgery, preferably not only esthetical, but radical interventions to excise the lipomatous masses.

Complementary treatment for associate diseases is necessary, but it does not influence the evolution of the lipomatous masses.

The disease remains rare, not necessarily due to low incidence, but because it is very seldom diagnosed, often being mistaken with simple lipomas or obesity.

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