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ABSTRACT



Lipomas, the most common type of benign tumours, are generally developed from adipose tissue and present an incidence of 2.1 per 1000 inhabitants. In addition to lipomas, at least three other maladies of the adipose tissue lead patients to consult a doctor, especially for aesthetic purposes: multiple familial lipomatosis, diffuse congenital lipomatosis, and adiposa doloris. Unlike lipomas, these maladies are characterized by numerous lipomas, encapsulated or not, of different sizes, symmetrical or not, which may appear in the neck, limbs, or the trunk, sometimes being painful. The life quality of these patients is affected, not only from an aesthetic point of view but also from medical considerations, like pain. Chemical lipolysis has proven unsatisfactory for patients due to several reasons: the prolonged therapy, high cost, the partial dissolution of the lipomatosis, and high recurrence at one year. Surgical treatment remains the only viable option; sometimes when numerous lipomatous tumors required large and numerous incisions, treatment was refused by patients. The result after laser liposuction is excellent, the recovery time is short, without much pain for the patient, with minimal ecchymoses and edemas, without any recurrence in time, and with an excellent degree of patient satisfaction.

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Introduction

Lipomas are the most common type of benign tumours developed from adipose tissue. These are generally well-located and of varying sizes, can appear at any age, in both sexes, and can manifest in several clinical forms. Benign adipose tumours can be classified into solitary lipomas, multiple familial lipomatosis, and diffuse congenital lipomatosis (benign symmetrical lipomatosis) [1].

Our practice has uncovered a number of cases of patients, from subjects who presented for a single lipoma (with clinical manifestations and/ or esthetic aspects) to those who presented with multiple lipomas of different sizes, sometimes more than 30 lipomas with or without clinical manifestations.

Most often lipomas did not have clinical manifestations but, even when these were present, the main reason for

consultation with the doctor was an aesthetic purpose, regardless of age. The main concern of these patients has been "How will it look after we remove it? Will, there be any scar?" Every surgeon is aware that the biological process of scarring has particularities from one patient to another, and that scarring is sometimes unpredictable as an esthetic result. Thus, if patients presented with one or more lipomas on areas of the body covered by clothing, they more easily accepted the surgery. In contrast, when patients presented with 10 or 20 lipomas, most on the upper limbs or even in the cervical region, more discussion and clarification with patients were needed. Usually, patients wanted to remove lipomas because they were aesthetically disturbing but, at the same time, they wanted the guarantee that they would not leave unsightly scars.

In this clinical context, and taking into account the psychological implications for the patient, we have tested

a variety of solutions in the treatment of multiple lipomas. The first therapeutic alternative was represented by chemical lipolysis. It consists of directly injecting an emulsifying substance into the adipose tissue, such as phosphatidylcholine (PPC) and deoxycholic acid (DOC). Injected active substances cause the slow progressive dissolution of the fat cells, without leading to an increase of triglycerides in the blood. The fat released is subsequently metabolized by the liver. Usually, 2-4 treatments are necessary (at 4-8-week intervals) for the procedure to be successful [2]. Treatments can also be performed at shorter intervals, more precisely about two weeks, in which case dose selection is essential. Each session lasts about 30 minutes and should dissolve 1-3 cm from the fat layer. In fact, the lipomas would not disappear completely in most women, and treatment/ healing times after each session were long, so that over time most patients became less compliant at treatment; in addition, we have noticed numerous recurrences, a finding confirmed by other authors [2, 3]. The degree of patient satisfaction, as well as our degree/ professional appreciation, was sometimes low, so that we sought other therapeutic options. The second alternative for us, as well as for other authors [4], was surgical ablation through small excisions. This solution was not very agreeable when the location of the lipomas was in aesthetic/visible areas, and in cases where the number of lipomas was very high, the patients objected to multiple incisions.

Given these goals (to treat lipomas through minimal scarring, in a short amount of time, and with a minimum recovery period), we decided to purchase a NdYag 1064 laser, Deka SmartLipo, whose preset indication and work schedule are specific to the treatment of lipomas. Since the 1980s, liposuction has been used in the treatment of multiple familial lipomatosis [5]. Laser lipolysis has been recently introduced in the treatment protocol for lipomas therapy, and the indications, procedures, and the long-term diagnosis/ outcomes are still under debate [6].

Discussions

The main difficulty/challenge is to understand exactly what the patient wants, and how important the aesthetic result is for him/her. Thus, before choosing the form of treatment, it is useful (both for the patient and physician) to identify the patient's wishes and expectations so as to obtain a maximum degree of post-therapeutic satisfaction. In this regard, we have developed a questionnaire that the patient must complete before surgery and during medical consultations.

Pre-treatment assessment questionnaire:

1. What is the main reason you want lipoma(s) removal?
 - for esthetic purposes
 - for medical purposes: localized pain
 - prophylactic purposes (fear of malignant transformation)

2. How important is the aesthetic result and a possible scar for you?
 - very important
 - important
 - little or no important
3. What is the time interval you could offer for treatment and recovery?
 - 1 week (for laser treatment)
 - 2-4 weeks
 - 1-3 months
4. What is your first treatment option?
 - laser lipolysis
 - chemical lipolysis
 - surgical ablation
5. What is the main criterion in choosing the treatment?
 - the cost of the treatment
 - duration of the treatment and recovery period
 - the esthetic result.

The second challenge was to establish indications and contraindications for laser treatment. The NdYag laser may be used for the following indications [7]:

- lipomas smaller than 5 cm, well-outlined, mobile, that do not affect any nerve and that have not presented an accelerated growth in the last months
- benign symmetrical lipomatosis (Madelung's malady)
- diffuse familial lipomatosis

Relative contraindication:

- Dercum's disease

Absolute contraindication:

- bulky lipomas with suspicion of liposarcoma

General contraindications of the laser for liposuction:

- uncontrollable high blood pressure
- cardiac failure
- decompensated diabetes
- pregnancy
- mental disorders

We also needed to consider the potential for malignancy, which is increased for lipomas over 5-6 cm and, from this perspective, laser-assisted liposuction has the disadvantage of not preserving tissue fragments for biopsy. In such cases, we prefer surgical excision of the large lipomas or, as a last resort, the classic liposuction with the histopathological examination of the various tissue fragments and, possibly, with the lipo laser.

Preoperatively, we recommend a minimal set of laboratory tests and, for painful lipids or a location near a nerve or vessel, soft tissue ultrasound is recommended.

The treatment is performed under local anesthesia for small lipomas, or intravenous sedation / general anesthesia for large lipomas, numerous lipomas, or patients with a history of panic attacks or phobias of different etiologies.

The procedure is relatively accessible. The anesthesia is followed by the minimal infiltration of the lymphomas with Klein solution [6], followed by a 2-3 mm incision through which the lipo laser cannula is inserted. The program is preset for lipids by the device, but can be adjusted manually, depending on the size of the lipids and the response to treatment. For lipomas larger than 1 cm, classical liposuction can be combined with laser lipolysis.

The working technique:

For liposuction, small cannulas 3-4 cm thick were used, with a single minimal incision. For laser lipolysis, a 300 µm fiber, with 6-8 W power and 3,000-6,000 J energy was used for a single lipoma depending on its size. The advantages of NdYag laser therapy are:

- a single session is usually necessary
- the recovery period is minimal, i.e., 2-4 days, with reduced discomfort
- it can also be performed with a local anaesthesia
- all lipomas can be treated in a single session
- it can concomitantly perform a skin tightening, so that for superficial and medium-sized lipomas the excision of the skin was not necessary
- in most cases no local skin bruising occur
- the aesthetic appearance is remarkable and often a 19G needle is sufficient (instead of making a minimal incision), while healing should not leave scars. The incisions are closed with intradermal 5.0 absorbable threads

After the procedure, patients are daily monitored, and prophylactic antibiotic therapy could be administered (Augmentin or Oxacylin of 500 mg for 5-7 days); painkillers and anti-inflammatory drugs (Paracetamol, Tador, Doreta) are also administered, and in case of small ecchymoses, arnica-based solutions (Arnigel) are administered as well. For the prevention of unaesthetic scars, Contractubex or Stratamed can be applied for three months after the intervention.

The results obtained with Deka SmartLipo laser are generally very good. In addition to all the advantages mentioned above, patients are aesthetically satisfied, an important aspect because most patients present themselves to the doctor with concern about the aesthetic aspects of the lipomas.

After treatment, the patient should evaluate his/her degree of satisfaction:

1. Are you satisfied with the treatment administered?
 - very satisfied (3 points)
 - satisfied (2 points)
 - unsatisfied (1 point)
2. Are you satisfied with the final esthetic result?
 - very satisfied (3 points)
 - satisfied (2 points)
 - unsatisfied (1 point)
3. How much has your quality of life improved?
 - very much (4 points)
 - satisfactorily (3 points)
 - a little (2 points)
 - very little (1 point)

Based on this form, the patient's degree of satisfaction after the laser-assisted liposuction can be established:

- 9-10 points – an excellent result, a high degree of satisfaction
- 7-8 points – very good result, a good degree of satisfaction
- Under 7 points – the average result, low degree of satisfaction

The lipoma is a benign affliction, with an incidence of 2.1 per 1000 persons. The location of these lipomas can sometimes be atypical. They may be encountered in various areas, such as at the level of the scrotum; when lipomas present low consistency they can be confused with external hernias [8]. In the case of development of lipomatous masses within the mediastinum, the differential diagnosis must be made with tumours or even with diaphragmatic hernias. Other possible differential diagnoses are with neurofibromas, schwannomas, synovial cysts, etc., depending on location [9, 10]. The treatment of solitary lipomas is usually surgical, but the laser lip may be considered, depending on the location, size, and preference of the patient. For lipomas larger than 5 cm and with rapid growth, the only safe therapeutic approach remains surgical ablation, with a histopathological examination to exclude possible liposarcoma.

Multiple familial lipomatosis was first described in 1970 by Das Gupta as a benign affliction characterized by the occurrence of numerous encapsulated lipomas [11], unlike diffuse congenital lipomatosis in which the lipomas are not encapsulated. The angioliipoma differentiates from the lipoma through the presence of capillary proliferation and slight fibrosis of the connective tissue. The incidence of multiple familial lipomatosis is approximately 0.002%, being rarely encountered. It is a disease with predominantly autosomal dominant transmission, although cases of recessive autosomal transmission have also been reported [12]. Lipomatosis can also be associated with

Madelung's disease, Gardner's syndrome (a hereditary disease characterized by the presence of multiple polyps in the colon, in association with bone tumours and soft tissue tumours), or Dercum's disease (painful adiposity, which mainly affects women at menopause) [13]. Even if they are frequently associated with polyneuropathy, the relationship between these maladies is still under discussion, the main causative factor being represented by the cytopathy of the mitochondria and the disorders of the lipid metabolism [14].

Benign symmetrical lipomatosis is characterized by the presence of some adipose masses of large dimensions, slightly circumscribed, of soft consistency, painless, non-encapsulated, usually located at the cervical level and the extremities. The lipomatous masses develop in the subcutaneous cellular tissue and frequently infiltrate the adjacent planes. The disease generally affects men between 30-60 years old, the men/women ratio ranging between 15/1 and 30/1, the most extensive spread being recorded in Mediterranean countries [15]. Benign symmetrical lipomatosis can occur sporadically, or it may be familial (with dominant, autosomal transmission). The incidence of the disease is 1 to 250,000 [16]. It is also known as Madelung's disease, Launois-Bensaude's adenolipomatosis, Brodie's syndrome, or Buschke's disease. The disease is frequently associated with alcohol consumption, over 90% of the patients being chronic alcohol users [17] and with polyneuropathy [18]. More than two-thirds of the patients are overweight, which is also an aggravating factor of the disease, accelerating the development of lipomatous masses [16].

From a clinical perspective, two types have been described. Type I, in which lipomas are located in the cervical region and the supraclavicular and deltoid regions (with the occurrence of the so-called "bull-neck"/Madelung's collar), sometimes with the invasion of the mediastinum manifested through the feeling of suffocation of the patient as a result of the tracheal compression. Type II, in which lipomas are located throughout the body, except for the neck, giving the impression of ordinary obesity without profound involvement. The possibility of malignant transformations is exceptional, although some cases of malignancy of familial symmetrical lipomatosis have been reported. The diagnosis of symmetrical lipomatosis is based on the symmetrical distribution of fat deposits and on the fact that the arms and the legs do not exhibit areas of lipodystrophy [19-21]. The leading causes for the occurrence of this malady could be represented by an enzymatic defect or an alteration of the membranous receptors (which would lead to a decrease in adrenergic lipolysis), or sympathetic denervation of brown adipocytes (which would lead to hypertrophy and mitochondrial DNA mutations) [22, 23]. It can be associated with different metabolic disorders: insulin resistance, hyperuricemia,

renal tubular acidosis, the increase of hepatic enzymes (cytolysis, cholestasis), disorders of the thyroid gland, of the adrenal glands, of the hypophysis. Paradoxically, there is an increase in high-density lipoproteins (HDL) [24-26]. Liposuction seems to be the best treatment option for those that are superficially located, although it cannot prevent recurrences [27, 28]. The prognosis mainly depends on the concomitance of neuropathy which may significantly increase mortality [16].

Dercum's disease, also called *adiposis dolorosa* or *neurolipomatosis*, is an unusually progressive disease of unknown etiology, characterized by the occurrence of some multiple lipomas, encapsulated or not, painful, which frequently occur in overweight women at menopause. The onset is insidious. The pain is due to the compression of the lipomas on the nerves, being described by the patients as "the fat that hurts". Its hereditary transmission is dominantly autosomal, from mother to daughter [29-31]. The mechanisms of the disease are still unknown, and the origin of the pain remains uncertain. The histopathological exam does not show any differences between these tumours and the regular lipomas. The diagnostic criteria for neurolipomatosis comprise the four cardinal symptoms: multiple and painful fat masses; generalized obesity especially at menopause; asthenia, weakness, and fatigue; and mental changes with emotional instability, depression, confusion, and dementia. The conditions associated with *adiposis dolorosa* include sleep disturbances, irritable bowel, carpal tunnel syndrome, Tietze syndrome, thyroid dysfunction, tendonitis and myalgia [32-35].

Three clinical types of Dercum's disease have been described:

- type I, the juxta-articular type, with folds or painful fat in the knees and the thighs
- type II, diffuse/ generalized, with the extension of the pain
- type III, the nodular type, with intense pain in and around the multiple lipomas attached to the adjacent tissue.

The diagnosis is difficult to make, because there are no specific signs or symptoms, and even the histopathological examination cannot provide a diagnosis of certainty. Differential diagnosis must be made with progressive lipodystrophy, Proteus syndrome, fibromyalgia, myasthenia gravis, Madelung's syndrome, neurofibromatosis, and Cushing's syndrome [36, 37]. Moreover, associated pathologies at the dermal-epidermal level can overlap the lipomas [38-40].

No treatment can alter the course of the disease, and those available are symptomatic only. The use of systemic corticosteroids, intravenous anesthetics, and analgesics are indicated. Liposuction produces a significant improvement

of the pain and the quality of life with the mention that the lowest laser energies should be used since lipomas are often connected to nerves that should be protected from heat emitted by the laser, this aspect generating thus distinct options (the relative indication or contraindication) of the lipo laser for this sickness [41, 42].

Highlights

- ✓ Lipomatosis has a relatively rare incidence, is well localized and occurs at any age in both sexes in patients with congenital or familial lipomatosis.
- ✓ Taking into account the psychological implications for the patient we have always tried alternative solutions in the treatment of multiple lipomas, and laser therapy with NDYAG 1064 NM LASER seems to be an optimal choice.

Conclusions

Although multiple lipomatosis is relatively rare, its treatment option is still challenging because most patients present to the doctor for an aesthetic purpose. Chemical lipolysis proved to have poor results, with a long period of treatment and high costs for the patient, so we no longer consider it a feasible therapeutic alternative. Surgical excision is often refused by patients, even if it involves minimal incisions, mainly due to the numerous resulting postoperative scars, whose evolution is often unpredictable. In this context, we consider that laser liposuction would be the optimal treatment for these maladies, with mention that patients must be well examined preoperatively. When lipomas are large or painful, the ultrasound of soft parts is also necessary to specify the anatomical relationships with the surrounding tissues. There were no recurrences in the studied group until the date of publication of this paper.

Conflict of interest disclosure

There are no known conflicts of interest in the publication of this article. The manuscript was read and approved by all authors.

Compliance with ethical standards

Any aspect of the work covered in this manuscript has been conducted with the ethical approval of all relevant bodies and that such approvals are acknowledged within the manuscript.

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