CLINICO-PATHOLOGICAL ASPECTS OF CUTANEOUS LIPOMAS AND LIPOMATOSES

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Tumors issued from the normal fatty tissue of the skin or differentiating fat cells within the skin are quite common. Most of them are benign (lipomas) but not necessarily easy to remove (diffuse lipomatoses). Primary liposarcomas of the skin and hibernomas are rare conditions. The pathological variants are numerous but only few are specific of the skin. The prevalence of lipomas is 2.1. per thousand people.

1. Lipomas

Lipomas are solitary or multiple capsulated tumors of the fatty layer of the skin. They are mainly constituted by mature lipocytes and they disclose a slow growth.

1.1. Solitary lipomas

ETIOLOGY

In most cases the etiology is unknown. The occurrence of rare lipomas following shearing injuries, heavy bruising or hematoma of other massive usually blunt trauma has been reported as the consequence of fat "fractures". Chronic pressure has also be believed to be responsible for some asymmetric lipomas ("porter's lipoma", "beer porter's lipoma").

CLINICAL FEATURES

Lipomas occur predominantly between the 4th. and 7th. decade (mean age around 45-50 years) with a light but controversial prevalence in female patients.

A solitary lipoma presents as a hemispherical subcutaneous tumor which may reach a diameter of 20 cm. The overlying skin moves freely and does not show inflammatory changes. The tumor, excepted for large tumors, moves also freely below the skin surface. Its palpation may be slightly tender. The usual localisations are the shoulders, the head and neck, the upper back, the buttocks and the upper part of the thighs.

Some clinical variants are most typical:

* the solitary fibrolipoma of the nape of neck and shoulders, in elderly men, from 45 to 65 years, is poorly limited and its fibrous component contributes to its adhesion to the deep fascias of the neck; its histological counterpart is sometimes a spindle cell or pleomorphic lipomas;
* the lumbar midline lipoma has a triangular form with its top down- side: it first appears in pubescent adolescents and it is often related to a hidden spinal dysraphy;
* the subgaleal lipoma of the forehead occurs in adult men; 50 per cent of the lipomas of the head are located on the forehead between the galea and the periosteum of the skull; it presents as a disk-like flat lipoma which needs for its removal an incision of the aponeurosis.

PATHOLOGY

The histological variants are not necessarily related to the clinical aspects. Most solitary lipomas are well differentiated lipocytic lipomas; the fatty cells are tightly grouped together in lobules separated by thin collagenous septae and surrounded by a fibrous capsule. The presence of the capsule allows an easy surgical removal of these tumors, which pop out through a short incision with the help of a light pressure. Other connective tissue components may be present between the adipocytes: a fibrous tissue (fibrolipoma), a rich capillary network, a myxoid degeneration (myxolipoma). Some further pathological variants may be isolated:

* the angiolipoma is a small tender capsulated lipoma which rarely exceeds 2 cm and is usually located on the forearm; it is characterized by a rich peripheric network of capillaries which are often thrombotic; bundles of smooth muscles originating from the vessel walls may also be present (angiomyolipoma). The tenderness of this variant is ascribed to the inextensibility of the capsule, to the capillary thromboses and to the contractile smooth muscle cells. In the cellular angiolipoma, the cellular angiomatous tissue is so dense and the amount of adipose tissue so minimal that the diagnosis is first of all the diagnosis of a lobulated vascular tumor of the fatty layer. Some cutaneous angiomyolipomas composed of smooth muscles, vascular spaces, connective tissue and mature fat have such a predominant smooth muscle component that they can hardly be considered as lipomas and should rather be classified as lipomatous variants of angioleiomyomas (angiolipoleiomyoma). It must be mentioned that they are always in acral lotion as most vessel derived leiomyoma. They do not have any association with tuberous sclerosis or angiomyolipomas of kidneys.
* the spindle cell lipoma is a variant most often located on the neck and shoulders: the main cellular type is a spindle cell intermingled with the typical mature lipocytes; these cells and their nuclei are often pleomorphic.
* the pleomorphic lipoma is another variant where the polygonal and spindle cells are associated with large multinucleated cells throughout the tumor often suggesting a pleomorphic liposarcoma.
* the adenolipoma is also a distinct variant which derives from the adipose lissue around the sweat gland coils; it develops in the dermis and in the fatty layer. Displaced and distorted sections of sweat glands and ducts are observed within the tumorous lobules. This superficial solitary lipoma is mainly located on the upper thigh and its clinical aspect does not deviate from this of an usual lipoma.
* the lipoblastoma is a variant of the early childhood occurring on the extremities in less than 3 years old boys. It is a lobulated tumor characterized by immature round vacuolated lipoblasts; It has a benign course and does not recur after complete surgical removal. The rare diffuse form or juvenile lipoblastomatosis has the clinical aspect of inharmonious obesity.

DIAGNOSIS

The clinical aspect is in most cases so typical that the diagnosis can be made without any difficulty. The ultrasound sonography contributes weakly to the pre-operative diagnosis because most lipomas are poorly or variably echogenic. The freezing of the tumor has been proposed to differentiate lipomas from other conditions; lipomas are expected to become more rapidly solid by freezing in vivo than subcutaneous cysts or adnexal tumors. Practically this procedure is of poor help and in dubious conditions it seems more wise to get an excisional (or incisional) biopsy.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis has to be made clinically with all the nodular solitary lesions which develop in the dermis and in the fatty layer of the skin: epidermal and adnexal cysts usually adhere to the overlying epidermis and are less movable below the skin surface;

neural, muscular and vascular mobile capsulated tumors, such as capsulated neuromas, nodular angioleiomyoma, lobulated subcutaneous angiomas, may also be tender as capsulated angio(myo)lipomas.

The so-called "mobile encapsulated lipoma" is a nodular-cystic fat necrosis presenting as solitary or multiple subcutaneous nodules. Each lesion is characterized by a thin fibrous capsule surrounding groups of non-nucleated adipocytes whose outlines are well preserved. The occurrence of these dead fat lobules seems to be related to trauma or rapid vascular insufficiency leading to circumscribed aseptic fat necrosis with subsequent fibrous encapsulation without vascular supply. The lesions, ranging in size from 1 to 15 mm, are easily movable below the skin surface as loose bodies ("skin mice"); they are also easily removable by a single surgical excision.

Hisologically the main difficulty is the differentiation of a solitary nevus lipomatosus superficialis. This connective tissue hamartoma occurs on the buttocks or somewhere around the pelvic girdle. It may be nodular, multiple or linear and sometimes present at birth. It discloses heterotopic foci of fatty cells, lipocytes and even liopblasts, in the dermis up to the papillary layer, especially around the venous structures. The skin surface is uneven and sometimes slightly papillomatous. The main difference with the lipoma is the intradermal extension of the fatty tissue; only some eccrine adenolipomas may have such an intradermal growth.

Large skin tags (acrochordons, fibroma pendulum) may also be confused with superficial lipomas with an intradermal extension. The stroma of a large based-skin tag is often infiltrated by mature fat cells in continuity with the normal panniculus; if the slides do no show the encapsulation of the fatty tissue in the depth, it is difficult to distinguish the hernial bulge of the fatty layer in a skin tag from the intradermal growth of an hypodermal lipoma. It must be underlined that primary intradermal lipomas do not exist.

TREATMENT

Capsulated solitary lipomas can be easily removed by a single surgical excision. The only ones which provide some surgical problems are the subgaleal lipomas of the forehead and scalp and the fibrolipomas of the neck. In the former it must be remembered that the epicranial aponeurosis has to be incised to get access to the lipoma; in the latter the lack of a cleavable capsule needs a careful dissection of the soft tissues of the nape of the neck, It is not necessarily indicated to remove the lumbar midline lipoma; if it is the patient's imperative request it is wise to refer him to a neurosurgical ward. Solitary, but especially rapidly growing lipomas of more than 5 cm, should always be submitted to a histological control.

1.2. MULTIPLE LIPOMAS

Multiple capsulated easy movable lipomas are characteristic of the multiple familial lipomatosis (mesosomatic lipomatosis, lipomatosis of Roch-Leri). They appear predominantly in adult males after the third decade and in most families the inheritance is autosomal dominant. Most of these patients have a normal karyotype; gene arrangements on chromosome 12 (loci 12q13-q14) and ring chromosomes have been described in this condition. The lipomas characteristic of this condition rarely exceed a diameter of 5-6 cm; they may be very numerous, up to hundred lesions, They are distributed in the middle part of the body (mesosomatic lipomatosis) from the level of the lower third of the arms down to the upper third of the thighs. They have a special propensity for the forearms and the evidence of multiple hypodermal lipomas in this location in a single individual allows the diagnosis of this inherited entity. The neck and the shoulders are never involved. In the segmental lipomatosis (of Touraine & Renault), the lipomas are arranged according to a metameric or blaschkolinear pattern.

Histologically they are common lipomas or angiolipomas. This explains why they are

often so tender and why the request of the patients for a surgical removal is so frequent. They can easily be removed like solitary lipomas. Nosologically this entity has for a longer time be confused with the multiple symmetric lipomatosis in the English literature.

2. LIPOMATOSES

2.1. THEMULTIPELE SYMMETRIC LIPOMATOSIS

It is also denominated adenolipomatosis of Launois-Bensauide or Madelung's disease. It occurs in adult males and is closely related to chronic alcoholism.

CLINICAL FEATURES

The fatty bulks appear around the neck, on the shoulders and upper arms ("buffed sleeves" lipomatosis), on the upper back. They have unprecise limits and a soft consistency and their confluence lead to a monstruous difformity of neck and upper trunk. One can distinguish 2 types: in the type I the lipomatosis predominates on the neck and around the scapular girdle and contrasts with the atrophy of the fatty layer of the non-involved skin areas of the limbs and a normal or deereased total body weight; in the type II, the lipomatosis extends largely on the trunk and on the limbs and may mimick a common obesity with an increase of the total body weight.

PATHOLOGY

Histologically the fatty masses are not capsulated and, expecially in the type 1, they infiltrate in their depth the muscles of the neck and penetrate in the mediastinum and in the cervical spine. The deep growth of the tumorous fatty tissue may provoke a compression of the trachea, the oesophagus and the vessels and nerves of the mediastinum. They are often associated (84 p. cent) with peripheral neuropathies which may partially ascrived to the chronic alcoholism; such neuropathies have been observed in multiple symmetric lipomatoses in patients who were not alcohol-addicts. The pathophysiology of this lipomatosis is not clearly understood: some patients have an hyper - α - or -B- lipoproteinemia and an increased storage of triglycerides in the fatty layers, but this pathogeny is controversial. Rare familial cases have been reported.

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

The type I has to be differentiated from the multiple familial lipomatosis: there are more confusisng data in the English literature and in the terminology than real difficulties to differentiate these two entities. The type II may be confused with a common obesity. Histopathology is not of any help in the diagnosis of lipomatoses.

TREATMENT

The best therapy of the Launois-Bensaude's disease is to combine iterative liposuctions and suppression of alcohol intake. Because of the poor limitation of the fatty bulges, surgical excisions usually fall and are no longer recommended. However on the neck the liposuction has to be performed with extreme caution because of the vicinity of nerves and jugular veins and some surgeons recommend to associate classical surgical resections with liposuction surgery.

2.2. The neurolipomatosis (Dercum's disease, adiposis dolorosa) is very rare and predominates definitely in menopausal women. The lipomas are solid, nodular or plaque-like and their main distinctive symptom is their painful tenderness. The pain is spontaneous or provoked by pressure; it may be paroxystic and associated with redness and oedema. The female patients frequently exhibit other symptoms such as bruisability, obesity and hypogonadism, asthenia, psychic instability. To relieve the pain attacks, the injections of lidocaine (intralesional, over even intravenous) seem to be the best therapeutical choice.

2.3. THE FRONTIERS OF LIPOMATOSES

Some dystrophic obesities and hypertrophic lipodystrophies are located at the frontiers of the lipomatoses.

The steroid lipomatosis associated with primary (Cushing's disease) or iatrogenic hypercorticism is characterized by an enlargement of the fatty layer around the neck (buffalo's neck) and shoulders. In the lipodystrophy of Barraquer and Simmons, the fally layer of the lower body may be bulky and monstruous and contrasts with the total lipoatrophy of the face and the upper part of the trunk.

The female bulging fat storage known in French speaking countries by the name of "cellulite" , enlarging the hips ("riding breeches") and pitting the thighs ("waffle thighs"), cannot be considered as a pathological lipomatosis. In these adipose conditions, the only components are normal large lipocytes filled up with fat pushing the laminated vacuolated nuclei to the cell periphery.

In infants a dystrophic obesity can be the expression of a diffuse lipoblastomaTosis. A generalized superficial lipomatous nevus presents clinically as a "Michelin tyre baby" mimicking a monstruous bulging lipomatosis.

3. Miscellaneous lipomas and lipomatoses related to gonetic disorders

In the Gardner-Richards syndrome, miscellaneous mesenehymal benign or malignant tumors may occur. Lipomas belong to the list of these soft tissue tumors; they do not have a special prognostical signification.

In the encephalocraniocutaneous lipomatosis, a congenital unilateral lipomatous infiltration of the face and scalp is associated with other skin hamartomas (sebaceous nevus) and a homolateral porencephaly with seizures and mental deficiency; this rare entity has sometimes a lethal outcome through the neurological complications.

In the Proteus syndrome, multiple lipomas and diffuse superficial or deep lipomatoses have been described; subcutaneous lipomas belong also to the three leading symptoms of the Bannayan syndrome whose other clinical symptoms are the macrocephaly and the hemangiomas. The localized gigantism in the congenital macrodactyly is partially due to a lipomatous dystrophy of the involved fingers kor toes. Congenital lipomas may also occur unrelated to other developmental anomalies.

4. Hibernoma (brown fat lipoma)

This rare benign tumor originates from the embryonic remnants of the brown fat. It appears in young adults predominantly in females, exceptionally in children. It is a solid, mobile, painless, well circumscribed tumor of 5 to 10 cm diameter; often if feels warm. The elective localization is the interscapular area, but other sites may also be concerned such as shoulders, neck, thighs, axillar or inguinal folds, anterior aspect of the trunk and even the face.

Histologically it appears as a well capsulated and lobulated tumor disclosing a yellowish-brown or red colour. The tumorous cells are large and round with a central nucleus and dispersed eosinophilic and P.A.S. positive granulae and / or microvacuoles in their cytoplasm. Monovacuolated lipocytes and numerous blood vessels are intermingled with the granular and microvacuolated lipocytes. The differential diagnosis has to be made with the granular cell neurinoma, the lipoblastoma, the pleomorphic lipoma and normal lobules of brown fat casually found in skin surgically removed from the upper back or the neck or the axillae.

Except for extremely rare malignant forms, the hibernoma does not recur after surgical removal.

5. Liposarcomas

Cutaneous primary liposarcomas usually do not coplicate the above described lipomas and lipomatoses. They appear de novo and have a regular growth reaching rapidly a diameter of 5 cm and more in elective sites such as thighs, groins, buttocks and popliteal fossae. Four main histological variants are known: lipocytic (well differentiated) liosarcoma, liposarcoma with myxoid stroma (myxoid liposarcoma), round cell liposarcoma and pleomorphic liposarcoma. These

morphological variants may occur together in the same tumor; immature cells are often spindle-shaped in a myxoid or sclerosing stroma and undifferentiated cells can only be definitively recognized by immunohistochemical staining (vimentin, S100 protein).

The liposarcomas appear in 50-60 years old adults, extremely seldom in childhood. In the skin, most cases are histologically well differentiated or of the myxoid type (in 40 p. cent). In most studies and comprehensive reviews the liposarcomas of the skin and those of the extracutaneous soft tissues are not considered apart. Only few separate informations dealing with skin liposarcomas alone are available.

A liposarcoma may be suspected if a subcutaneous tumor of the lower limbs has a continuous growth distorting the skin relief; the tumor is seldom painful; compression of veins or peripheral nerves may occur. The suspicion of malignancy can be strenghened by the arteriography (increased vascular supply, vascular stops, haemorrhages, thromboses) and the CT scan which shows a deep penetrating non capsulated tumor invading the aponeouroses and muscles. A tumor larger than 5 cm, located in the thigh, growing in depth, is more likely to be a liposarcoma than a benign condition.

A wide excision is requested if the tumor is located proximally; in acral locations on the lower limbs below the knee level an amputation is necessary. The postoperative recurrences are frequent, 50 to 80 p. 100 within 5 years; metastases, especially hematogenic lung metastases, appear in 5 p. cent and the survival rate after 10 years is approximately 60 to 70 p. cent. Few complementary results may be expected from radiotherapy and chemotherapy. The chemotherapeutical regimen usually proposed in non - surgical and metastatic forms associates cyclophosphamid, vincristine and doxorubicine. It provides a rate of 15 to 50 p. cent of objective responses but does not improve the survival rate.