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Clinical considerations on the retroperitoneal liposarcomas

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AIM: *It presents a clinical case of undifferentiated retroperitoneal liposarcoma with 5 years' recurrence from the first operation for the rarity of the occurrence, the problems related to surgery and complementary therapeutic approach.*
MATERIAL OF STUDY: *Male patient aged 73 was operated for removal of retroperitoneal mass with involvement of the right kidney at the Second University of Naples in the 2003. In accordance with the interdisciplinary board, complementary therapy is not indicated and follow-up program. The successive controls were negative until at least 2007. Reoperation for recurrence in 2008 for the presence of massive bone formation occupying a large part in the right half of the abdomen at the sub-hepatic level. In both cases histological examination showed undifferentiated liposarcoma.*
DISCUSSION: *It is of unknown etiology and only 25% occurs in well-differentiated cells are also more than 100 histological subtypes, 85% are malignant. The most affected is the male sex and from the beginning looks like malignancy. The trend of growth in general is slow, and in most cases tends to recur over time. The role of chemotherapy and radiation therapy is controversial.*
CONCLUSIONS: *The peculiarity of our case is higher than the average survival despite advanced age and presence of recurrence. This confirms the importance of surgical treatment, thus offering the patient a chance of better long-term survival.*

KEY WORDS: Liposarcomas, Recurrence, Retroperitoneum.

Introduction

Un-differentiated retroperitoneal liposarcoma is classified among tumours deriving from mesenchymal tissues; among these ones, it is certainly one of the most widespread and is associated with a low life expectancy, especially in relation to its dimensions, seat, histological subtype, radicality of surgical treatment, presence of metastasis at distance [1]. Liposarcomas have an incidence ranging from 0,2% and 1% of all solid tumours [2].
One of the distinctive features of this pathology is that of achieving substantial dimensions (and weight); in reference to dimensions, a distinction can be made between liposarcomas >25 cm and liposarcomas <25 cm, and this is useful in demarcating differences in terms of the prognosis [3].
The slow growth involves a subtle symptomatological scenario, with lack of objectivity in the first years of the illness, until it reaches remarkable dimensions and is manifested with abdominal pains and signs that are easily identifiable [3].

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Complete excision represents the gold standard of the treatment with complete exeresis with excision margins in healthy tissue. Liposarcomas tend to recur locally in time, while presenting a low tendency to metastasise at distance, often forcing the patient to undergo many surgical treatments.
Ten years survival is about 16% and five years survival does not exceed 30%, relapses occur in 50% of the cases in five years [4].
Given the rarity of the disease, the problems connected to surgical treatment and the complementary therapeutic approach, it seemed of interest to expose a clinical case of retroperitoneal liposarcoma with recurrence in five years from the first surgical treatment and presence of metastasis. We then got insights for developing considerations on this pathology.

Materials and Methods

A 73 year-old man, hospitalized for the first time in 2003 at the "Second University of the Study of Naples" to undergo surgical treatment in order to remove a retroperitoneal mass detected by means of TC check.
An attack via xiphi-pubic region was chosen, since it allows for a better exposure. The surgical treatment was very laborious and all the attempts to avoid simultaneous removal of the right kidney were useless because it was incorporated in the mass. This mass was removed as a unique block up to the diaphragm, after having isolated the cave and having performed resection of lower ureter (Fig. 1).
Histologic diagnosis revealed a liposarcoma with extended un-differentiated areas and mixoids. In accordance with the interdisciplinary board, complementary therapy was excluded, while a yearly follow-up program comprising haematic checks, chest and complete abdomen TC and Pet total body was chosen. The successive controls were negative until at least 2007, when the patient did not show up at the fixed appointment.
In 2008, the total body Pet showed the presence of a massive area with intense metabolic activity, occupying a large part of the right half of the abdomen at the subhepatic level; moreover, the presence of small areas of slight increase in metabolic activity was evident in the anterior and posterior segments of the upper lobe of the right lung, in the anterior segment of the upper lobe of the left lung and in the right costophrenic recess; TC of the complete abdomen confirmed inhomogeneous swelling starting from the epiploon rear-cave with net margins, compatible with a sarcoma swelling in the retroperitoneal area.
The operation was again performed via the xiphi-pubic region and provided for the complete removal of the swelling, which was full of lobes, whitish, with greater manifestation in the right mesocolon. A bigger mass was defined and a small part of it was removed (Figg. 2, 3).

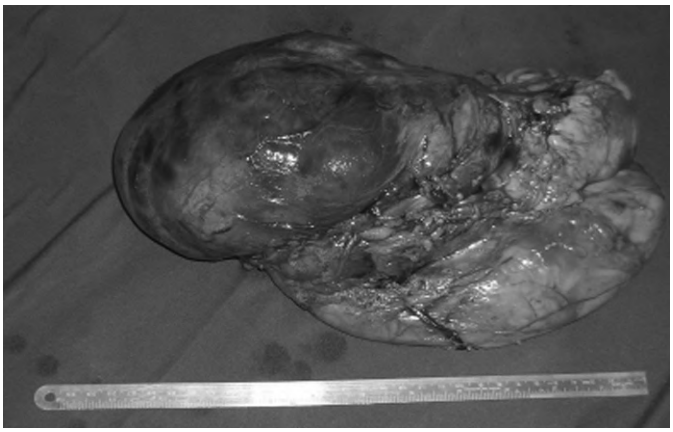

Fig. 1: Liposarcomas encompassing the right kidney (2003).

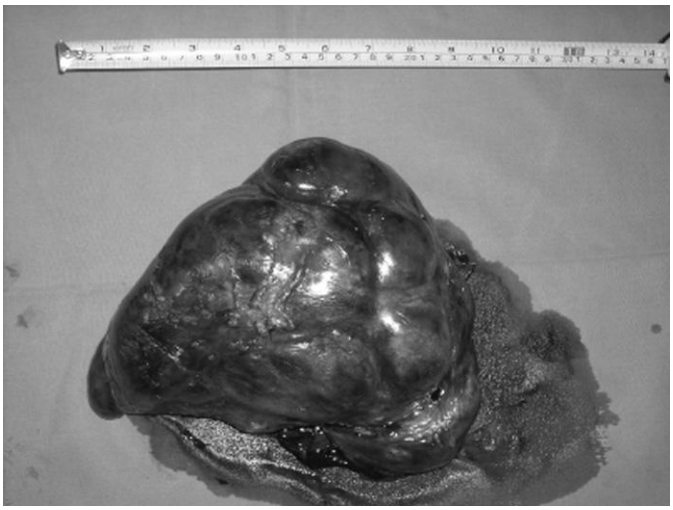

Fig. 2: The removed bigger part of the mass (2008).

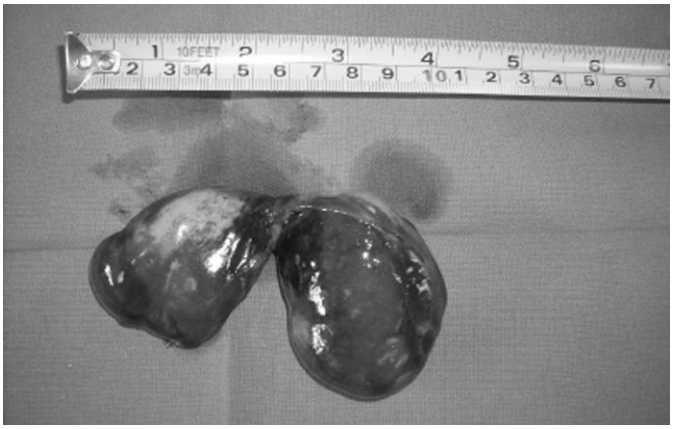

Fig. 3: The smaller part of the mass (2008).

The histologic check showed that both masses were undifferentiated liposarcomas. Even in this circumstance, taking into account the age of the patient, none of the complementary therapies was chosen.

Discussion

Although liposarcomas represent the second most widespread of the soft tissues' sarcomas in adults, usually they are not localized in the areas rich in fat, such as the subcutaneous tissue and the tela subserosa of the intestinal tract, where lipomas are situated, but in the retroperitoneal area (20-40% of the cases). In most of these cases, liposarcomas are embedded within the retroperitoneal fat. Only 25% of the patients present well-differentiated cells and there are more than 100 histologic subtypes, 85% of which malignant. Liposarcomas, besides being of fat consistency and hyper-vascularised, they have unknown aetiology, even if recent studies document genetic alteration in the region 12q 13-15 of the gene MDM2, CDK4 with related amplification [1,5]. In the future, if this hypothesis is confirmed, it could serve as a starting point for an early diagnosis and a better prognosis of such a pathology.

From the epidemiological viewpoint, males are more affected by liposarcomas, while racial differences are not registered [6,7].

From the beginning, liposarcomas appear as a malign neoplasm, few are the cases in which it is possible to observe the evolution from benign lipoma to liposarcomas. The rate of tumour growth is not constant; in general, however, it is possible to observe a slow growth, sometimes inactive for months (or years), with final exacerbation. Furthermore, the ascertainment that the retroperitoneal area, where the mass grows, is a silent clinical region, is a key element that permits to the tumour to reach sensible dimensions (all the more, given the fact that the frequent involvement of renal and perirenal areas almost never gives rise to hematuria or colics, thus entailing a diagnostic delay). Once sensible dimensions are achieved, liposarcomas show up with a sense of weight at the abdominal region, accompanied by symptoms of compression on nearby organs, e.g. constipation as in the case we are presenting.

An accurate classification (Table I) and state detection are particularly important to facilitate the choice of an appropriate surgical therapy, to determine the prognosis and to possibly associate extra therapies. The American Joint Committee Staging System, which takes into account the histological grade, the tumour extension and the depth with respect to the muscular strip, the presence or absence of lymph node involvement and the presence or absence of at-distance metastasis (Table II), is based on the TNM classification, and is the most commonly used [2,8].

When retroperitoneal liposarcomas metastasise, they localise at the level of the big vessels and nearby organs, often at the lung, abdominal organs, peritoneal serum[9]. The prognosis factors with respect to at-distance metastasis and recurrence have the attitude of becoming almost superimposed. Such factors are: the dimensions of the primary lesion (<10 cm; between 10 and 20 cm; >20cm, thus 3 categories), histology (liposarcomas or others) and grading (Grades 1-3, see Table I); in this way, the operations following Enneking criteria are practically excluded [4].

In accordance with Enneking criteria, it has to be pointed out that operations with intra-lesion margin (curettage, non "en-bloc" removal) could leave macroscopic or microscopic residuals of the illness, while surgery with the so called perilesion margins (block removal by means of pseudo-capsule or reactive area) exposes to the risk of leaving satellite lesions or skip metastasis (neoblastic nodules localised inside the same structure of the tumour but not adjacent to it); broad margins (block excision by means of a healthy tissue) do not allow avoiding skip lesions. Only drastic methods (excision of the whole interested area) avoid the risk of leaving local residuals of the illness.

The high grading, that is grade 3, and the histologic subtype different from the liposarcomas represent the

TABLE I - *Classification* [2]

Histologic rank (G)	G1	well-differentiated
	G2	moderately well-differentiated
	G3	little or poorly-differentiated
Main Site (T)		
NB : retroperitoneal and pelvic sarcomas are ranked as deep	T1	diameter <5 cm
	T1a	surface tumour
	T1b	deep tumour
	T2	diameter ?5 cm
	T2a	surface tumour
	T2b	deep tumour
Lymph node involvement (N)	N0	no metastasis at lymph nodes
	N1	involvement at regional lymph nodes
At-distance metastasis (M)	M0	no at-distance metastasis
	M1	presence of distant metastasis

TABLE II - *Grade of sarcomas in soft tissues according to the American Joint Committee* [2]

Grade	Classification	Description
IA	G1, T1, N0, M0	Tumour of grade I diameter <5 cm, no regional lymph nodes involved and/or no at-distance metastasis
IB	G1, T2, N0, M0	Tumour of grade I diameter ≥ 5 cm, no lymph nodes or metastasis
IIA	G2, T1, N0, M0	Tumour of grade II diameter < 5 cm, no lymph nodes or metastasis
IIB	G2, T2, N0, M0	Tumour of grade II diameter ≥ 5 cm, no lymph nodes or metastasis
IIIA	G3, T2, N0, M0	Tumour of grade III diameter <5 cm, no lymph nodes or metastasis
IIIB	G3, T1, N0, M0	Tumour of grade III diameter ≥5 cm, no lymph nodes or metastasis
IIIC	G1-3, T1-2, N1,M0	Tumours of any grade with involvement of lymph nodes, no metastasis
IVA	G1-3, T3, N0-1,M0	Tumours of any grade, invading bones, vessels or nerves with or without involvement of lymph nodes, no metastasis
IVB	G1-3, T1-3, N0-1, M1	Tumour with at-distance metastasis

TABLE III - *Complete Resection and Survival in the main published studies* [4,12-19].

References	Period	Number of patients	Complete resection (%)	CS at 5 years (%)	CS at 10 years (%)
Lewis et al., 1998[13]	1982-1997	231a	80	54	35
Stoeckle et al., 2001[14]	1980-1994	145a	65	49	NR
Ferrario and Karakousis, 200[15]	1977-2001	130	95	60	48
Dalton et al., 1989[16]	1963-1982	116	54	59	NR
Catton et al., 1994[17]	1975-1988	104	43	36	14
Singer et al., 1995[12]	1970-1994	83	NR	60	50
Van Doorn et al, 1994[18]	1973-1990	70	43	35	NR
Kilkenny et al., 1996[19]	1970-1994	63	78	48	37
Gronchi et al., 2004[4]	1982-2001	167	88	54	27

Note: CS: complete survival; NR: not reported ; a, only patients with primary tumour.

most significant and independent high risk for at-distance metastasis[10]; generally, negative prognostic factors are also considered: the age of the patient >50 years, the presence of positive surgical margins, the involvement of other organs, the number of mitosis and the extent of necrosis [1,6].

Pleomorphic, mixed, un-differentiated subtypes present a strongly unfavourable prognosis; the average survival is about 119 months for the well-differentiated subtype or lipoblast, 113 for the mixed one, 59 for the un-differentiated, 24 for the pleomorphic [1]. It has to be taken into account that among the above subtypes, the un-differentiation is a rare phenomenon manifested in about 15% of the well-differentiated liposarcomas [11].

Even the subtype with the best prognosis, the lipoma-like (lipoblast or with spherical cells), which presents a low tendency to produce at-distance metastasis, has a high incidence of loco-regional recurrence [11].

The radical surgery is a prerequisite for right treatment of the disease, as evidenced by the majority of the studies published (Table III) [4,12-19], which compare the percentage of resection and the global survival.

The therapeutic role of chemotherapy and radiotherapy is controversial in this type of tumour, the most of the authors agree on its non-significant influence on both main lesions and metastasis. Consequently, it is not always adopted as a complementary therapy, even though some authors believe in the usefulness of chemotherapy and radiotherapy, especially in neoplasms that are not well-encapsulated as the post surgical therapy, because it would favour cell differentiation from an un-differentiated state [13].

Conclusions

The presented case reflects the standard features of the disease; even if our patient is old and had recidivism, he tends to have a higher survival attitude with respect to the average life expectancy. It is then confirmed the importance of a radical surgical treatment, so that a better long term survival possibility can be offered to the patient.

Moreover, we agree that chemotherapy and radiotherapy are not useful in such a pathology, since the main objective of the therapeutic choice is the radicality of surgical treatment.

Thus, the complete and broad exeresis is the centre of the therapy of this kind of tumour and it remains, still at present, one of the few application fields of a certain

type of surgical demolition, which, for its extremely aggressive character, often seems to be of second choice for most of the tumour pathologies.

Riassunto

OBIETTIVO: Si espone un caso clinico di liposarcoma dedifferenziato retroperitoneale con recidiva a 5 anni dal primo intervento per la rarità d'insorgenza, per i problemi connessi al trattamento chirurgico e per l'approccio terapeutico complementare.
MATERIALI E METODI: Paziente di sesso maschile di anni 73 operato nel 2003 di asportazione di massa retro peritoneale con interessamento del rene destro presso la Seconda Università degli Studi di Napoli. In accordo con il collegio interdisciplinare si escluse terapia complementare e si indicò programma di follow up. I successivi controlli furono negativi almeno fino al 2007.
Nel 2008 reintervento per recidiva per presenza di voluminosa neoformazione occupante gran parte dell'emiaddome destro in sede sottoepatica. In entrambi i casi l'esame istologico evidenziò liposarcoma dedifferenziato.
DISCUSSIONE: È ad eziologia sconosciuta e solo il 25% si presenta a cellule ben differenziate inoltre esistono più di 100 sottotipi istologici, l'85% di essi maligni. Il sesso più colpito è quello maschile e fin dall'inizio si presenta come neoplasia maligna. L'andamento di crescita, in generale, è lento; nella maggioranza dei casi tende a recidivare nel tempo. Il ruolo terapeutico di chemioterapia e radioterapia è controverso.
CONCLUSIONI: La peculiarità del nostro caso è la sopravvivenza superiore alla media pur con età avanzata e presenza recidiva. Si conferma l'importanza di un trattamento chirurgico, così da offrire al paziente una chance di sopravvivenza a lungo termine migliore.

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