Case-based review

Cutaneous leiomyosarcoma arising after CO₂ laser therapy of an unknown lesion: case report and review of the literature

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Summary

We report the case of a Caucasian man that presented with a cutaneous leiomyosarcoma (cLMS) on the medial surface of the right knee. Eight months before, a similar lesion was excised by a CO₂ laser treatment in the same anatomical area. Histology and immunohistochemistry confirmed the diagnosis of cLMS. We performed a Mohs micrographic surgery (MMS) to enlarge the surgical scar and we staged the tumor.

Leiomyosarcoma (LMS) is a rare mesenchymal tumor originating from smooth muscle cells and cLMS represents its superficial form. cLMS appears as a smooth nodular cutaneous lesion but clinically should be differentiated with other cutaneous tumors. It requires histology and immunohistochemistry to confirm the diagnosis. Heterogeneity of the data make it difficult to establish biological behaviour, prognosis and response to therapy. The recommended therapy is surgical but guidelines are not plainly defined. We believe that the best surgical therapeutic approach is MMS. Adjuvant radiotherapy and chemotherapy have not shown any advantages in patients’ survival. Long-term follow-up is requested for the frequent recurrences.

KEY WORDS: cutaneous leiomyosarcoma; superficial leiomyosarcoma; treatment of cutaneous sarcoma.

Case report

A 67-year-old Caucasian man was referred with an asymptomatic nodular lesion localized on the medial surface of the right knee (Figure 1). Physical examination showed a nodule of 1.3x1.1 cm size, sessile, slightly erythematous. Adenopathy was not present. The patient reported that eight months before, he was admitted to another hospital for CO₂ laser treatment of a similar lesion in the same anatomic region. The patient reported a diagnosis of Gilbert’s disease due to a permanent hyperbilirubinemia. Otherwise, he was apparently in good health. The nodular lesion on the right knee was excised surgically. Histology revealed elongated cells with a clear and eosinophilic cytoplasm, minute interposition of collagen and nucleus with scattered chromatin or “blunt-ended” nuclei, included in the reticular dermis (Figures 2, 3, 4). Cytology was clearly sarcomatoid, occasionally pleomorphic, with rare phenomena of necrosis and low mitotic index. Immunohistochemistry was positive for smooth muscle actin (Figure 5), desmin, myosin and caldesmon. Taking into account the diagnosis of cutaneous leiomyosarcoma (cLMS) infiltrating the reticular dermis, we staged the tumor and performed a Mohs micrographic surgery (MMS) to enlarge the surgical scar (Figures 6, 7). The total body computed tomography (CT) scan and the ultrasound scan of the armpit, groin and laterocervical lymph nodes, did not reveal any sign of lymphadenopathy or metastases. Surgical excision was performed cutting to a distance of 8-10 mm from the surgical scar deep to the muscle band. The patient performed clinical examination and ultrasound of the superficial lymph nodes after three, six and twelve months and total body CT scan one year later without local relapses or metastases. The patient actually is apparently in good health after almost two years of follow-up.

We cannot endorse that the previous lesion was a LMS.

Introduction

Leiomyosarcoma (LMS) is a rare mesenchymal tissue tumor that originates from smooth muscle fibrocells (1). LMS of the skin includes superficial LMS (sLMS) arising from cutaneous structures and metastatic LMS that derives from distant visceral sites (2). sLMS represents 2-3% of all soft tissue sarcomas. Approximately 400 cases have been reported (3, 4). sLMS is classically classified as cutaneous (cLMS) and subcutaneous (scLMS) depending on histological features.
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Figure 1 - Nodular lesion, sessile, slightly erythematous, localized on the medial surface of the right knee.

Figure 2 - Hematoxylin and eosin (H&E) stained histology image of the tumor that infiltrates all the reticular dermis but it is not ulcerated.

Figure 3 - Histological image (H&E) of elongated cells with a clear and eosinophilic cytoplasm and nucleus with scattered chromatin in the reticular dermis.

Figure 4 - Histological image (H&E) of “blunt-ended” nuclei in the reticular dermis and a low mitotic index.

Figure 5 - Positive immunohistochemistry for smooth muscle actin.

Epidemiology

sLMS can develop from adolescence to old age but generally afflicts between 50 and 60-year-old patients; localized in the dermis but can extend to the superficial soft tissue. scLMS is more deeply situated, predominantly in subcutaneous tissue (2).

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Etiology

cLMS develops in the dermis usually from smooth muscle cells surrounding the sudoriferous glands and the erector muscle of hair while scLMS arises from smooth muscle of vessels (3). Etiology of sLMS is unknown but traumas, burns, chemical agents, solar exposer, vaccines, tick bites, radiation, venous stasis or lupus have been implicated (6, 8-11). In a study including 80 cases affected by sLMS, 15 patients referred a history of trauma (5). West et al. reported a 41-year-old man with a cLMS localized in the proximity of a tattoo performed approximately 10 years before (12). Gonzales-Vela et al. reported a 74-year-old man that developed a cLMS close to a titanium pacemaker installed 15 years before (13). Although the development of this tumor in these areas could be just a coincidence, Authors suggest that chronic inflammation or irritation could be a plausible etiopathogenetic mechanism (13). Other case reports describing malignant tumor arising in the proximity of metallic implants and/or chronic inflammation sites support this theory (14-16). Gonzalez-Sixto et al. described a case of cLMS arising from scrofuloderma scar, suggesting that the absence of lymphatic or blood circulation in
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the scar could have induced a local environment able to stimulate the tumor (17). The risk of developing a LMS from a leiomyoma is still not defined (18). However, it has been recently demonstrated a case of a clLMS arising from a symplastic pilar leiomyoma, an atypical type of smooth muscle tumor (19).

Clinical presentation

Both clLMS and sclLMS appear as smooth nodular cutaneous lesions, firm and coloured from pink to brown. Usually they are sessile, sometimes pedunculated or even ulcerated (3). sclLMS usually grows more than clLMS. The size when they are excised is generally less than two centimetres (7). Clinically, it is a single lesion but sometimes, in cases of cutaneous metastases from visceral malignancies such as the uterus, it could appear as groups of nodular lesions (8, 20). Signs and symptoms include itching, burning, bleeding, spontaneous pain or induced by digitopressure (6). sLMS can arise in different anatomical sites like lower extremities, genitalia, head, neck, areola, nipple, ectopic nipple, buttocks and trunk (2, 21-26). Lower extremities are frequently involved in sclLMS (65%) respect to clLMS (33%) (27). While this latter tumor involves mainly head and neck (48%) and, in a minority of cases, extremities (31%) and trunk (21%) (2). Clinical features are atypical and sometimes do not induce suspicion of malignant lesions (28). Clinically sLMS should be differentiated from dermatofibrosarcoma protuberans, cysts, lipomas, neurofibromas, atypical fibroxanthoma, basal cell carcinoma, squamous cell carcinoma and pyogenic granuloma (6, 8).

Histology and immunohistochemistry

cLMS localized mainly in the dermis sometimes infiltrates the superficial subcutaneous tissue, while sclLMS grows mostly in the subcutaneous tissue (8). sclLMS presents as a circumscribed mass surrounded by a pseudocapsule of collagen. Usually it arises between the junction of dermis and hypodermis. Histology shows atypical smooth muscle cells with irregular pattern (3). cLMS is characterized by dermal proliferation of interlacing fascicles of spindle cells with blunt-ended nuclei and multiple mitotic figures (3). Tumor borders show an irregular aspect with smooth muscle cells through collagen and adipocytes, defining an atypical morphological pattern. These features explain why a radical surgical excision is often difficult (29).

Histopathological diagnosis requires the presence of a dense cellularity composed by spindle cells with eosinophilic cytoplasm, nuclear atypia represented by stretched and blunt-ended nuclei, variable nucleoli, pleomorphism with at least one mitotic figure per 5 or 10 high power fields (HPF) (3, 5, 20). Immunohistochemistry is an essential method to diagnose LMS. Smooth muscle actin (alpha-actin), localized in smooth muscle cells and skeletal muscle with contraction function, is always present in sLMS (2, 30). Vi-
The drugs used in chemotherapy are doxorubicin, vincristine and carboplatin, either in monotherapy or in association (8, 40). Recently Vorinostat, a competitive inhibitor of histone deacetylases approved for cutaneous T-cell lymphoma, has been utilized in monotherapy in a patient who had been treated with multiple chemotherapeutic agents and obtained a partial response (48). Based on literature data we believe that the best therapeutic approach in both forms of sLMS is radical surgical removal, independent of the grade. The MMS represents the optimal therapeutic approach. First, it allows a total excision and furthermore, in esthetically important sites such as the face, it spares healthy tissue to obtain acceptable esthetic results.

**Patient management**

The guidelines for the management of patients affected by sLMS are still not established. Recent literature shows the utility of AJCC criteria for the assessment and management of both cutaneous and subcutaneous types of sLMS (2). A multivariate analysis considering 105 cases of sLMS has demonstrated that AJCC staging and size of the tumor are the only features statistically significant and more reliable for the prognosis and survival of the patient (4, 36). Physical examination and staging exams like lymph nodes ultrasound and total body CT scan are necessary (2). A chest x-ray is useful considering the high frequencies of lung metastasis (8). Subsequent to the diagnosis, the patient should have a follow-up of at least five years (2, 49).

**Conclusions**

sLMS is a rare tumor of the skin. The correct management, histopathological evaluation and therapy still need to be clarified. Regarding the follow-up, we believe that it should be extended for at least five years, in both forms. Furthermore, the subcutaneous forms, presenting a higher risk of metastases, should be followed with periodic instrumental examinations. Moreover, it is necessary to identify univocal criteria for the recognition of cutaneous and subcutaneous forms. Considering both forms, the best surgical therapeutic approach is the MMS. Even if there are no controlled studies between the traditional surgical techniques with a wide or limited excision and MMS for the treatment of sLMS, MMS is the preferred modality.

For the reason that there are not specific guidelines, we believe large scientific studies will help define a shared therapeutic approach that allows a correct management of patients affected by sLMS.

**Conflict of interest statement**

All the authors state no conflict of interests.

**References**


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tasis confirming the data in the literature, that depth, histological grade and surgical therapy of the tumor are important prognostic factors (31). sLMS has a worse prognosis in comparison with cLMS intuitively because arising from smooth muscle cells of the vessels, it could diffuse to blood circulation developing metastases (37).

**Therapy**

The guidelines for the treatment of sLMS are not clearly defined in the literature. The recommended treatment is surgical and implies a wide local excision for cutaneous forms, as well as for the subcutaneous ones. From the literature data, it is difficult to define the surgical margins used by the Authors, as in most cases they generally describe wide or limited margins. A universally accepted concept is that surgical excision should have 2-5 cm margins, and a depth close enough to include the subcutaneous tissues up to the muscular band (6, 38, 39).

Some Authors suggest that limited margins are sufficient to the treatment of cutaneous forms with low grade malignancy. High grade malignancies and subcutaneous ones require a wide excision with minimum lateral margins set at 2 cm and deep to the muscular band (3, 40). The use of wide surgical margins represents a significant reconstructive challenge both under a functional and an esthetic point of view. It has not been demonstrated that this strategy has a higher advantage in patient survival or in the reduction of loco-recurrences (2, 4, 27, 41, 42).

Narrow surgical margins with MMS showed a considerable reduction in the risk of local recurrences, preservation of normal tissue and ensure a more rewarding functional and esthetic result (2, 3, 27, 28, 41-47). Lymphadenectomy is not indicated in cases without lymph node involvement.

Adjuvant radiotherapy and chemotherapy in sLMS treatment did not demonstrate any advantages in patients’ survival. These techniques are generally reserved for subcutaneous and deep tumors, with a high grade malignancy, with dimensions greater than 5 cm and with positive surgical margins (2, 6).

The radiotherapy used for LMS are the cobalto-therapy and the external beam radiotherapy with dosages of 50 Gy [2 Gy fractioning and additional (boost) dose] in the areas with macroscopic and microscopic residual tumor (8, 40).

The guidelines for chemotherapy are doxorubicin, methotrexate, dacarbazine, cyclophosphamide, vincristine and carboplatin, either in monotherapy or in association (8, 40). Recently Vorinostat, a competitive inhibitor of histone deacetylases approved for cutaneous T-cell lymphoma, has been utilized in monotherapy in a patient who had been treated with multiple chemotherapeutic agents and obtained a partial response (48).

Based on literature data we believe that the best therapeutic approach in both forms of sLMS is radical surgical removal, independent of the grade. The MMS represents the optimal therapeutic approach. First, it allows a total excision and furthermore, in esthetically important sites such as the face, it spares healthy tissue to obtain acceptable esthetic results.
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