



REVIEW ARTICLE

Cutaneous leiomyosarcoma: A rare cutaneous soft tissue neoplasm. Clinicopathologic Features and Review of Literature

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OPEN ACCESS

PUBLISHED

30 April 2025

CITATION

Tinguria, M., 2025. Cutaneous leiomyosarcoma: A rare cutaneous soft tissue neoplasm. Clinicopathologic Features and Review of Literature. Medical Research Archives, [online] 13(4).

<https://doi.org/10.18103/mra.v13i4.6437>

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DOI

<https://doi.org/10.18103/mra.v13i4.6437>

ISSN

2375-1924

ABSTRACT

Leiomyosarcomas of the skin are divided into two subtypes based on their origin and location: superficial dermal leiomyosarcoma believed to originate from the arrector pili muscles and sweat glands, and subcutaneous leiomyosarcoma arising from vascular smooth muscle of subcutaneous adipose tissue. Preoperative misdiagnosis is common because it is a rare malignant tumor, and the diagnosis is based on histopathological and immunohistochemical studies. Although superficial cutaneous leiomyosarcoma is usually treated with surgical excision, high rates of local recurrence (30–50%) have been reported. Subcutaneous leiomyosarcomas tend to be more aggressive, and since they are usually diagnosed at a more advanced stage, they are usually larger than superficial dermal based neoplasms. Recurrence rates are higher at 50–70%, and up to 60% of distant metastases have been reported. Guidelines for surgical management and role of radiation and chemotherapy as adjuvant treatments are not clearly defined. The clinicopathological features of this rare cutaneous soft tissue neoplasm are described, along with a review of the literature. Differential diagnoses, possible histogenesis, clinical behavior, management, and prognostic factors are also discussed.

Keywords: Cutaneous leiomyosarcoma, smooth muscle tumor, cutaneous neoplasm, dermatopathology.

Introduction

Cutaneous Leiomyosarcoma (cLMS) is a rare malignant neoplasm representing around 2% to 3% of all cutaneous soft tissue sarcomas and 0.04% of all neoplasms¹. Leiomyosarcomas of the skin can be divided into 2 subtypes based on origin and location: primary dermal leiomyosarcoma believed to originate from the arrector pili muscles and sweat glands, and subcutaneous leiomyosarcoma arising from vascular smooth muscle of subcutaneous adipose tissue²⁻¹⁴. Cutaneous leiomyosarcoma and subcutaneous leiomyosarcoma differ in both primary site of origins and prognosis¹⁵⁻¹⁸. Preoperative misdiagnosis is common because it is a rare malignant tumor, and direct diagnosis requires histopathologic examination.¹⁹⁻²⁴ Guidelines for surgical management are not clearly defined, and recommendations for excision margins range from conservative (1 cm) to wide (2, 3, and 5 cm), including subcutaneous fat and deep fascia^{4,26-31,3,25-30} as well as Mohs micrographic surgery^{21,29}. There are no specific recommendations regarding adjuvant therapy, namely radiation and chemotherapy, for the management of cutaneous LMS.

The review highlights clinicopathologic features of cutaneous leiomyosarcoma. The review discusses the differential diagnoses, current staging system and management as well as prognostic factors. Recommendations about treatment of this rare cutaneous neoplasm is also discussed in detail.

Epidemiology

Cutaneous Leiomyosarcoma (cLMS) represents around 2% to 3% of all cutaneous soft tissue sarcomas and 0.04% of all neoplasms¹. On the skin, leiomyosarcoma is the third in frequency, behind dermatofibrosarcoma protuberans and Kaposi's sarcoma.³¹ The incidence rates of cLMS, have been estimated at 0.2/100,000/year^{3,32}.

Clinical features

Most cLMS occur in the fifth to seventh decades of life²⁻⁵. Male to female ratio appears to be 2:3⁴⁻⁶. The sites involved include head and neck, gluteal region, trunk, areola and nipple, but it frequently occurs on the lower extremities and shows a predilection toward the hair-bearing extensor surfaces³⁻⁶. Annest et al reviewed patients with cLMS and reported that 48% of them have tumors occurring on the head and neck⁹. The other body sites involved include scrotum³³, and face^{27,34}. Taylor et al described differences in tumor location between males and females, where females exhibited higher rates of truncal and lower extremity tumors and males had higher rates of head/ neck and upper extremity tumors³⁵.

The clinical presentation of cutaneous LMS is nonspecific. Clinically, cLMS is a slow growing lesion

and appear as solitary or multiple well circumscribed nodules. Morphologic characteristics include irregular contours, pedunculation, umbilication, and reddish-brown discoloration of the skin²⁻¹⁴. Cutaneous leiomyosarcoma lesions typically range from 0.3 to 3 cm in diameter²⁻⁷. Subcutaneous lesions are usually larger, seem better delimited than dermal ones and remind a lipoma, but with more solid consistency. Cutaneous leiomyosarcomas may be asymptomatic or the patients may complain of pain, pruritus, burning sensation, and bleeding. Pain is the most common symptom of cLMS, occurring in 80% to 95% of patients^{6,8,14}. The clinical differential diagnosis includes cysts, lipomas, fibromas, persistent insect bites, granulomas, dermal nevi, pyogenic granulomas, neurofibromas, dermatofibromas, and carcinomas. In elderly patients, cutaneous leiomyosarcoma of the head and neck may clinically mimic basal cell carcinoma, squamous cell carcinoma, or pyogenic granuloma^{8,15}. Clinical diagnosis of cLMS is difficult. Dermoscopic features of LMS are also nonspecific, consisting of asymmetrical, ulcerated, multilobulated tumors with linear, irregular, and polymorphic atypical vessels, in addition to white structures³⁶.

Pathology

Cutaneous leiomyosarcoma is now believed to be a distinct entity separate from the subcutaneous forms, as in the past cutaneous and subcutaneous leiomyosarcomas were viewed as a single entity^{8,15,24,37,38}. Both the lesions are composed of fascicles of smooth muscle fibers. The cells are spindle-shaped, with elongated nuclei and blunt ends, inconspicuous nucleolus, and fibrillar eosinophilic cytoplasm. Some cells have a clear perinuclear halo characteristic of the muscle cell³¹. (Figure 1). The degree of nuclear pleomorphism is variable, mitosis is usually present (>1 mitosis per 10 high-power field) and necrosis can be present or absent³⁹. (Figure 2). The presence of cellular atypia and one mitotic figure per 10 high-power fields (HPFs) are suggestive of LMS according to the WHO recommendations⁴⁰. Ki-67 can be used to assess proliferative activity in difficult cases. Phosphohistone H3 (PHH3) immunostains may also be employed to identify mitotic figures⁴¹. Two architectural patterns have been described: the nodular pattern, characterized by greater cellularity, atypia and mitotic figures, and the diffuse pattern, which is less cellular and with a lower mitotic burden. Occasionally, there is no obvious cellular atypia, making a differential diagnosis with leiomyoma difficult. In these instances, the histological diagnosis should be based on the overall architecture of the lesion, with an infiltrative pattern and increased cellularity being suggestive of malignancy. Rare histologic variants of leiomyosarcoma include clear cell variant⁴²,

desmoplastic leiomyosarcoma⁴³⁻⁴⁶. LMS of epithelioid cells, LMS of multinucleated giant cells, LMS of

granular cells, sclerotic LMS, and pleomorphic and myxoid variants³¹.

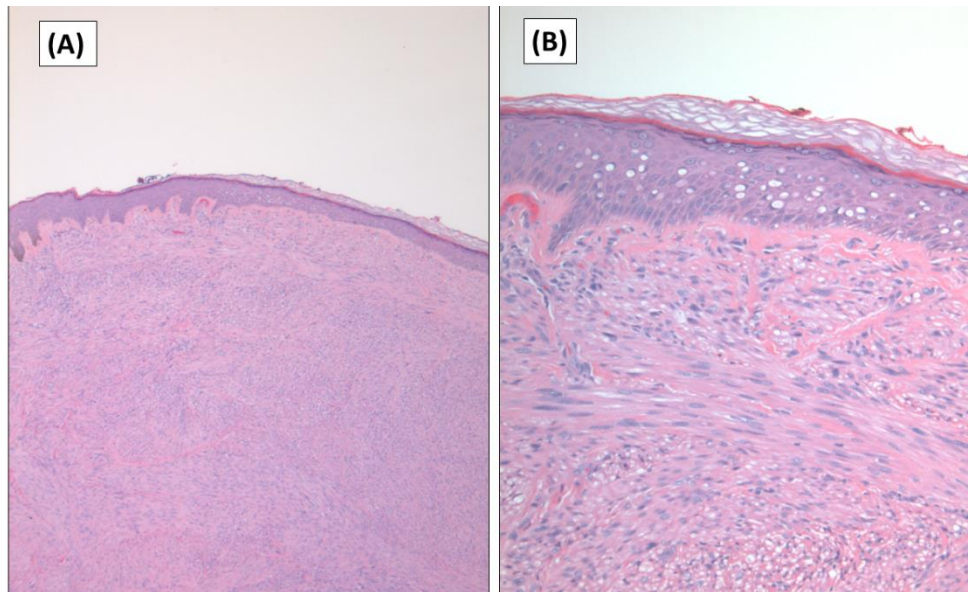


Figure 1. Histologic features of cutaneous leiomyosarcoma. A. Sections shows a dermal based soft tissue neoplasm. The overlying epidermis is unremarkable (Hematoxylin and Eosin stain x 25). B. Higher magnification showing fascicles of elongated spindle cells with elongated nuclei, abundant eosinophilic cytoplasm and mild cytologic atypia. The overlying epidermis is unremarkable (Hematoxylin and Eosin stain x 100).

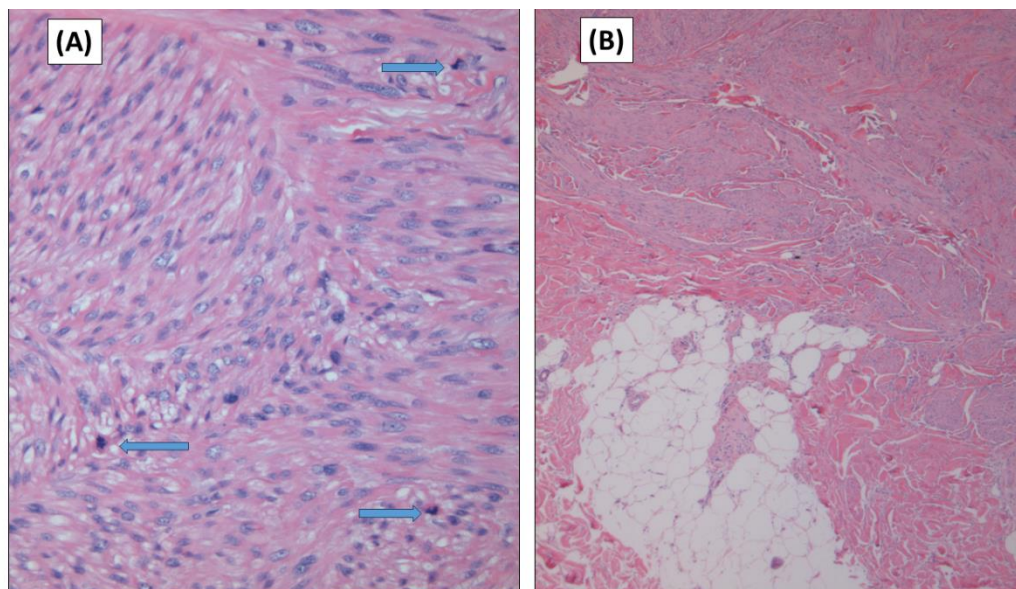


Figure 2. A. Higher magnification of the neoplasm. Numerous mitoses are noted (Blue arrows) (Hematoxylin and Eosin stain x 100). B. The neoplasm is confined to the superficial dermis with no infiltration of the subcutaneous adipose tissue (Hematoxylin and Eosin stain x 25).

Differential Diagnosis

Entities, which may have overlapping features with leiomyosarcoma include spindle cell squamous cell carcinoma, atypical fibroxanthoma (AFX), pleomorphic undifferentiated sarcoma, desmoplastic malignant melanoma, cellular neurofibroma, benign fibrous histiocytoma/dermatofibroma, cellular dermatofibroma, dermatofibrosarcoma protuberans and leiomyoma. Immunohistochemical analysis is essential for accurately diagnosing muscle-specific antigens and facilitating differentiation of smooth muscle tumors from malignant spindle cell cutaneous tumors. Cutaneous leiomyosarcomas are generally positive for vimentin, desmin, smooth muscle actin, HHF-35^{4,17,18}. (Figure 3). Vimentin and smooth muscle actin positivity is noted in 100% of cLMS, and desmin, in 60% of

cLMS^{6,8,17}. Actin expression may be a more sensitive marker of myogenic differentiation than desmin¹⁷. Absence of desmin expression has been observed in poorly differentiated neoplasms and may represent a feature of neoplasms that arise from vessel walls¹⁷⁻¹⁹. Cytokeratin and S100 stains may rarely be positive, causing difficulty in differentiating these tumors from other spindle cell neoplasms such as squamous cell carcinoma and malignant melanoma. The positivity of p53 has been demonstrated in some studies^{20,47}. Diffuse overexpression of p53 has been described in cutaneous LMS but not in leiomyomas, being helpful in the differential diagnosis between these two conditions. The loss of PTEN was noted by Hall et al, but its significance is unknown⁴⁸. Estrogen and progesterone receptors were also expressed by some soft tissue

LMS⁴⁹. Other immunohistochemical stains performed to rule out other spindle-cell lesions (spindle cell carcinoma, desmoplastic melanoma, dermatofibrosarcoma protuberans, nodular fasciitis, malignant peripheral nerve sheath tumor, spindle cell atypical

fibroxanthoma, fibrosarcoma, synovial sarcoma, and vascular tumors) include EMA, CD34, CD117, CEA, HMB45, Mart-1, Melan A and CK7; all of them are negative in LMS³¹.

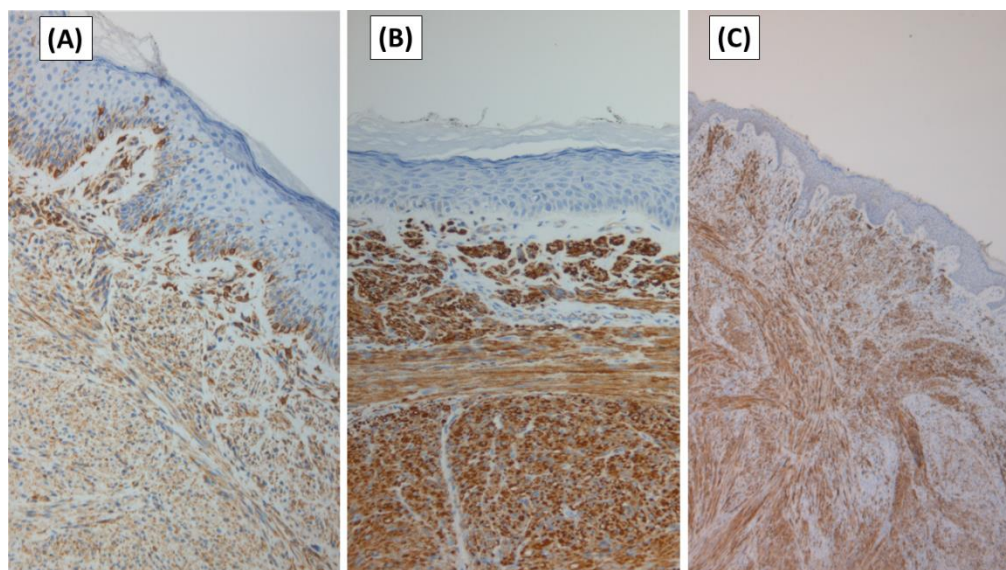


Figure 3. Immunohistochemical studies confirm smooth muscle origin of the neoplasm. The lesional cells show positivity for vimentin (A. x 100), smooth muscle actin (B. x 100), and desmin (C. x 100).

Staging

There are currently two staging systems for LMS. The Federation Nationale des Centres de Lutte Contre Le Cancer (FNCLCC) grading system is determined by three parameters, including differentiation, mitotic activity, and extent of necrosis (Table 1)⁵⁰ and the American Joint Committee on Cancer (AJCC) Cancer Staging (Table 2)⁵¹ Recent literature demonstrated the utility of the American Joint Committee on Cancer GTNM (Grade, Tumor, Nodes, Metastasis) staging criteria for soft tissue sarcoma in the assessment of

both forms of superficial leiomyosarcoma. Recently, multivariate analysis of 105 cases of superficial leiomyosarcoma (both cutaneous and subcutaneous types) demonstrated that AJCC stage and overall tumor size were the only statistically significant prognosticators of 5- year patient survival²³.

Table 1. FNCLCC Histologic Grading System⁵⁰

Tumor Differentiation Grade	
1	Sarcoma closely resembling normal adult mesenchymal tissue
2	Sarcoma for which histologic typing is certain
3	Embryonal and undifferentiated sarcoma, sarcoma of uncertain type, synovial sarcoma, soft tissue osteosarcoma, and Ewing sarcoma/primitive neuroectodermal tumor (PNET) of soft tissue
Mitotic count score	
1	0–9 mitoses per 10 HPF
2	10–19 mitoses per 10 HPF
3	≥20 mitoses per 10 HPF
Tumor necrosis score	
0	No tumor necrosis
1	<50% tumor necrosis
2	≥50% tumor necrosis
Grade definition	
Low	Total differentiation, mitotic count, and a necrosis score of 2–3
Intermediate	Total differentiation, mitotic count, and a necrosis score of 4–5
High	Total differentiation, mitotic count, and a necrosis score of 6–8

FNCLCC : Fédération Nationale des Centres de Lutte Contre Le Cancer. HPF: High-powered field, assessed using a 40× objective.

Table 2. AJCC (American Joint Committee on Cancer) staging of leiomyosarcoma⁵¹

T – Tumor				
Tx	Primary tumor cannot be assessed			
To	No evidence of primary tumor			
T1	Tumor ≤5 cm in greatest dimension			
T2	Tumor >5 cm and ≤10 cm in greatest dimension			
T3	Tumor >10 cm and ≤15 cm in greatest dimension			
T4	Tumor >15 cm in greatest dimension			
N – Lymph node				
No	No regional lymph node metastasis or unknown lymph node status			
N1	Regional lymph node metastasis			
M – Metastasis				
cMo	No distant metastasis			
cM1	Distant metastasis			
pM1	Distant metastasis, microscopically confirmed			
Clinical staging				
Stage IA	T1	No	Mo	G1, GX
Stage IB	T2, T3, T4	NO	MO	G1, GX
Stage II	T1	No	Mo	G2, G3
Stage IIIA	T2	No	Mo	G2, G3
Stage IIIB	T3, T4	No	Mo	G2, G3
Stage IV	Any T	N1	Mo	Any G
Stage IV	Any T	Any	M1	Any G
	N			

Treatment / Management

Complete excision with clear margins is considered the gold standard. Recommendations or guidelines for the size of margin are, however, lacking^{3,5}. Margins of 3–5 cm have been proposed by some investigators for both cutaneous LMS and subcutaneous LMS^{21,28}. In the study by Deneve et al., excision, with a 1 cm margin was performed for 33 cases of cutaneous LMS, with no recurrence observed in more than 15 months of follow-up³⁰. It is important to note that, however, the average size of lesions included was 1.3 cm, and 88% were low-grade histologically³⁰. There are no reports on dependence of either the survival benefit or the rate of local recurrence on the excision width³⁰. The rate of recurrence has been claimed to decrease with wider excision, but there are no documented figures for these claims^{28–30}. If microscopic margins are negative for soft tissue sarcomas, then local recurrence and survival are not affected by increasing the soft tissue excisional margin^{25,30,52}. The deep margin should reach up to the fascia, and in more infiltrating cases the muscle should be included⁵³. It is estimated that up to 20% of patients may require repeated excisions to achieve negative

margins⁵³. MMS, a time-honored tissue-conserving technique that allows for optimal cosmetic outcome, has been shown to be an equally effective, if not superior, modality in treating spindle cell neoplasms, including cutaneous LMS^{18,21,26,29,38,48,54–59}. Kazlouskaya et al. reviewed 47 cases of cutaneous LMS treated with MMS. There were only two cases of recurrences and one case of metastases identified among 47 cases of LMS treated with MMS⁶⁰. MMS has a distinct advantage over surgical excision in certain cases, i.e., a simultaneous closure can be performed after confirming clear margins. Despite this, MMS is still underutilized for cutaneous LMS, with only about 5% of cases being treated with this method⁶¹.

There are no specific recommendations regarding adjuvant therapy, namely radiation and chemotherapy, for the management of cutaneous LMS. Indications for adjuvant chemoradiotherapy include tumor size greater than 5 cm, positive excision margins, high grade of atypia, local recurrence, as well as the presence of metastasis^{53,62}. Radiotherapy can also be used in local palliative control in cases with metastasis⁵³. No clear survival benefit has been

demonstrated with the use of adjuvant chemotherapy or radiotherapy; however, external beam radiation is commonly administered in cases of high-grade tumors^{6,27,63,64}. No survival benefit after adjuvant radiotherapy^{7,14,28} or systemic chemotherapy^{4,6,14}. has been demonstrated in treating superficial LMS.

Advanced therapies, such as immunotherapy and gene therapy, are being developed. Targeted therapies using tyrosine kinase inhibitors are also currently being investigated in clinical trials³².

Clinical Behaviour and Prognosis

The reported biologic behavior of superficial leiomyosarcoma varies widely in the literature. This is due to three factors. First, these tumors are extremely rare. Second, calculations and reports include cutaneous lesions only in some cases^{20,65}, subcutaneous lesions only in others⁶³, and an admixture of both lesions in yet other reports^{21,57}. Many published series do not specify surgical margins, listing only “excised”⁶ or “wide excision”²¹ as tumor treatments, henceforth creating difficulty in systematically reviewing treatment responses and overall biologic behavior. Jensen et al described several poor prognostic factors, including tumor size more than 5 cm, deep location with fascia involvement, high malignancy grade, and acral distribution, and their only patient with local recurrence as having incomplete microscopic margins at initial surgery⁵².

The clinical behavior is correlated to the depth of invasion with cLMS demonstrating a more benign tumor biology than leiomyosarcoma (LMS) arising within the subcutaneous tissue. It is therefore critical to evaluate the entire depth of the tumor to assess its origin⁶⁰. Based on the low rate of recurrence and absence of metastases, the name “atypical intradermal smooth muscle neoplasm” was proposed in 2011 for these tumors. The local recurrence rate for superficial cutaneous leiomyosarcoma is approximately 30%; however, reported rates range widely from 0% to 50% depending upon treatment modality and duration of follow-up^{6,8,21,24,66}. By contrast, subcutaneous leiomyosarcomas have a much higher rate of local recurrence. These tumors recur locally in 50% to 70% of cases.⁶ Inability to achieve clear margins is one of the most important factors in predicting recurrence¹⁸. Oliver et al proposed that the risk of local recurrence is related to the adequacy of excision, whereas metastatic spread is related to depth, histologic grade of the tumor, and DNA content²⁴.

The metastatic potential of cutaneous and subcutaneous leiomyosarcoma is also dramatically different. Cutaneous LMS rarely metastasizes and has a favorable prognosis overall. Kraft and Fletcher reported no metastases among 83 cases of cutaneous LMS and proposed that the term “sarcoma” be omitted altogether.⁵ Other studies reported a rate of metastasis

of up to 12% for cutaneous LMS^{6,18,21,56,67}. The metastatic rate for subcutaneous LMS, in contrast, is much higher, ranging from 27.3% to 63%^{5,6,18,21,56,67}. Higher histological grade, size greater than 5 cm, presence of necrosis, and deeper location increase the likelihood of cutaneous LMS metastases.¹⁸ Distant metastases are most commonly observed in the lungs, but superficial LMS may also metastasize to other cutaneous sites, namely to the scalp; scalp metastases may even be a harbinger of poor outcomes^{32,18}.

Only few cases of mortality have been associated with cutaneous LMS. Fauth et al. reported only one patient with cutaneous LMS (1/14; 7.14%) developing lung metastases and subsequently expiring from the disease in about a year⁵⁶. Similarly, Winchester et al. reported two deaths out of 48 cases with cutaneous LMS (4.2%)¹⁸. On the contrary, subcutaneous LMS has a significantly higher mortality rate that ranges from 25% to 41.2%^{5,6,18,21,39,56,67}. The Scandinavian Sarcoma Research Group has estimated the overall survival rate for LMS to be 64% for 5 years and 46% for 10 years, with the presence of metastases being the most important prognostic factor⁶². Bresler et al in their retrospective analysis of 36 cases of subcutaneous LMS reported metastasis in 12 cases (33%) with lung being the most common site of metastasis. Six of 36 patients (17%) died from the disease at an average of 47 months after diagnosis (range 16 to 94 months). Metastasis or death from disease was significantly associated with the Fédération Nationale des Centers de Lutte Contre le Cancer grade ($P = 0.0015$), the presence of necrosis ($P = 0.032$), tumor size ($P = 0.049$), and AJCC tumor stage ($P = 0.036$). These data demonstrate that subcutaneous LMS are more aggressive than dermal-based tumors and have a prognosis akin to that of deep-seated LMS⁶⁸. The prognosis of dermal LMS is usually better, with 5-year-survival rates over 95%⁵³. Subcutaneous LMS has a greater tendency for recurrence and metastasis, therefore resulting in lower 5-year-survival rates of around 65%^{39,62}. Wong et al. retrospectively reviewed all patients with dermal and subcutaneous leiomyosarcoma managed at the Peter MacCallum Cancer Centre, Australia from January 2003 to December 2018. Eighty-three patients were identified (64 with dermal leiomyosarcomas and 19 with subcutaneous leiomyosarcomas). Dermal leiomyosarcoma had an excellent prognosis, particularly after definitive surgical excision, with margins of at least 10 mm. Subcutaneous leiomyosarcoma had poorer outcomes and should be managed by wider excision and considered for adjuvant radiotherapy⁶⁹. In a multivariate analysis of prognostic factors for superficial LMS, such as size, depth of invasion, histological grade and proliferative activity (Ki67), only tumor size was shown to be an independent prognostic factor in relation to decreased survival⁵². In this study and in a univariate analysis, a tumor size

equal to or greater than 5 cm, deep location with fascia involvement and a high histological grade have been correlated with decreased survival. Additionally, in subsequent studies, histological grades II and III (according to the Fédération Nationale des Centres de Lutte le Cancer, or FNCLCC grading system) have been associated with recurrence and metastasis⁵⁶. Fernandez reviewed the literature to study the evolution and prognostic factors of primary and cutaneous leiomyosarcoma. The published data were reviewed to assess the rates of recurrence and metastasis, mortality, recommended follow-up periods, and prognostic factors. This review included 112 subcutaneous LMS and 313 cutaneous LMS cases. In subcutaneous LMS, the rates of recurrence, metastasis, and mortality were 36.63%, 43.23%, and 37.82%, respectively, after a median follow-up period of 4.40 years, while in cutaneous LMS, these rates were 24.40%, 4.22%, and 3.33%, respectively, after a median follow-up period of 3.45 years⁴⁷. The cutaneous LMS have a potential risk of metastasis, and in certain cases, they may be the cause of death. The collected data suggest that the term "atypical intradermal smooth neoplasm" should be avoided to identify dermal LMS⁴⁷.

Taylor et al. explored the presentation of LMS and disease-specific survival (DSS) with respect to sex. Males demonstrated higher 5- and 10-year DSS rates (69.0% and 60.0%, respectively) than females (50.0% and 36.0%) ($p < 0.001$). Multivariate analysis adjusted for age, race, ethnicity, income, rural–urban living, disease stage, and primary tumor location revealed that female sex independently increased disease-specific mortality risk compared to male sex³⁵.

There are no standard guidelines for LMS follow-up, but clinical examination is recommended every 4 months during the first two years, for early detection of possible local recurrences. Thereafter, controls every 6 months until the fifth year after surgery are advised; subsequently, once a year until 20 years, since very late relapses have been described^{18,39}. However, the practice of a simple annual chest radiograph in the first five years after surgery and clinical evaluation of the surgical bed and regional lymph nodes appears to be a reasonable strategy. In some cases, magnetic resonance imaging may be helpful, especially in recurrent or hypodermic lesions, or in cases where surgery is complex.

Histogenesis / Genetics

Most cLMS arise de novo rather than via malignant transformation of leiomyoma as a precursor lesion^{2-7,52}. Although the etiology of cutaneous leiomyosarcoma is unclear, predisposing factors such as exposure to trauma, radiation, chemicals, and sunlight have been emphasized^{10,70}. Recently, cLMS arising from a tattoo¹¹, pacemaker pocket¹², or scar^{10,13} has been reported. In

immunocompromised pediatric patients, including those with HIV, an increased incidence of LMS was associated with Epstein-Barr virus infection^{71,72}.

Although the underlying genetic abnormalities responsible for the development of cutaneous LMS are poorly understood, one study has identified defects in the 13q4-q21 chromosome region^{88,73}. LMS can also be seen in the setting of Reed syndrome⁷⁴, with fumarate hydratase gene mutation being implicated as an important factor⁷⁵. Moreover, aberrations in the p53 and p16 genes may play a role and have been shown to be associated with poor prognosis^{76,77}. Kraft and Fletcher described a case of LMS and pleomorphic liposarcoma developing in a patient with Li–Fraumeni syndrome, a hereditary disorder associated with a germline mutation in the p53 tumor suppressor gene⁵. A 32-year-old patient with Li–Fraumeni syndrome, who developed cutaneous LMS with a hereditary disorder associated with a germline mutation in the p53 tumor suppressor gene⁷⁸.

Conclusion

Leiomyosarcoma of the skin is a rare tumor of smooth muscle derivation that is diagnosed by histopathological and immunohistochemical studies. There are two subtypes of superficial leiomyosarcoma: cutaneous and subcutaneous. Although cutaneous LMS has a better prognosis than subcutaneous LMS, it is unclear whether larger tumors or those that secondarily involve the subcutis exhibit different behaviors. The AJCC staging criteria for soft tissue sarcomas provide valuable prognostic information for cutaneous leiomyosarcomas. Although surgical excision is regarded as the mainstay treatment for cutaneous LMS, more prospective studies are needed to standardize the margins. The clear differences in biological behavior between cutaneous and subcutaneous tumors provide compelling evidence that not all types of superficial leiomyosarcomas should be treated equally, with more aggressive treatment warranted only in subcutaneous tumors. Although MMS can be a promising surgical modality, fewer than 50 cases have been performed, with insufficient follow-up to demonstrate its long-term effectiveness. MMS may be safely introduced for small cutaneous LMS; however, the tumor characteristics and patient selection criteria remain to be established. Although radiation and chemotherapy may be employed as adjuvant treatments for larger, recurrent, and subcutaneous LMS, the optimal regimens still need to be elucidated. Adjuvant therapy may be employed, after multidisciplinary discussions until specific guidelines for adjuvant therapy are established. There are no standard guidelines for LMS follow-up, and further studies are required to establish follow-up guidelines.

Conflict of Interest:

None.

Acknowledgements:

None.

Funding Statement:

None.

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