E.B. SATBAYEVA¹, N.A. MUCHAMETGALIEV¹, E.E. ISKAKOVA¹

¹Kazakh Institute of Oncology and Radiology, Almaty, the Republic of Kazakhstan

Cutaneous leiomyosarcoma/ atypical smooth muscle sarcoma

Relevance: Cutaneous leiomyosarcoma is a rare primary dermal neoplasm, accounting for up to 2-3% of all superficial sarcomas. It can occur at any age, most likely between the ages of 50 and 70 years. This tumor has a high recurrence potential in case of insufficiently deep excision. Recurrent tumors are more aggressive and characterized by subsequent metastasis.

The purpose of the study was to demonstrate the results of the histopathological examination of a cutaneous leiomyosarcoma / atypical smooth muscle tumor.

Results: Cutaneous leiomyosarcoma was represented by spindle-shaped cells with high cellularity located in bundles and growing expansively, surrounded by a capsule. The nuclei of the cells were elongated, hyperchromic. Cells with atypical abnormal nuclei were present in smaller quantities. The mitoses, including atypical, were numerous. IHC staining for SMA, Desmin, H-Caldesmon – diffusely positive on tumor cells. The reaction for S100, Myogenin – negative.

Conclusion: A cutaneous leiomyosarcoma can be finally diagnosed only after a pathomorphological examination of the specimen and differential diagnostics using additional research methods.

Keywords: cutaneous leiomyosarcoma; pathomorphological examination; pathological examination; atypical smooth muscle tumor.

Introduction: Cutaneous leiomyosarcoma (also known as “atypical smooth muscle tumor”, “piloleiomyosarcoma”) is a rare dermal tumor. It belongs to superficial leiomyosarcomas, which can be cutaneous and subcutaneous, depending on their origin. Cutaneous leiomyosarcoma develops from smooth hair retraction

muscle cells and/or muscle cells surrounding the sweat gland [1, 2]. In contrast, a subcutaneous leiomyosarcoma develops from the blood vessel muscle membrane cells [1-3]. The cutaneous and subcutaneous leiomyosarcomas account for 2–3% of all cutaneous soft-tissue sarcomas [1-3] (Table 1).

Table 1 – The frequency of superficial leiomyosarcomas

Leiomyosarcoma (7-10% of all soft-tissue sarcomas in adults)					
Localization	common		rare		
	Retroperitoneal leiomyosarcomas	Intra-abdominal leiomyosarcomas (uterus and gastrointestinal tract)	Leiomyosarcomas arising from deeply located blood vessels	Superficial leiomyosarcomas (2-3% of all superficial sarcomas)	
				Cutaneous leiomyosarcomas	Subcutaneous leiomyosarcoma

The rare occurrence of this nosology does not provide precise data on its etiology. Some scientists associated dermal leiomyosarcoma with Li-Fraumeni syndrome. EBV-associated leiomyosarcomas occur in immunosuppressive patients [4]. There are also reports on dermal leiomyosarcoma on areas of the skin previously subjected to injuries or radiation therapy [2, 3].

Dermal leiomyosarcoma can occur at any age but is most common between 40 and 60 years of age. Recent reports show the same incidence in both sexes in contrast to previous data, which indicated a higher prevalence in women [1, 3]. Most observations report the lesion of the proximal limbs, mainly on the skin with hair [1, 2]. Other localizations (head, neck, and body) are less likely to be affected [3, 5]. The skin above the surface of the dermal leiomyosarcoma is inactive, maybe slightly swollen, the color of the surface may change, it may also be in the form of a formation on the “leg.” Some researchers note possible ulceration on the surface. At the same time, the skin above a subcutaneous leiomyosarcoma does not change color and does not lose mobility. Cutaneous leiomyosarcoma

is a single small red-pink nodule with a diameter of 0.5-2.0 cm [1, 3], with slow growth, which can be painful constantly or from time to time. Subcutaneous leiomyosarcoma has several nodules (multifocal location), which can suggest the metastases of leiomyosarcoma from the retroperitoneal space, uterus, digestive tract, or deep vessels [2, 3, 6]. A macroscopic examination of the incision shows a whitish-gray tumor tissue with a fibrous structure; the fibers are twisted. The tumor boundaries are blurred since the tumor structures penetrate and “twist” the collagen fibers and smooth muscle cells of the hair follicle. The tumors which expand into the subcutaneous fat forming a pseudo capsule have more distinct boundaries.

Almost all intradermal leiomyosarcomas are well-differentiated (Low Grade), although even unusual intradermal leiomyosarcomas with a low degree of differentiation (High Grade) were characterized by benign behavior [1-3, 7]. On microscopic examination, cutaneous leiomyosarcoma is represented by highly or moderately differentiated spindle cells located in bundles. The nuclei of the cells are elongated, slightly rounded, and hyperchromic. To a less-

er extent, there are less differentiated areas with atypical irregular nuclei and eccentric mitoses and the presence of atypical giant cells with bizarre nuclei. For the most part, the tumor is well-differentiated, as evidenced by the absence of regressive and degenerative changes. Almost no hemorrhages, necrosis, myxoid changes, and hyalinosis are detected, probably due to their small size. With highly differentiated dermal leiomyosarcoma, the main criteria for malignancy include rapid growth of formation,

high cellularity of the tumor tissue, a significant frequency of mitoses (three or more x 10 HPF). Figures of mitosis, including atypical forms, are easily detected. The number of mitoses can be high in anaplastic regions, even in the absence of metastases [1-3]. In dermal leiomyosarcoma, so-called "mitotic hot spots" may be present, which also may be absent in individual samples. The percentage of S-phase cells correlates with mitotic numbers; a comparison is shown in Table 2.

Table 2 - Superficial leiomyosarcomas

Subtype	Precursor tissue	Morphology	Prognosis
Cutaneous	Hair raising muscle	Differentiated spindle cell skin cells	Local relapse of 32%
Subcutaneous	Vascular wall	Atypical smooth muscle cells located in adipose tissue	Distant metastases in 30-40%

Most of the soft-tissue leiomyosarcomas are characterized by overexpression of αSMA (alpha-smooth muscle actin), Desmin, H-caldesmon (high molecular weight caldesmon), MSA (muscle-specific actin), Cytokeratin (can be positive in 45% of cases), and Vimentin. Normally, the overexpression of at least two of the smooth muscle markers speaks for leiomyosarcoma [6, 8]. CD34, S100, and EMA are also expressed in some cases, but they are not specific for leiomyosarcoma. CD117 is not expressed in most cases, which distinguishes soft tissue leiomyosarcoma from GIST. Another interesting fact is the expression of estrogen and progesterone receptors by some leiomyosarcomas [6].

Dermal leiomyosarcoma is associated with a favorable biological behavior/clinical course. The relapses develop in 32% of cases (some researchers report up to 50% of relapses [6, 7]). However, metastases are rare and, according to the analysis, correlate with the original tumor invasion depth [3]. Tumors localized in the dermis only do not metastasize [3, 7]. Tumors that are deeper advanced into the hypoderm (subcutaneous fat) metastasize in about 30-40% of cases [2, 8]. They metastasize through the blood vessels to the lungs, with sporadic lesions of regional lymph nodes in about 25% of cases [2, 3, 9].

Treatment of dermal sarcoma. The proper surgical removal of the primary tumor with sufficient capture of the surrounding tissue is critical. If the excision is not deep enough, cutaneous leiomyosarcoma has a high recurrence potential. A recurring tumor is characterized by a more aggressive course, which implies a greater amount of damage in the horizontal direction and a spread to deeper structures with subsequent metastasis [9].

Given the rarity of the occurrence of an atypical smooth muscle tumor, we describe our observation of a clinical case of cutaneous leiomyosarcoma. A 60-year-old female patient appealed to the outpatient department of the Kazakh Institute of Oncology and Radiology, complaining of a protruding formation in the skin of her left leg. After physical exercise, the formation has changed color and became painful. Ultrasound examination suggested a fibrolipoma. The surgeon found a skin lesion in the lower third of the left lower leg sized 2.5 cm x 1.5 cm. A skin lesion was excised; the biopsy sample was sent for histopathological examination.

The material was fixed for 24 hours in 10% neutral buffered formalin. Pieces of tissue were processed in a tissue processor as per the standard procedure and paraffined. Paraffin sections 3-4 μm thick were dyed with hematoxylin and eosin. The pathomorphological study was performed

using an Axiostar plus microscope (Carl Zeiss, Germany) with a total magnification of X100, X200.

A nodular formation with clear boundaries was detected in the dermis. A tumor had a tufted structure in the form of interwoven bundles of elongated cells. The cell nuclei were elongated, hyperchromic. Less differentiated cells with atypical irregular nuclei and atypical giant cells with bizarre nuclei were also present. The tumor spread expansively into the subcutaneous fat tissue. Mitoses, including pathological (10 x 10 HPF) ones, were present.

Figure 1 – Cutaneous leiomyosarcoma (atypical smooth muscle tumor). A nodular formation with clear boundaries located in the skin extends into the subcutaneous fat. HE, x100

Figure 2 – Cutaneous leiomyosarcoma (atypical smooth muscle tumor), pathological mitosis. HE, x100

The immunohistochemical (IHC) study was made using the Ventana BenchMark Ultra platform with monoclonal antibodies to SMA (Smooth muscle actin), Desmin,

H-Caldesmon, S100, Myogenin, as well as the UltraView imaging system.

In the IHC study, the tumor cells were brightly positive to antibodies to SMA, Desmin, H-Caldesmon (Figures 4, 5, 6), and negative to S100 and Myogenin antibodies. The two latter reagents are not specific for leiomyosarcoma. The histopathological and IHC studies showed the morphological picture and immunophenotype relevant for cutaneous leiomyosarcoma / atypical smooth muscle tumor, ICD-O code: 8897/1.

Figure 3 – Cutaneous leiomyosarcoma (atypical smooth muscle tumor), bright diffuse immunostaining of tumor cells, and vascular wall smooth muscle cells with SMA. x100

Figure 4 – Cutaneous leiomyosarcoma (atypical smooth muscle tumor), bright, positive staining of tumor cells with Desmin. X100

So, we described a case of cutaneous leiomyosarcoma in a 60-year-old female patient who noticed the first symptoms of a tumor after physical exercise. The tumor was clinically manifested by skin protrusion, discoloration, and periodic painfulness. The diagnosis was verified by histopathological and IHC studies. The dermal localization, size,

and histological differentiation of the tumor spoke for a favorable prognosis. The size and the histological stage of the primary neoplasm correlated with the depth of the lesion.

Figure 5 – Cutaneous leiomyosarcoma (atypical smooth muscle tumor), bright diffuse staining of tumor cells with H-caldesmon. x100

The demonstrated case is of great clinical interest due to the rarity of this pathology.

References:

1. Torres T., Oliveira A. Superficial cutaneous leiomyosarcoma of the face: report of three cases // *J. Dermatol.* – 2011. – Vol. 38(4). – P.373–376;
2. Ciurea M.E., Georgescu C.V., Radu C.C., Georgescu C.C., Stoica L.E. Cutaneous leiomyosarcoma – Case report // *J. Med. Life.* – 2014. – Vol. 7(2). – P. 270–273;
3. Deyrup A.T., Lee V.K., Hill C.E. et al. Epstein Barr virus-associated smooth muscle tumors are distinctive mesenchymal tumors reflecting multiple infection events: a clinicopathologic and molecular analysis of 29 tumors from 19 patients // *Am. J. Surg. Path.* – 2006. – Vol. 30. – P. 75;
4. Lee K.C., Kim M.S., Choi H., Na C.H., Shin B.S. Rapid growing superficial cutaneous leiomyosarcoma of the face // *Ann. Dermatol.* – 2013. – Vol. 25(2). – P. 237–241;
5. Jensen M.L., Myhre Jensen O., Michalski W. et al. Intradermal and subcutaneous leiomyosarcoma: a clinicopathological and immunohistochemical study of 451 cases // *J. Cutan. Pathol.* – 1996. – Vol. 23. – P. 458;
6. Cutaneous leiomyosarcoma (atypical smooth muscle tumors). In: *World health organization classification of skin tumors.* – IARC, 2018. – P. 330;
7. Snowden R.T., Osborn F.D., Wong F.S., Sebelik M.E. Superficial leiomyosarcoma of the head and neck: case report and review of the literature // *Ear Nose Throat J.* – 2001. – Vol. 80(7). – P. 449–453;
8. Humphreys T.R., Finkelstein D.H., Lee J.B. Superficial leiomyosarcoma treated with Mohs' micrographic surgery // *Dermatol. Surg.* – 2004. – Vol. 30. – P. 108;
9. Huether M.J., Zitelli J.A., Brodland D.G. Mohs' micrographic surgery for the treatment of spindle cell tumors of the skin // *J. Am. Acad. Dermatol.* – 2001. – Vol. 44. – P. 656.