

**Figure 2** Cells with a polygonal morphology, abundant granular eosinophilic cytoplasm, and large vesicular nuclei. The cells are arranged in an interlinked fascicular pattern. Hematoxylin-eosin, original magnification  $\times 40$ .

Primitive polypoid granular cell tumor is a rare neoplasm or uncertain origin that affects middle-aged adults. It usually arises on the trunk or limbs as a polypoid or elevated lesion with a smooth surface; its size can be variable. The distinctive characteristic that differentiates it from conventional granular cell tumor is its histopathology, which shows a tumor in the mid dermis that is clearly surrounded by an epidermal collarette; the tumor is formed of large polygonal, round or spindle-shaped cells with marked nuclear pleomorphism, an elongated nucleus, abundant eosinophilic cytoplasm containing fine granules, and mitotic activity of around 1 to 3 mitoses per mm,<sup>2</sup> usually with no atypia and minimal or absent epidermal hyperplasia. These histopathology findings satisfy the criteria proposed by Enzinger and Weiss for the classification of malignant or atypical granular cell tumor, but the tumors can be differentiated by immunohistochemistry, as primitive polypoid granular cell tumor is usually negative for S-100 and positive for CD68 and neuron-specific enolase.<sup>5</sup>

Despite the histological characteristics, this is a tumor of low-grade malignancy. In the series reported there is only 1 case of metastasis, which arose in the cheek 25 months after excision of the lesion and did not present an epidermal collarette on histology.<sup>6</sup>

We have presented a new case of primitive polypoid granular cell tumor, a variant that is not clearly distinguished from the conventional tumor. Its atypical histological characteristics allow it to be classified as a new entity and distinguished from granular cell tumor of neural origin.

## References

1. Philip E, LeBoit MD, Ronald J, Barr MD. Primitive polypoid granular-cell tumor and other cutaneous granular-cell neoplasms of apparent nonneural origin. *Am J Surg Pathol.* 1991;15:48–58.
2. Chaudhry IH, Caljonje E. Dermal non-neural granular cell tumor (so-called primitive polypoid granular cell tumor): A distinctive further delineated in a clinicopathological study of 11 cases. *Histopathology.* 2005;47:179–85.
3. Torrijos-Aguilar A, Alegre-de Miquel V, Pitarch-Bort G, Mercader-García P, Fortea-Baixauli JM. Tumor de células granulares cutáneo: análisis clínico-patológico de treinta y cuatro casos. *Actas Dermosifiliogr.* 2009;100:126–32.
4. Di Martino B, Soskin A. Cutaneous granular cell tumor. Report of three cases and review of the literature. *Our Dermatol Online.* 2012;3:46–51.
5. Weiss SW, Langloss JM, Enzinger FM. Value of S-100 protein in the diagnosis of soft tissue tumors with particular reference to benign and malignant Schwann cell tumors. *Lab Invest.* 1983;49:299–308.
6. Lazar AJF, Fletcher CDM. Primitive nonneural granular cell tumors of skin: Clinicopathologic analysis of 13 cases. *Am J Surg Pathol.* 2005;29:927–34.

M.T. López-Villaescusa,<sup>a,\*</sup> M. Rodríguez-Vázquez,<sup>a</sup>  
M. García-Arpa,<sup>b</sup> R. García-Angel<sup>c</sup>

<sup>a</sup> *Servicio de Dermatología, Complejo Hospitalario Universitario de Albacete, Albacete, Spain*

<sup>b</sup> *Servicio de Dermatología, Hospital de Ciudad Real, Ciudad Real, Spain*

<sup>c</sup> *Servicio de Anatomía Patológica, Complejo Hospitalario Universitario de Albacete, Albacete, Spain*

\*Corresponding author.

E-mail address: [lopezvillaescusa@hotmail.com](mailto:lopezvillaescusa@hotmail.com)

(M.T. López-Villaescusa).

## Dermal Leiomyosarcoma at the End of the Left Eyebrow<sup>☆</sup>



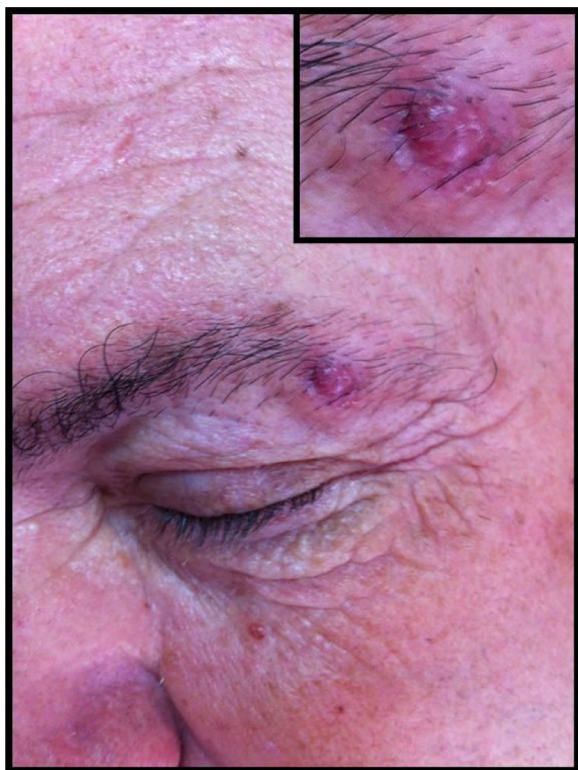
### Leiomiosarcoma dérmico en la cola de la ceja izquierda

Cutaneous sarcomas constitute less than 1% of superficial soft tissue neoplasms. Leiomyosarcomas (LMSs), which account for between 3% and 6.5% of cutaneous sarcomas, are

classified as dermal (derived from the hair erector muscle) or subcutaneous (derived from the smooth muscle of vessel walls).<sup>1</sup> This classification has prognostic relevance, as dermal LMS has a more favorable clinical course and outcome; metastasis occurs in 5% to 10% of dermal cases as compared with 30% to 40% of subcutaneous cases.<sup>2</sup>

We report the case of a 63-year-old man with a medical history of hypertension, hyperuricemia, and dilated cardiomyopathy, who presented with an asymptomatic and progressively growing nodular lesion in the ciliary region of the left eye that had appeared 6 months previously (Fig. 1). Physical examination revealed a raised, indurated, and erythematous lesion, with destruction of hair follicles, that was surrounded by a halo of firm, edematous skin.

<sup>☆</sup> Please cite this article as: Lozano Salazar A, Márquez García A, Ortega Medina I, Ríos-Martín J. Leiomiosarcoma dérmico en la cola de la ceja izquierda. *Actas Dermosifiliogr.* 2014;105:879–882.



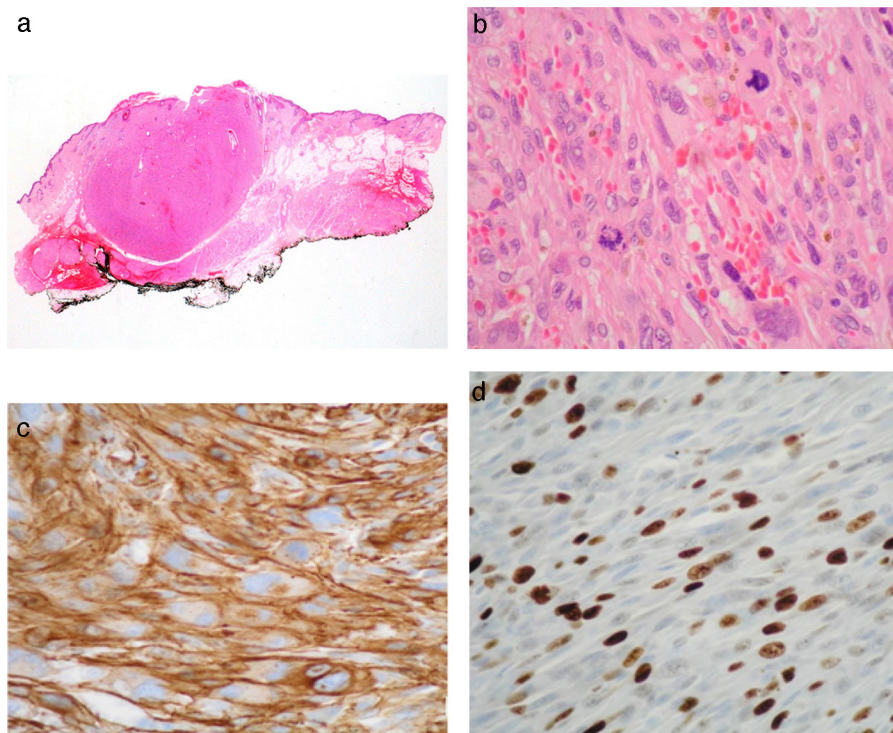
**Figure 1** Nodular lesion of 7 mm in diameter located at the tail of the left eyebrow. A higher magnification image of the lesion is shown in the inset.

Dermoscopy showed a homogeneous brown pattern with no other notable features. Based on a clinical diagnosis of basal cell carcinoma the lesion was excised and the surgical defect reconstructed with a transposition flap.

Histologic examination revealed a malignant mesenchymal neoplasm of 7 mm in diameter, with expansive borders. The tumor occupied the entire thickness of the dermis, extended into the hypodermis, and was located within 1 mm of the deep resection margin (Fig. 2). The tumor was composed of spindle cells arranged in intersecting fascicles. The nuclei were atypical, pleomorphic, elongated, and had rounded edges. The mitotic index was 15 mitoses per 10 high power fields (HPF). Immunohistochemistry was positive for muscle markers (smooth muscle actin, desmin, caldesmon) and negative for S-100 and CD34. The Ki-67 proliferative index was 20%. A diagnosis of dermal leiomyosarcoma with infiltration of the hypodermis was established. No metastasis was detected in the staging study. Ten months after surgery, the patient remains free of disease.

LMSs are rare cutaneous neoplasms that occur in middle-aged men, some of whom may have a medical history of trauma. The most common site of LMS is the flexor surfaces of the lower extremities, followed by the scalp and trunk. Facial localization is rare.

While LMSs that are confined to the dermis do not usually metastasize,<sup>3</sup> the rate of recurrence is over 30%. Deeper tumors may metastasize in up to 30% to 40% of cases, especially to the lungs.<sup>4</sup> In general, LMSs are asymptomatic and grow slowly. In rare cases these tumors can cause pain, itching, tenderness, or bleeding.<sup>3</sup> They usually appear as



**Figure 2** A, Panoramic microscopic image shows a neoplasm with an expansive growth pattern, which does not affect the resection margin (hematoxylin-eosin, original magnification  $\times 4$ ). B, The neoplasm is composed of spindle cells arranged in fascicles with marked atypia and abundant mitotic figures (hematoxylin-eosin, original magnification  $\times 40$ ). C, Expression of smooth muscle actin (Papanicolaou, original magnification  $\times 40$ ). D, The proliferative index (Papanicolaou, Ki-67) is 20%.

**Table 1** Immunohistochemistry of Cutaneous Spindle-Cell Tumors.

| Marker Tumor | CD10 | CD34 | Vimentin | Desmin | Smooth Muscle Actin | S-100 Protein | HMB-45 | HMW Cytokeratins |
|--------------|------|------|----------|--------|---------------------|---------------|--------|------------------|
| DFSP         | -    | +    | +        | -      | -                   | -             | -      | -                |
| AFX          | +    | -/+  | +        | -      | -/+                 | -             | -      | -                |
| MFH          | -    | -/+  | +        | -      | -/+                 | -             | -      | -                |
| SCSCC        | -    | -    | +/-      | -      | -                   | -             | -      | +                |
| LMS          | -    | -/+  | +        | +      | +                   | -             | -      | -/+              |
| DM           | -/+  | -    | -/+      | -/+    | -/+                 | +             | -      | -/+              |
| AS           | +    | +    | +        | -      | -                   | -             | -      | +/-              |

Abbreviations: AFX, atypical fibroxanthoma; AS, angiosarcoma; DFSP, dermatofibrosarcoma protuberans; DM, desmoplastic melanoma; HMW, high molecular-weight; LMS, leiomyosarcoma; MFH, malignant fibrous histiocytoma; SCSCC, spindle-cell squamous cell carcinoma.

a solitary, firm, raised lesion of between 0.5 cm and 3 cm, sometimes with ulceration.

Histologically, LMS tumors have infiltrative borders, consisting of spindle cells embedded in a collagenous stroma. They sometimes show a fascicular arrangement and may be accompanied by a peritumoral or intratumoral lymphocytic inflammatory infiltrate.<sup>5</sup> Two growth patterns have been described: a nodular pattern, with high cellularity, nuclear atypia, and mitoses, and a diffuse pattern, with low cellularity and proliferative activity.

The malignancy criteria established by the World Health Organization include high cellularity, nuclear atypia, and at least 1 mitosis per 10 HPF.<sup>6</sup>

Clinical suspicion of LMS is uncommon.<sup>3</sup> Histopathological examination is usually necessary for diagnosis, as physical examination reveals no specific findings that facilitate the identification of LMS. The differential diagnosis includes other soft-tissue spindle-cell tumors (e.g., fibrosarcoma, malignant histiocytoma, dermatofibroma, atypical fibroxanthoma, spindle cell melanoma, sarcomatoid carcinoma, leiomyoma) and immunohistochemical techniques are required for proper grading (Table 1).<sup>2,7,8</sup> A recent study described the usefulness of phosphohistone H3, an immunohistochemical marker of mitosis, in distinguishing between leiomyosarcoma and leiomyoma.<sup>7</sup>

In 2003 Hornick and Fletcher<sup>5</sup> proposed the term *atypical smooth muscle tumors* for cutaneous smooth muscle tumors with mitotic figures and cellular atypia, and proposed reserving the term *leiomyosarcoma* for tumors affecting subcutaneous tissue. In 2011, Kraft and Fletcher<sup>9</sup> published an analysis of 84 cases of primary LMS (atypical smooth muscle tumors); 61 (72.9%) of these were limited to the dermis and 23 (27.1%) involved superficial extension into the subcutaneous tissue. No metastasis was detected in any of these cases, with a mean follow-up of 51 months. Given the low (or absent) risk of metastasis, those authors concluded that it was inappropriate to classify this lesion as a sarcoma, preferring the term *atypical intradermal smooth muscle neoplasm*. We disagree with this view, as other histologically malignant cutaneous neoplasms (e.g., dermatofibrosarcoma protuberans) have a more benign biological behavior, with very low metastatic potential in most cases, and thus should be referred to using the original terminology.<sup>10</sup>

The treatment for cutaneous LMS is excision with wide margins (at least 3-5 cm). These tumors show a poor response to chemotherapy and radiation therapy, although the latter may be indicated for high-grade tumors of more than 5 cm in diameter, in cases of excision of recurrent tumors, or after surgery with inadequate margins.

## References

1. Kilgour CS. Cutaneous leiomyosarcoma. *Br J Plast Surg.* 1955;8:144-6.
2. Hollmig ST, Sachdev R, Cockerell CJ, Posten W, Chiang M, Kim J. Spindle cell neoplasms encountered in dermatologic surgery: A review. *Dermatol Surg.* 2012;38:825-50.
3. Fields JP, Helwig EB. Leiomyosarcoma of the skin and subcutaneous tissue. *Cancer.* 1981;47:156-69.
4. Jensen ML, Myhre Jensen O, Michalski W, et al. Intradermal and subcutaneous leiomyosarcoma: A clinicopathologic and immunohistochemical study. *J Cutan Pathol.* 1996;23:458-63.
5. Hornick JL, Fletcher CD. Criteria for malignancy in non-visceral smooth muscle tumors. *Ann Diagn Pathol.* 2003;7:60-6.
6. Weedon D, Williamson RM, Patterson JW. Smooth and skeletal muscle tumors. In: LeBoit PE, Burg G, Weedon D, Sarasin A, editors. *World Health Organization classification of tumors pathology and genetics skin tumors.* Lyon: IARC Press; 2006. p. 251.
7. Idriss MH, Kazlouskaya V, Malhotra S, Andres C, Elston DM. Phosphohistone-H3 and Ki-67 immunostaining in cutaneous pilar leiomyoma and leiomyosarcoma (atypical intradermal smooth muscle neoplasm). *J Cutan Pathol.* 2013;40:409-12.
8. Feigenbaum L, Skinner D, Golda N. Atypical cutaneous leiomyosarcoma with skip-lesion behaviour. *Dermatol Surg.* 2013;39:660-2.
9. Kraft S, Fletcher CD. Atypical intradermal smooth muscle neoplasms: Clinicopathologic analysis of 84 cases and a reappraisal of cutaneous «leiomyosarcoma». *Am J Surg Pathol.* 2011;35:599-607.
10. Llombart B, Serra-Guillén C, Monteagudo C, López Guerrero JA, Sanmartín O. Dermatofibrosarcoma protuberans: A comprehensive review and update on diagnosis and management. *Semin Diagn Pathol.* 2013;30:13-28.

A.D. Lozano Salazar,<sup>b,\*</sup> A. Márquez García,<sup>a</sup>  
I. Ortega Medina,<sup>b</sup> J.J. Ríos-Martín<sup>b</sup>

<sup>a</sup> Unidad de Gestión Clínica de Dermatología,  
Hospital Universitario Virgen Macarena, Sevilla,  
Spain

<sup>b</sup> Unidad de Gestión Clínica de Anatomía Patológica,  
Hospital Universitario Virgen Macarena, Sevilla, Spain

\* Corresponding author.

E-mail address: [analozano@hotmail.com](mailto:analozano@hotmail.com)

(A.D. Lozano Salazar).

## Increased Sensitization to Kathon CG (Methylchloroisothiazolinone plus methylisothiazolinone) in the South of Gran Canaria, Spain<sup>☆</sup>



### Aumento de sensibilización al Kathon CG<sup>®</sup> (clorometilisotiazolinona/metilisotiazolinona) en el área sur de Gran Canaria

Kathon CG is a preservative that contains methylchloroisothiazolinone (MCLI) and methylisothiazolinone (MI) in a 3 to 1 ratio. It is used in cosmetics as well as in industrial and domestic cleaning products. An increase in sensitization to MCLI/MI has recently been reported, probably due to an increase in sensitization to the MI component.<sup>1</sup>

We have performed a retrospective analysis of the data from patients who underwent patch testing in our hospital to discover whether this situation has also arisen in our setting. The sample of patients sensitized to MCLI/MI includes from January 1, 2005, to July 31, 2013, and the sample of those sensitized to MI includes from January 1, 2012, to July 31, 2013. The  $\chi^2$  test (Epidat 4.0<sup>®</sup>, Servicio Gallego de Salud) was used to determine whether significant differences existed between the groups studied. Sensitization to MCLI/MI was diagnosed using the True Test (Smartpractice DENMARK ApS, Hillerød, Denmark) and all patients evaluated during the study period underwent patch testing for MI at a concentration of 0.05% in water (alergEAZE, Marti-Tor, Barcelona) and at 0.2% in water in those patients patch tested with the cosmetics series (Chemotecnique, Vellinge, Sweden).

Patch testing for MCLI/MI was performed in 863 patients, of whom 85 (9.85%) were sensitized. Analysis of the frequency of sensitization by years revealed a marked increase starting in the year 2010 (Fig. 1). When the study period was divided at the 2010 time point, we observed an increase in the frequency of sensitization from 5.97% to 14.11% ( $P < .05$ ,  $\chi^2$  test). Comparison of the MOAHLFA indices of the sensitized patients in these 2 periods showed no significant differences; this would suggest there had been no epidemiological changes that might justify this increase in frequency.

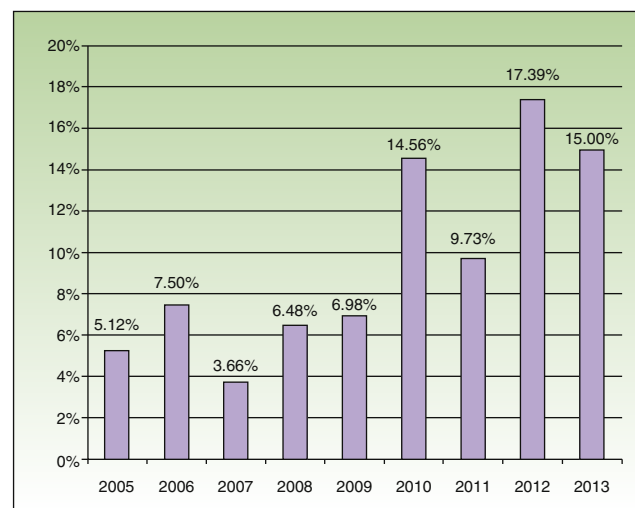
<sup>☆</sup> Please cite this article as: Liuti F, Hernández Hernández Z, Borrego Hernando L. Aumento de sensibilización al Kathon CG<sup>®</sup> (clorometilisotiazolinona/metilisotiazolinona) en el área sur de Gran Canaria. *Actas Dermosifiliogr.* 2014;105:882–883.

However, evaluation of the cause of the eczema showed a statistically significant increase in sensitization related to the use of cosmetic products in the second period ( $P < .05$ ,  $\chi^2$  test) (Table 1).

MI was studied in 195 patients, of whom 8.2% (16 patients) were sensitized. It should be noted that 5 of the 16 patients patch tested with MI at both concentrations (0.05% and 0.2%) were negative at the lower concentration. All the patients sensitized to MI were positive with MCLI/MI, and 50% of those sensitized to MCLI/MI were positive with MI.

Since its introduction in the eighties, MCLI/MI has been found to be a powerful sensitizer, and the maximum permissible concentration in cosmetic products has therefore been reduced to 15 ppm. Despite this regulation, the frequency of sensitization prior to 2008 was stable in Europe at levels between 1% and 4%,<sup>2</sup> and in Spain at figures between 3% and 4%.<sup>3,4</sup> However, since that date, the frequency of sensitization in Europe has doubled<sup>1,5,6</sup> and, in 2012, reached 8% in Spain.<sup>7</sup> Our data show that sensitization levels were already very high and that they have doubled in the past 3 years.

In 2005, MI was approved for use in cosmetic products at a maximum concentration of 100 ppm, but its concentration has not been regulated in industrial products. It is estimated that the prevalence of sensitization to MI in Europe was around 1.5% prior to 2010, and it has increased in parallel with MCLI/MI sensitization in recent years. This finding allows us to state that this new sensitization "epidemic"



**Figure 1** Frequency of sensitization to Kathon CG by study year.