SOMATO PUBLICATIONS

Archives of Clinical Case Reports

Case Report

Novel Collision Tumor: Melanocytic Tumor of Uncertain Malignant Potential (MELTUMP) and Leiomyoma

Michael L. Wang[1], May P. Chan[1,2], Rajiv M. Patel[1,2], Lori Lowe[1,2], Min Wang[1], Aleodor A. Andea[1,2] and Douglas R. Fullen[1,2]

[1]Department of Pathology, University of Michigan Health System, Ann Arbor, MI 48109, USA

[2]Department of Dermatology, University of Michigan Health System, Ann Arbor, MI 48109, USA

***Address for Correspondence:** Douglas R. Fullen, NCRC Bldg. 35, 2800 Plymouth Rd., Ann Arbor, MI 48109, USA, Tel: (734)764-4460; Fax: (734)764-4690; E-mail: dfullen@med.umich.edu

Received: 11 May 2019; **Accepted:** 07 June 2019; **Published:** 10 June 2019

Citation of this article: Wang, ML., Chan, MP., Patel, RM., Lowe, L., Andea, AA., Fullen, DR. (2019) Novel Collision Tumor: Melanocytic Tumor of Uncertain Malignant Potential (MELTUMP) and Leiomyoma. Arch Clin Case Rep, 2(2): 012-016.

ABSTRACT

Cutaneous collision tumors comprising melanocytic and smooth muscle proliferations are rare. We present a skin lesion taken from the flank of a 29-year-old woman, consisting of intermingled melanocytic and smooth muscle elements confirmed by immunohistochemistry. The melanocytic component was histopathologically ambiguous and demonstrated multiple chromosomal aberrations by array-comparative genomic hybridization, best regarded as a melanocytic tumor of uncertain malignant potential (MELTUMP). The smooth muscle component was morphologically bland, most in keeping with a leiomyoma. Previous reports of cutaneous collision tumors of melanocytic and smooth muscle proliferations are predominantly composed of blue nevi and smooth muscle hamartomas. To our knowledge, this is the first reported cutaneous collision tumor composed of MELTUMP and leiomyoma.

Keywords: Collision tumor, Melanocytic tumor of uncertain malignant potential (MELTUMP), Leiomyoma, Array comparative genomic hybridization (aCGH)

Introduction

Cutaneous collision tumors composed of melanocytic and smooth muscle proliferations are exceedingly rare. A literature review revealed 21 reported cases, with the majority involving a blue nevus [1-8]. Borderline melanocytic tumors or melanoma have not been previously reported as a component of these collision tumors. We present a cutaneous collision tumor comprised of a leiomyoma and a histopathologically ambiguous melanocytic tumor with multiple chromosomal aberrations by array comparative genomic hybridization (aCGH), best regarded as a melanocytic tumor of uncertain malignant potential (MELTUMP).

Case Report

A 29-year-old female in good health presented with a longstanding left flank pigmented skin lesion that had enlarged over the past few years. The lesion was 1 cm in diameter and asymptomatic. The clinical differential diagnosis included dysplastic nevus and scar. A punch biopsy was performed and submitted to our Dermatopathology Service for consultation.

The hematoxylin and eosin-stained sections demonstrated a cellular dermal proliferation of intermingled melanocytic and smooth muscle cells (Figure 1 and 2A). The melanocytic component was composed of epithelioid to occasionally spindled cells with eosinophilic cytoplasm, smooth to irregular nuclear contours, and conspicuous nucleoli, extending into the deep reticular dermis. Few melanocytic cells contained melanin pigment. Some epithelioid cells displayed cytologic atypia (Figure 2B). The smooth muscle component, which lacked cytologic atypia, was composed of fascicles of spindled cells with eosinophilic cytoplasm and elongated oval nuclei with blunted ends and indistinct nucleoli. No mitotic figures were identified in either component. The overlying epidermis showed

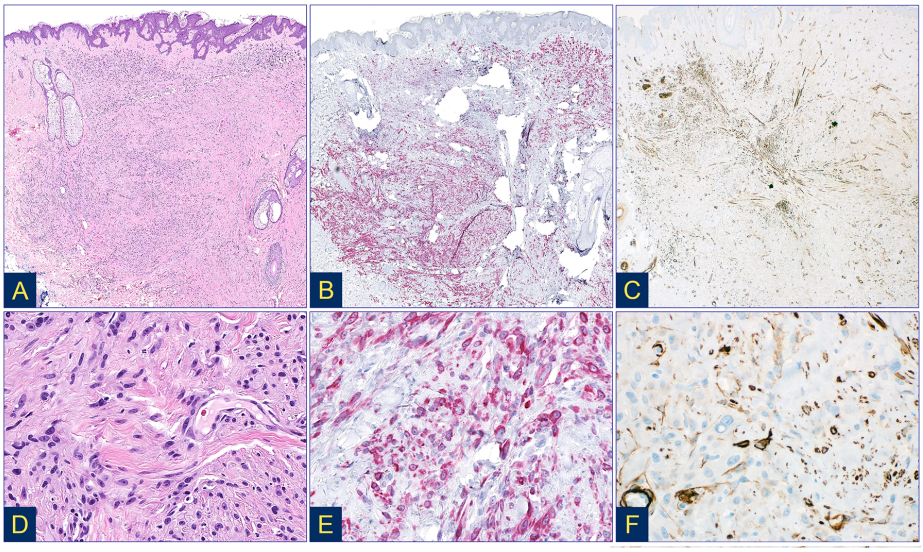

Figure 1: Collision tumor comprising MELTUMP and leiomyoma. Cellular dermal proliferation thatwas distinctly biphenotypic (A and D), consisting of intermingled melanocytic and smooth musclecomponents. The melanocytic component is positive for Melan-A (B and E). The smooth muscle component is positive for caldesmon (C and F). Original magnification: A-C at 20X and D-F at 400X.

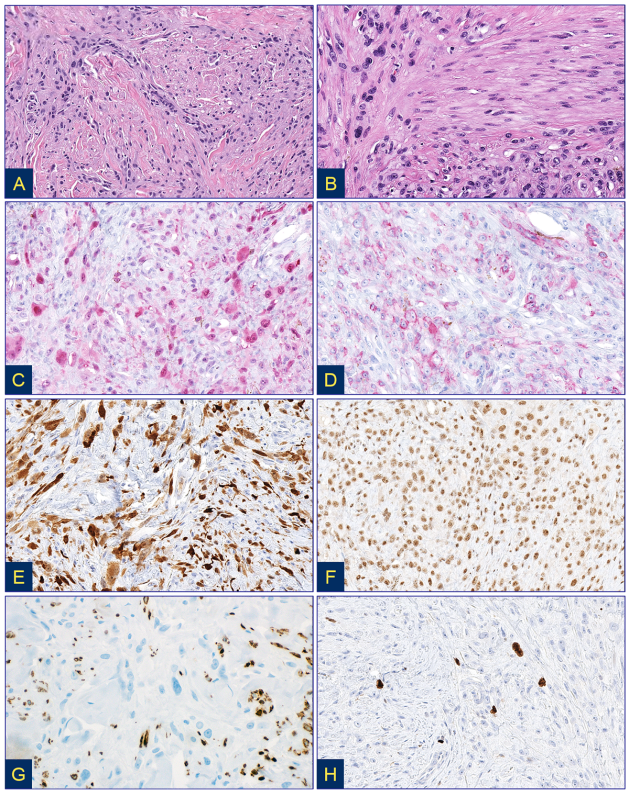

Figure 2: Histomorphology and immunohistochemistry of collision tumor. Intermingled proliferation of epithelioid and spindled melanocytes and smooth muscle cells (A). Atypical epithelioid melanocytes juxtaposed to a bundle of bland smooth muscle cells (B). Positive immunostaining of melanocytes for S-100 (C), HMB-45 (D), p16 (E), and BAP-1 (F). Positive immunostaining of smooth muscle cells for desmin (G). Ki-67 immunostain shows a proliferation index of 2-3%, presumably highlighting a few melanocytes (H). Original Magnification: A at 260X and B-H at 400X.

slight acanthosis and elongation of rete ridges without junctional melanocytic proliferation. The subcutaneous tissue was spared.

Immunohistochemical studies were performed. The melanocytic component was positive for S-100, Melan-A, and HMB-45; there was no loss of p16 or BAP-1 (Figure 1 and 2). The melanocytes were negative for smooth muscle actin (SMA), caldesmon and desmin. The smooth muscle component was positive for SMA, caldesmon and desmin (all cytoplasmic) (Figure 1 and 2) and negative for S-100, Melan-A, HMB-45, p16, and BAP-1. The Ki-67 proliferation index was 2-3% (Figure 2H).

Array comparative genomic hybridization was performed by single nucleotide polymorphism microarray analysis using the Affymetrix OncoScan(TM) FFPE Assay Kit. Multiple chromosomal copy number changes were detected, including gains of whole chromosomes 4, 5, 6, 8, 10, 11, 13, 15, 18, 20, and 22, partial gains of chromosomes 2p, 2q, 12p, 12q, and 17q, and copy neutral loss of heterozygosity in chromosomes 7 and X (Figure 3). Additionally, no mutations were identified in the following genes: BRAF, NRAS, KRAS, IDH1, IDH2, PIK3CA, EGFR, PTEN, and TP53.

Integrating the histopathologic, immunohistochemical, and molecular findings, the melanocytic component was challenging to classify and best regarded as MELTUMP, while the smooth muscle component was morphologically a leiomyoma. Given the ambiguity of the melanocytic component, the case was discussed at melanoma tumor board regarding appropriate therapy. Following discussion between the clinician and patient, the decision was made to treat with wide local excision and sentinel lymph node biopsy. Both the excision and the sentinel lymph node biopsy were negative for a melanocytic tumor.

Follow-up full body skin examination revealed a 0.8 x 0.3 cm pigmented skin lesion between the left first and second toes. A biopsy demonstrated an atypical compound nevus with severe

junctional atypia. Margins were free in the wide local excision. To our knowledge, the patient has not been seen for recurrent or new melanocytic lesions since.

Discussion

Only 21 collision skin tumors of melanocytic and smooth muscle lineages have been reported in the literature to date (Table 1) [1-8]. Of these, 18 cases involved a blue nevus, 1 involved a compound nevus, 1 involved an intradermal nevus, and 1 involved a desmoplastic Spitz nevus. The most common type of smooth muscle proliferation was smooth muscle hamartoma (16/21; 76%). The average age of the patients at presentation was 53 years (range: 31 to 80). The majority of patients were male (14 males, 4 females, 3 unspecified). These tumors most commonly arose on the back (14/21; 67%) followed by the extremities (3/21; 14%) and the abdomen (1/21; 5%); the anatomic site was unknown in 3 cases. The majority of the lesions were under 0.6 cm in diameter, except for 3 cases composed of plaque-type blue nevus (9 cm), compound nevus (within Becker's nevus) (2 cm), and intradermal nevus [3-5].

Our case was unique because the melanocytic component exhibited ambiguous histopathologic and immunohistochemical findings. Although the melanocytes demonstrated cytologic atypia, no mitotic figures were observed. Additionally, the melanocytes retained p16 and BAP-1 expression and the Ki-67 proliferation index was minimally increased (2-3%). Thus, the lesion was further characterized by aCGH.

Array comparative genomic hybridization is a useful adjunct in the diagnosis of melanocytic lesions difficult to classify based on histopathology and immunohistochemistry alone. The test detects chromosomal aberrations frequently present in melanoma (>90%) and relatively rare in benign nevi [9-11]. Melanomas typically show partial chromosomal gains or losses, though abnormalities involving entire chromosomes may also be present. Common abnormalities in benign melanocytic lesions include whole chromosomal gains or losses in proliferative nodules arising in congenital melanocytic nevi and 11p gain in Spitz nevi [9-13].

Table 1: Summary of 21 previously reported collision tumors involving melanocytic and smooth muscle proliferations.

Author	Year	Number of Cases	Collision Tumor
Tieche	1906	1	Blue nevus with fibromatous and myomatous elements
Montgomery	1959	2	Blue nevus and smooth muscle tumor
Park	1999	1	Plaque-type blue nevus and nevus spilus with smooth muscle hyperplasia*
Patrizi	2007	1	Becker's nevus, compound nevus and smooth muscle hamartoma*#
Zarineh	2008	1	Intradermal nevus and smooth muscle hamartoma
Tzu	2013	12	Combined (blue nevus and common-type) nevus and smooth muscle hamartoma
Townsend	2015	2	Combined (blue nevus and common-type) nevus and smooth muscle hamartoma Common blue nevus and smooth muscle hamartoma
Ieremia	2015	1	Desmoplastic Spitz nevus and cutaneous leiomyoma

*Adjacent melanocytic and smooth muscle proliferations without intimate comingling of the two components.
#A basal cell carcinoma was also present within the Becker's nevus.

Table 2: Summary of results from immunohistochemical studies performed to characterize the collision tumor.

Component	Positive	Negative
Melanocytic	S-100, Melan-A, HMB-45, p16, and BAP1	SMA caldesmon and desmin
Smooth muscle	SMA, caldesmon and desmin	S-100, Melan-A, HMB-45, p16, and BAP1

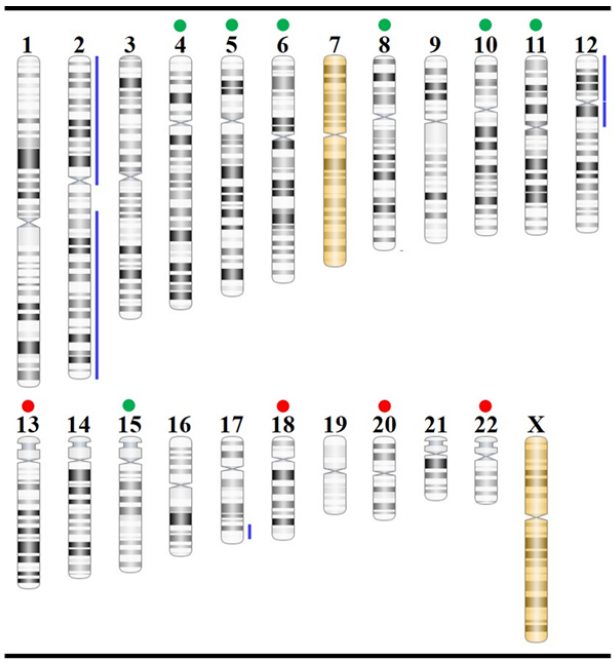

Figure 3: aCGH data: represented on karyotype. Green dots represent triploid gains, red dots represent tetraploid gains, blue lines represent partial gains, and orange chromosomes represent copy neutral loss of heterozygosity.

In our tumor, aCGH demonstrated multiple partial and whole chromosomal gains. Many of these chromosomal alterations have been described in melanoma, including gains of 2p and 20 in blue nevus-like melanoma, 2q in metastatic melanoma, 12q in acral melanoma, 17q in melanoma on sun-damaged skin and acral, mucosal, and metastatic melanomas, and 22 in uveal melanoma [9-13]. Given these findings, this melanocytic tumor was regarded as MELTUMP. With potential for aggressive behavior, it was treated as melanoma following discussion of treatment options between the clinician and patient.

Data from aCGH represents the average of the entire cell population. Due to the intermingled nature of the collision tumor, cells from the smooth muscle component would also have been included. Data regarding chromosomal copy number variation in cutaneous smooth muscle tumors is lacking. However, aCGH has been used to help classify ambiguous uterine smooth muscle tumors. Uterine leiomyomas were found to harbor no or very few alterations, whereas leiomyosarcomas contain numerous copy number alterations [14]. In our case, the histomorphology of the smooth muscle component was

unambiguously benign (leiomyoma). Therefore, the chromosomal aberrancies detected are best attributed to the atypical melanocytic component.

Biphasic tumors may arise from the collision of two unrelated tumors, tumor-to-tumor metastasis, or divergent differentiation. A collision tumor is defined as two distinct tumors coinciding at the same location [15,16]. It has been previously suggested that collision tumors of melanocytic and smooth muscle lineages may arise from dermal stem/pluripotent cells [6-8]. Various stem cell populations have been isolated from the epidermis, dermis, and hair follicles, some of which have the capability of differentiating into both melanocytic and smooth muscle cells [17-19]. These may be the source of dermal melanocytic lesions, smooth muscle lesions, and collision tumors of the two. We propose that the intermingled nature of the two components in our case may support this theory.

Tumor-to-tumor metastasis is a very rare but well-described phenomenon, and a variety of neoplasms have been documented as donor or host tumors [20,21]. Melanoma has been reported as the donor in tumor-to-tumor metastasis in 2 cases: one metastasized to a colonic polyp [22] and another to a prostatic adenocarcinoma [23]. In contrast to previous collision tumors of melanocytic and smooth muscle components, tumor-to-tumor metastasis was considered in our case because of the chromosomal abnormalities and, therefore, potential for aggressive (metastatic) behavior. However, the extensive intermingling of the two components and lack of a definitive known primary melanoma argue against this mechanism.

Lastly, melanomas can exhibit various divergent differentiation [24]. Only 4 cases of melanoma developing smooth muscle differentiation have been reported [25-28]; 3 of which were diagnosed in metastatic lesions [25-27]. In all cases, areas of smooth muscle differentiation (supported by SMA and desmin positivity) were malignant appearing with nuclear pleomorphism and high mitotic activity including atypical mitotic figures, and demonstrated variable expression of melanocytic markers. Our case is unlikely to represent a melanocytic tumor with divergent smooth muscle differentiation without a definitive melanoma diagnosis and given the absence of malignant features in the smooth muscle component.

Other entities that must be considered in the histopathological differential diagnosis include cutaneous perivascular epithelioid cell tumor (PEComa) and clear cell sarcoma. Cutaneous PEComas are rare, well-demarcated dermal lesions composed of perivascular epithelioid cells. There may be admixture of spindle cells and nuclear pleomorphism. In addition, the lesional cells exhibit both melanocytic and smooth muscle immunophenotypes [29]. Cutaneous clear cell sarcomas are rare dermal lesions composed of fusiform to epithelioid cells arranged in fascicles and nests separated by delicate fibrous septa. Immunohistochemically, these are indistinguishable from melanocytic tumors; some even produce melanin [30]. Although our collision tumor shares some morphologic and immunophenotypic characteristics with these entities, it also demonstrates features not seen in either – a distinctly biphasic appearance of juxtaposed atypical and bland cell populations of either melanocytic or smooth muscle differentiation without a perivascular or nested arrangement.

In summary, collision tumors with melanocytic and smooth muscle components occur rarely, and may be a diagnostic challenge. Previous reports have predominantly involved blue nevi and smooth muscle hamartomas. To our knowledge, this is the first case involving a MELTUMP and a leiomyoma.

Acknowledgement

We would like to thank Dr. Reena Singh for her help in the translation of the German language reference. We also would like to thank Elizabeth Walker for her assistance revising the figures.

References

1. Tieche, M. (1906) Uber benigne Melanome (Cromatophorome) der Haut-"Blaue Naevi". Virchow's Arch Pathol Anat, 186: 212.
2. Montgomery, H., Winkelmann, RK. (1959) Smooth-muscle tumors of the skin. AMA Arch Derm, 79(1): 32-40.
3. Park, YM., Kang, H., Cho, BK. (1999) Plaque-type blue nevus combined with nevus spilus and smooth muscle hyperplasia. Int J Dermatol, 38(10): 775-777.
4. Patrizi, A., Medri, M., Neri, I., Fanti, PA. (2007) Becker naevus associated with basal cell carcinoma, melanocytic naevus and smooth-muscle hamartoma. J Eur Acad Dermatol Venereol, 21(1): 130-132.
5. Zarineh, A., Kozovska, ME., Brown, WG., Elder, DE., Rabkin, MS. (2008) Smooth muscle hamartoma associated with a congenital pattern melanocytic nevus, a case report and review of the literature. J Cutan Pathol, 35(1): 83-86.
6. Tzu, J., Goldman, C., Perry, AE., Meehan, SA. (2013) Combined blue nevus-smooth muscle hamartoma: a series of 12 cases. J Cutan Pathol, 40(10): 879-883.
7. Townsend, M., Wald, J., Murphy, M., Kristjansson, A. (2015) Blue Nevus-Smooth Muscle Hamartoma: A Rarely Reported Entity. Am J Dermatopathol, 37(8): 662-663.
8. Ieremia, E., Taylor, M., Calonje, E. (2015) Desmoplastic Spitz Nevus Combined With Cutaneous Leiomyoma: A Rare Collision Tumor. Am J Dermatopathol, 37(9): 732-733.
9. Bastian, BC., Olshen, AB., LeBoit, PE., Pinkel, D. (2003) Classifying melanocytic tumors based on DNA copy number changes. Am J Pathol,163(5): 1765-1770.
10. Wang, L., Rao, M., Fang, Y., Hameed, M., Viale, A., Busam, K., et al. (2013) A genome-wide high-resolution array-CGH analysis of cutaneous melanoma and comparison of array-CGH to FISH in diagnostic evaluation. J Mol Diagn, 15(5): 581-591.
11. Shain, AH., Yeh, I., Kovalyshyn, I., Sriharan, A., Talevich , E., Gagnon, A., et al. (2015) The Genetic Evolution of Melanoma from Precursor Lesions. N Engl J Med, 373: 1926-1936.
12. Bauer, J., Bastian, BC. (2006) Distinguishing melanocytic nevi from melanoma by DNA copy number changes: comparative genomic hybridization as a research and diagnostic tool. Dermatol Ther, 19(1): 40-49.
13. North, JP., Vemula, SS., Bastian, BC. (2014) Chromosomal copy number analysis in melanoma diagnostics. Methods Mol Biol, 1102: 199-226.
14. Croce, S., Ribeiro, A., Brulard, C., Noel, JC., Amant, F., Stoeckle, E., et al. (2015) Uterine smooth muscle tumor analysis by comparative genomic hybridization: a useful diagnostic tool in challenging lesions. Mod Pathol, 28(7): 1001-1010.
15. Moody, P., Murtagh, K., Piduru, S., Brem, S., Murtagh, R., Rojiani, AM. (2012) Tumor-to-tumor metastasis: pathology and neuroimaging considerations. Int J Clin Exp Pathol, 5(4): 367-373.

16. Abrahão-Machado, LF., Abrahao-Machado, EF., Abrahao-Machado, ECF., Guimarães, FP., Alvarenga, M., Adami, AM., et al. (2015) Tumor-To-Tumor Metastasis: Intracranial Meningioma Harboring Metastatic Breast Carcinoma. Ann Clin Pathol, 3(2): 1049-1053.

17. Grichnik, JM. (2008) Melanoma, nevogenesis, and stem cell biology. J Invest Dermatol, 128(10): 2365-2380.

18. Li, L., Fukunaga-Kalabis, M., Herlyn, M. (2013) Isolation, characterization, and differentiation of human multipotent dermal stem cells. Methods Mol Biol, 989: 235-246.

19. DeLellis, RA., Tischler, AS., Wolfe, HJ. (1984) Multidirectional differentiation in neuroendocrine neoplasms. J Histochem Cytochem, 32(8): 899-904.

20. Campbell, LV Jr., Gilbert, E., Chamberlain, CR Jr., Watne, AL. (1968) Metastases of cancer to cancer. Cancer, 22(3): 635-643.

21. Petraki, C., Vaslamatzis, M., Argyrakos, T., Petraki, K., Strataki, M., Alexopoulos, C., et al. (2003) Tumor to tumor metastasis: report of two cases and review of the literature. Int J Surg Pathol, 11(2): 127-135.

22. Grignon, DJ., Ro, JY., Varona, OB., Ayala, AG. (1988) Malignant melanoma with metastasis to a colonic polyp. Am J Gastroenterol, 83(11): 1298-1300.

23. Grignon, DJ., Ro, JY., Ayala, AG. (1989) Malignant melanoma with metastasis to adenocarcinoma of the prostate. Cancer, 639(1):196-198.

24. Banerjee, SS., Eyden, B. (2008) Divergent differentiation in malignant melanomas: a review. Histopathology, 52(2):119-129.

25. Banerjee, SS., Bishop, PW., Nicholson, CM., Eyden, BP. (1996) Malignant melanoma showing smooth muscle differentiation. J Clin Pathol, 49(11): 950-951.

26. Ul-Mulk, J., Rasmussen, H., Breiting, L., Siim, E. (2012) A case of collision tumor or transdifferentiation between malignant melanoma and leiomyosarcoma. Indian J Pathol Microbiol, 55(4): 538-539.

27. Morimoto, A., Asai, J., Wakabayashi, Y., Komori, S., Hanada, K., Takenaka, H., et al. (2014) Malignant melanoma with probable smooth muscle differentiation. Case Rep Dermatol, 6(1):16-19.

28. Prieto-Torres, L., Alegría-Landa, V., Llanos, C., Córdoba, A., Kutzner, H., Requena, L. (2017) Cutaneous malignant melanoma with rhabdoid morphology and smooth muscle differentiation: achallenging histopathologic diagnosis. Am J Dermatopathol, 39(5): 397-403.

29. Llamas-Velasco, M., Requena, L., Mentzel, T. (2016) Cutaneous perivascular epithelioid cell tumors: A review on an infrequent neoplasm. World J Methodol, 6(1): 87-92.

30. Hantschke, M., Mentzel, T., Rutten, A., , Palmedo, G., Calonje, E., Lazar, AJ., et al. (2010) Cutaneous clear cell sarcoma: A clinicopathological, immunohistochemical, and molecular analysis of 12 cases emphasizing its distinction form dermal melanoma. Am J Surg Pathol, 34(2): 216-222.