



CUTANEOUS LEIOMYOMA: A CASE STUDY WITH REVIEW OF LITERATURE ON RARE VARIANTS AND CLINICAL BEHAVIOUR

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ABSTRACT

Cutaneous leiomyomas are unusual benign smooth muscle tumors that comprises of three distinct types such as piloleiomyoma, angioleiomyoma, and genital leiomyoma. However Cutaneous leiomyoma tumor arises from erector pili muscle sharing similar histological features with uterine atypical or symplastic leiomyoma showing atypical cellularity with pleomorphic nuclei with variable mitotic activity. Six other cases have been reported so far and, in spite of its name and of being a smooth muscle proliferation, no recurrences nor metastasis have been reported. The present study briefs a series of 5 interesting cases of cutaneous leiomyoma presented as subcutaneous masses with a brief note on its review of literature. The present study advocates the clinicians to include cutaneous leiomyoma as a differential diagnosis on all patients presenting with subcutaneous masses

KEY WORDS: cutaneous leiomyoma, smooth muscle proliferation, immunohistochemistry



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INTRODUCTION

Leiomyomas are a group of benign soft tissue neoplasms that arise from smooth muscles and were first described by Virchow in 1858. The hereditary form which presents with multiple leiomyomas was originally observed by Kloepper et al in 1958.^[2] The tumor tends to originate in the presence of smooth muscle and is a rare, benign tumor with many differential diagnoses. It has been divided into different subtypes according to skin adnexal structures from which they are derived:^[3]

1. Cutaneous pilar leiomyoma arising from erector pilae muscle of pilo sebaceous unit [multiple] and solitary pilo leiomyoma

2. Angioleiomyoma arising from vessel walls[solitary]

3. Genital leiomyoma from smooth muscles of scrotum and nipple

Recent research studies revealed that transmission of a particular gene group is associated with evolution of inherited multiple cutaneous leiomyoma and is in close association with uterine leiomyoma. This gene encodes for fumarate hydratase[FH], an enzyme of the tricarboxylic acid cycle, which acts as a tumour suppressor factor and it is located on 1q42.3-q43^[4] and further studies narrowed down the locus to a region of 4.55-7.17 centromere on chromosome 1. In familial conditions, with multiple cutaneous and uterine leiomyomata[MCUL] with hereditary leiomyomatosis in association of renal tumour [HLRCC], coexists as proposed by Alam et al^[5]. All mutated genes were associated with decreased enzyme activity suggesting the tumour suppressor role of FH^[6]. Previous case studies proposed that patients presenting with cutaneous leiomyoma with FH mutations association, 69% had both cutaneous involvement and uterine leiomyomata, 15% had only skin leiomyomata and rest 7% had only uterine leiomyoma^{[7][8]}. In the present study, we observed a series of 6 cases with features of cutaneous leiomyoma and its variants demonstrated on routine histopathological stains.

REVIEW OF LITERATURE

Epidemiology Frequency

Cutaneous leiomyoma and its variants are not so common especially genital leiomyomas tend to be the least common occurrence. Universal frequency incidence does not differ from the US frequency data^{2,3}.

Mortality/Morbidity

Cutaneous leiomyomas being a benign non-aggressive tumour, direct mortality impact is insignificant. However, one case report involves an angioleiomyoma that occurred in association with a leiomyosarcoma^{3,4}. The relevance of this association still remains an unknown etiology. Associated morbidity are usually localized including spontaneous lesional pain, as well as pain evoked by cold and/or tactile hypersensitivity. Additionally, multiple piloleiomyomas have the potential to be cosmetically disfiguring⁵.

Race

A racial predilection is not described yet on this entity, except in regard to angioleiomyomas occurring in oral cavity, with the frequency of white-to-black ratio of 3:1⁶.

Sex

The incidences of piloleiomyomas has equal incidence of males and females. Women with multiple cutaneous piloleiomyomas have concordant uterine leiomyomas⁷. With strong familial association are termed as *familial leiomyomatosis cutis et uteri, or Reed syndrome*^{8,9}. Angioleiomyomas are more common among females than in males, with a ratio of 2:1 the exception being venous and cavernous subtype having male preponderance. Genital leiomyomas being rare entity, data relevant to sexual predilection are inadequate.

Age

Cutaneous leiomyomas are more likely to occur in adults than in children. However, isolated reports of cutaneous leiomyomas in children

exist, with non specified type of solitary cutaneous leiomyoma on the heel of a neonate at birth⁸.

histological features are studied. Site distribution of cases are shown in Table1. Among 5 cases, 3 cases presented with solitary swelling and two cases presented with multiple leiomyomas in adjunction with uterine fibroids. Sex predilection was towards females than males and age distribution was predominantly third decade as described in Table 2

OBSERVATIONS

In the present study, 5 cases of cutaneous leiomyoma with varied clinical behavior and

Table 1
Site Distribution of cases with painful lesion

Site of the swelling	Distribution of cases	Association of Pain
Forearm	2	1
Palmar arch	1	-
Lower extremity	1	1
Oral /Cheek	1	1

Table 2
Distribution of cases with age, sex and clinical presentation

No. of Cases	Age[in years]	Sex	Association of uterine fibroids
3	25-30	Female	Positive[2Cases]
2	30-35	Male	-

Histological Features are classified into 3 types based on the pattern observed. Predominantly bundles and fascicles of smooth muscles with epidermal lining of stratified squamous epithelium are appreciated. 2 cases showed

increased pilosebaceous units and one case showed vascular proliferation of varying sized endothelial lined blood vessels as shown in table3.

Table 3
Distribution of Variants of Leiomyoma

Type of Leiomyoma observed	No. of cases
Cutaneous Leiomyoma	2
Pilar leiomyoma	2
Angioleiomyoma	1

FIGURES



Figure 1
Gross appearance- Well circumscribed grey white Solitary nodular mass with bulging out appearance with skin surface.

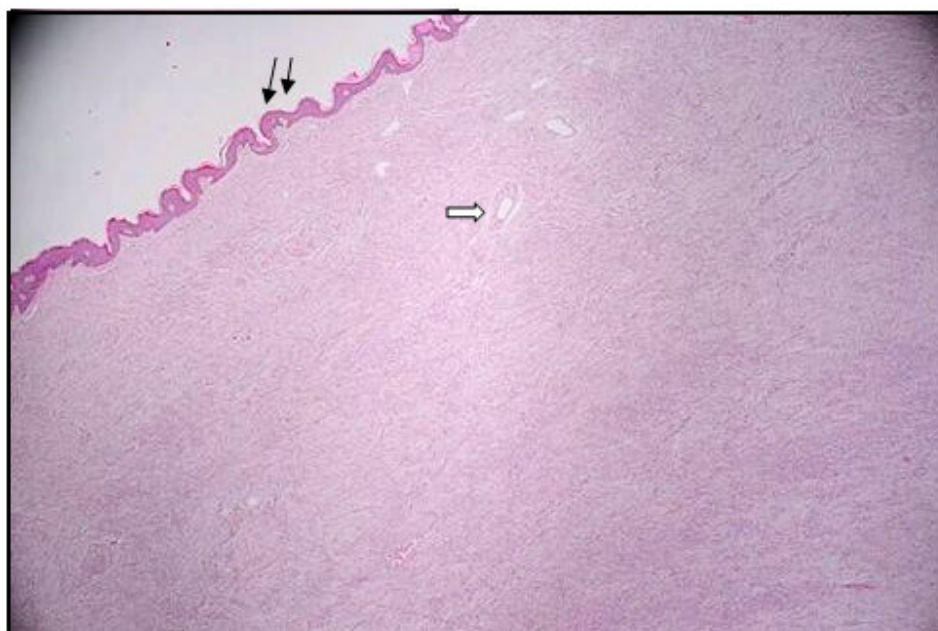


Figure2
Cutaneous leiomyoma with stratified squamous epithelium[double arrow] with bundles of underlying smooth muscles & blood vessels[arrow head], H&E, 4X[Low power]

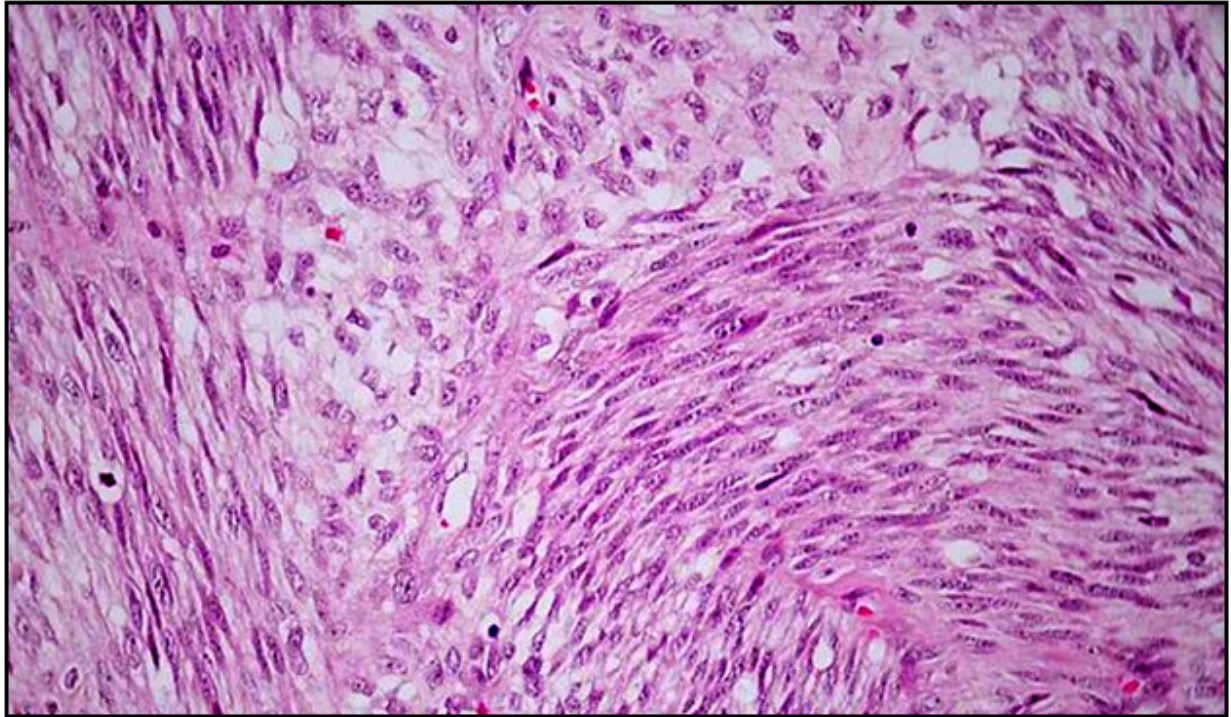


Figure 3
Smooth muscles bundles in fascicles with occasional mitotic figures and clear cell change H&E, 40X.

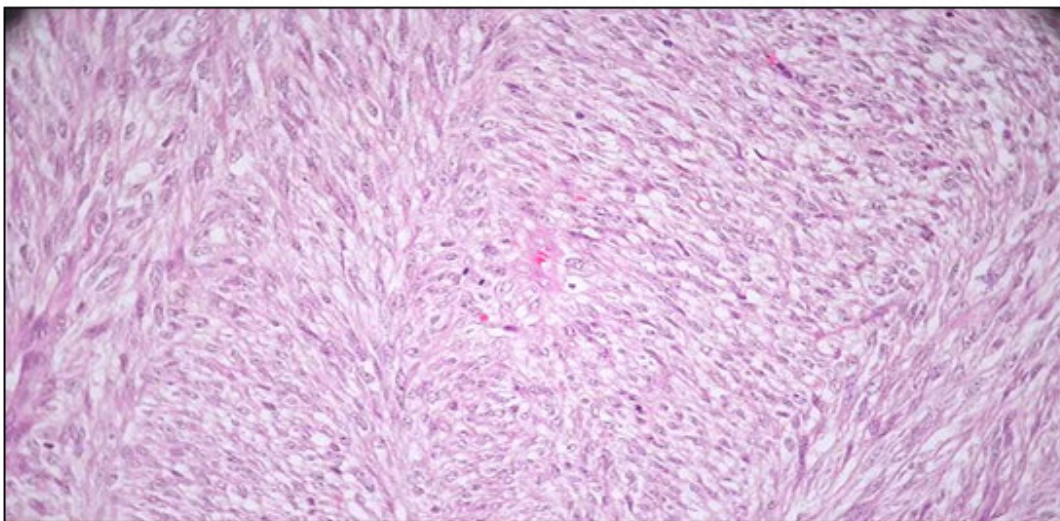


Figure4
Classic smooth bundles whorling with plump nuclei with moderate mitotic activity, H&E,40X

DISCUSSION

Cutaneous pilar leiomyoma are benign smooth muscle tumour with high incidence in elderly age group at second and third decades presenting as multiple painful red brown papulo nodules¹⁰. The common sites are malar region of face, back and extensor aspect of extremities. A germline mutation is noted as an underlying cause and the condition is usually in adjunction with uterine fibroids and renal cell carcinoma^{10,14}. Solitary piloleiomyomas are smooth, firm nodular lesions, lesser than 2 cm in diameter, and reddish brown with associated tenderness as observed in the patients our study¹⁴. Multiple presentation of piloleiomyomas can occur over the face, trunk, or extremities. Various distribution patterns are reported with varied clinical patterns Cutaneous leiomyomas in association with uterine leiomyoma shows a pattern of inheritance as Multiple leiomyomatosis termed as Reed Syndrome^{11,12} which was observed in two cases of our study.

Solitary cutaneous leiomyoma

Solitary cutaneous pilar leiomyoma on the other hand are usually asymptomatic and larger in size and typically presents as a well circumscribed, mobile nodular lesion ranging from 2 to 5cm in diameter, with intact overlying skin[Fig.1]. However solitary presentation of the lesion is uncommon and often found on lower extremity^{10,11} Since piloleiomyomas develop in the superficial dermis, they are fixed in the skin. However, they can be easily moved over the deeper subcutaneous tissues^[14]. Atypical leiomyoma or symplastic leiomyoma is an unusual variant of cutaneous pilar leiomyoma. Being a rare entity only 6 cases have been reported in the literature so far with male preponderance. The histological features are in concordance with symplastic leiomyoma of the uterus with atypical cellularity, pleomorphic nuclei with minimal mitosis¹⁴. However they share features common to schwannomas, fibrohistiocytomas, and neuromas¹⁶ and hence considered as a challenging tasks for the pathologists[Fig-2] The tumor stains positive for Immunohistochemistry like smooth muscle actin and desmin and negative for S100 and Ki67

marker. Based on the experience with uterine symplastic leiomyomas (a review of cases with a ten-year follow-up period found no recurrences nor metastasis), surgical excision of the tumor with free margins is the proposed treatment of choice for the cutaneous atypical leiomyoma^{10,14}. The pathogenesis of pain in cutaneous leiomyoma and its associated lesions is not been well established. Some authors have suggested that pain could result from local pressure by the tumor on cutaneous nerves. However, the histologic findings do not show that prominent nerve fibers are associated with these tumors. Angioleiomyoma have a classical presentation with painful lesions as observed in one of our case and is a benign neoplasm that originates from smooth muscle cells of arterial or venous walls and contains thick-walled vessels and are generally solitary in presentation. The usual site being subcutis and deep dermis of the extremities¹⁰, particularly the lower leg as presented in our study. Cases have been reported at unusual sites like lip, palate, buccal mucosa, tongue, mandible, floor of mouth, and gingival, structures such as the epididymis, spermatic cord and blood vessels could be sites of origin of angioleiomyoma. Macroscopically feature Presents as a slow growing, firm, gray white, round to oval nodules (usually less than 2cm in diameter). Histologically, well circumscribed and encapsulated tumour is usually noted in the lower dermis with interlacing bundles of smooth muscle fibres between vascular channels. The vessel walls (veins) display layers of smooth muscle fibres[Fig.3]. Degenerative changes may be present including vascular thrombosis, stromal hyalinization, Myxoid changes, dystrophic calcification and nuclear atypia. Adipocytes may be present in an exceptional cases which termed as Angiomyolipoma, where HMB45 stain has to be employed to rule out renal angiomyolipoma¹⁵ Variants of Angioleiomyomas, A.] Solid; B].Cavernous; C]. Venous D].Epithelioid ; Angioleiomyoma is often associated with pain and one case report indicates the angioleiomyoma in association

with leiomyosarcoma but the relevance is unknown^[12]

CONCLUSION

Cutaneous leiomyomas are rare lesions and form an important clinical differential diagnosis

REFERENCES

1. Alam N, Barclay E, Rowan AJ, Tyrer JP et al. "Clinical features of multiple cutaneous and uterine leiomyomatosis, an underdiagnosed tumor syndrome." *Arch Dermatol.* Vol.141:199-206.(2006).
2. Kloepfer HW, Krafchuk J, Derbes V. Hereditary multiple leiomyoma of the skin. *Am J Hum Genet.* Vol.10(1):48-52.1958
3. Sherwani RK, Rahman K, Akhtar K, Zaheer S et al. "Leiomyoma of scrotum". *Indian J Pathol Microbiol.* Vol. (51):72-3.(2008).
4. Alam NA, Bevan S, Churchman M, Barclay E, Barker K, Jaeger EE, et al. "Localization of a gene (MCUL1) for multiple cutaneous leiomyomata and uterine fibroids to chromosome 1q42.3-q43". *Am J Hum Genet.* Vol. 68(5):1264-67(2008).
5. Alam NA, Olpin S, Rowan A, Kelsell D, Leigh IM, Tomlinson IP, et al." Missense mutations in fumarate hydratase in multiple cutaneous and uterine leiomyomatosis and renal cell cancer". *J Mol Diagn.* Vol.7(4) : 437-43.(2005).
6. Wei MH, Toure O, Glenn GM, Pithukpakorn M, Neckers L, Stolle C, et al. "Novel mutations in FH and expansion of the spectrum of phenotypes expressed in families with hereditary leiomyomatosis and renal cell cancer". *J Med Genet.* Vol. 43(1):18-27.(2006).
7. Alam NA, Olpin S, Leigh IM. "Fumarate hydratase mutations and predisposition to cutaneous leiomyomas, uterine leiomyomas and renal cancer". *Br J Dermatol.* Vol.153(1):11-7.(2005).
8. Badeloe S, Geel M, Steensel MA, Bastida J, Ferrando J, Steijlen PM, et al. "Diffuse and segmental variants of cutaneous leiomyomatosis: novel mutations in the fumarate hydratase gene and review of the literature". *Exp Dermatol.* Sep 2006;15(9):735-41. 2006.
9. Ghaninejad H, Moeineddin F, Rajaei A, Asgari M, Salimzadeh A. "Hereditary leiomyomatosis and renal cell carcinoma syndrome: A case report". *Dermatol Online Journal.* Vol.14(1):16-20.(2008).
10. Lavanya K, Priyadarshini S.M, Dr. Saraswathi K." Leiomyoma of the Vulva". *Int. Journal of Pharma & Bio Sciences,* Vol5 (4). 1150-1152.(2014).
11. Weedon S. *Textbook of Dermatopathology-Colour Atlas.* 3 rd Ed. Elsevier Publication- Madrid, 795-6.(2002)
12. Kaddu S, Beham A, Cerroni L et al. "Cutaneous leiomyosarcom". *Am J Surg Pathol.* Vol (21) 979-87.(1997)
13. Nagata S, Nishimura H, Uchida M, Hayabuchi N, Zenmyou M, Fukahori S. "Giant angioleiomyoma in extremity: report of two cases". *J.Magn Reson Med Sci.* Vol5(2):113-116(2006)
14. Usmani N, Merchant W, Yung A. "A case of cutaneous symplastic leiomyoma-a rare variant of cutaneous pilar leiomyoma". *J Cutan Pathol.* Vol(35):229-3.2008.
15. Yagi K, Hamada Y, Yasui N. "A leiomyoma arising from the deep palmar arterial arch". *J Hand Surg [Br].* Vol.31 (6):680-82.(2006).

of painful papulonodules. Excision biopsy must be performed for histopathological study and also to differentiate from similar spindle cell lesions. A close follow up of the patients is recommended, especially if two or more mitoses per ten high power fields are present to rule out transformation to sarcomas.