Multiple Cutaneous and Uterine Leiomyomatosis with Renal Involvement: Report of a Rare Association

Gunjan Gupta, Rahul Sudan¹, Sabha Mushtaq²

Abstract
Cutaneous leiomyomas (CLs) are uncommon benign smooth muscle tumours characterised by solitary or multiple painful nodules. Based on origin, three types are recognised, namely piloleiomyoma, dartoic leiomyoma, and angioleiomyoma, with piloleiomyomas being the commonest one. Reed’s syndrome also known as multiple cutaneous and uterine leiomyomatosis (MCULs) is characterised by CLs in men and CLs and uterine fibroids in women. Association of Reed’s syndrome with renal cell carcinoma is labelled as hereditary leiomyomatosis and renal cell carcinoma (HLRCC). Both MCUL and HLRCC are caused by a heterozygous mutation in the fumarate hydratase gene. Besides renal cell carcinoma, there were extremely rare reports of association of MCUL with benign renal lesions. We report a case of a 55-year-old female with segmental tender papulonodular lesions suggestive of leiomyoma associated with uterine leiomyomas and unilateral renal cyst. The case is reported here for its rarity and uncommon association with asymptomatic benign renal cyst.

Key Words: Hereditary leiomyomatosis and renal cell carcinoma, leiomyoma, multiple cutaneous and uterine leiomyomatosis, Reed’s syndrome, renal cyst

What was known?
Reed’s syndrome is the simultaneous occurrence of multiple cutaneous and uterine leiomyomas. When associated with renal malignancy, the resulting condition is known as hereditary leiomyomatosis and renal cell cancer.

Introduction
Rudolf Virchow, a German physician, in 1854 coined the term “tuberculum dolorosum” for cutaneous leiomyomas (CLs) which are rare benign tumours of smooth muscle origin.[1] They can be classified into piloleiomyomas, angioleiomyomas, and dartoic leiomyomas arising from the arrector pili muscles of the hair follicles, vascular smooth muscles, and smooth muscles of genital skin and areola, respectively. Piloleiomyomas are the most common type and may be associated with internal organ involvement followed by angioleiomyomas and genital leiomyomas.[1,2] The tumour affects both sexes equally and is usually seen in the second to fourth decades of life. The tumours are painful in response to physical stimuli such as pressure and cold.[1,3]

Diagnosis is confirmed by histopathology which shows interlacing bundles of spindle cells with moderate amount of eosinophilic cytoplasm and an elongated, cigar-shaped nucleus. Immunohistochemical staining is positive for smooth muscle markers including actin and desmin.[4]

The association of CL with leiomyoma of the uterus is labeled as Reed’s syndrome.[9]

Herein, we report a case of Reed’s syndrome in a 55-year-old female with benign renal cyst. The present case highlights the association of Reed’s syndrome with renal involvement and lays emphasis on screening of such patients.

Case Report
A 55-year-old female presented to the outpatient clinic with multiple, intermittently painful raised skin lesions over the right shoulder, right chest, and right upper back. The lesions started appearing at the age of 40 years and were few in number to begin with involving only the right shoulder. After remaining stationary for 5 years, the number of lesions had gradually increased to involve the upper back and chest on the same side, associated with severe pain, especially on touch. There was a

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Address for correspondence:
Dr. Sabha Mushtaq,
H. No. 15, Lane 6, Talab Tillo,
Jammu - 180 002,
Jammu and Kashmir, India.
E-mail: smqazi.gmc@gmail.com

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history of excision of some of the skin lesions, but new lesions continued to appear. The patient had a history of menorrhagia for which hysterectomy was done 10 years back. Histopathology of the hysterectomy specimen had confirmed the diagnosis of uterine leiomyoma. There was no history of any associated systemic ailment. No other family members were affected.

General physical examinations were within normal limits. Cutaneous examination revealed multiple reddish brown papulonodular lesions ranging from 2 to 10 mm distributed in a segmental pattern over the right shoulder, upper back, and chest [Figure 1a and b]. The lesions were firm and tender to touch. Atrophic scar at the site of excision was present over the shoulder.

Histopathological examination of skin lesion showed well-defined benign spindle cell neoplasm composed of smooth muscle cells arranged in whorls in the dermis, confirming the diagnosis of leiomyoma [Figure 2a and b]. Special stains could not be done owing to unavailability and financial constraints.

The patient was screened for Reed’s syndrome. Routine investigations and ultrasonography of whole abdomen were within normal limits. However, computed tomography scan of whole abdomen showed a corticomedullary cyst involving mid pole of the right kidney measuring approximately 3.2 cm × 2.8 cm × 2.5 cm with no calcification or haemorrhage suggestive of a simple renal cyst [Figure 3a, b and c].

Based on the clinical evaluation, history of hysterectomy for uterine leiomyomas, and histopathological findings, a diagnosis of Reed’s syndrome associated with renal cyst was established. The patient was put on nifedipine 20 mg twice daily which resulted in significant improvement in pain.

Discussion

The most common site for leiomyoma is uterus followed by the skin, accounting for 5% of the cases. It has been reported that between 70% and 98% of women with CLs also had uterine fibroids. Piloleiomyomas, the most common type of CLs, can present as solitary, multiple, disseminated, or segmental lesions. Multiple leiomyomas may be inherited as an autosomal dominant trait or can occur sporadically. In almost 90% of cases, piloleiomyomas are painful, with cold, pressure, or stress being the triggering factors. Pressure on local nerve fibres or ischaemia due to smooth muscle contraction has been proposed as the mechanism underlying pain.

Reed et al in 1973 first described the term multiple cutaneous and uterine leiomyomatosis (MCUL) which is known by various other names in medical literature as multiple leiomyomatosis, Reed’s syndrome, and
leiomyomatosis cutis et uteri. Reed’s syndrome may be associated with renal malignancy, and the resulting condition is known as hereditary leiomyomatosis and renal cell cancer (HLRCC).

HLRCC mainly predisposes to type 2 papillary renal cell cancers, but renal cysts and primary adrenal lesions have also been documented. Although benign renal cysts are common in general population (4.6–8.2%), their incidence is high in HLRCC patients (36%).

Diseases reported to be associated with Reed’s syndrome include multiple endocrine neoplasia type 1, rheumatoid arthritis, breast cancer, prostate cancer, bladder cancer, renal and ovarian cysts, and adrenal cortical adenoma.

In a retrospective study of 13 cases of Reed’s syndrome by Congros et al, there were 10 women and 3 men with multiple CLs. The mean age at diagnosis was 53 years (range: 36–76 years) and the mean age of onset was 40 years (range: 14–53 years). The most common presentation was Type 2 segmental involvement and the most common histologic subtype was piloleiomyoma (in 12 of 13 patients). Nine (90%) of the ten women required hysterectomy for uterine fibroids before the diagnosis of MCUL as seen in our case. Out of the nine patients screened for renal involvement, four had renal lesions (cysts, calculi, or adrenal nodule). No evidence of renal cell carcinoma was detected. This was similar to our case where screening for renal involvement revealed a benign renal cyst.

Patients with multiple CLs should be screened for noncutaneous manifestations. Although the association of Reed’s syndrome with renal cyst may be coincidental, considering the previous reports, further association between the two needs to be determined.

**Conclusion**

Reed’s syndrome or MCUL is a rare condition with uncommon and unrecognized associations. It is important for dermatologists to identify CLs and obtain a targeted clinical history to rule out MCUL, as this syndrome is strongly associated with more aggressive uterine fibroids and a risk of renal cell carcinoma.

**Declaration of patient consent**
The authors certify that they have obtained all appropriate patient consent form. In the form the patient had given her consent for her images and other clinical information to be reported in the journal. The patient understood that her name and initial would not be published and due efforts would be made to conceal her identity, but anonymity could not be guaranteed.

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**Conflicts of interest**
There are no conflicts of interest.

**What is new?**
Reed’s syndrome may be associated with benign renal lesions.

**References**

1. Malik K, Patel P, Chen J, Khachemoune A. Leiomyoma cutis: A focused review on presentation, management, and association with malignancy. Am J Clin Dermatol 2015;16:35-46.
2. Calonje E. Soft tissue tumours and tumour-like conditions. In: Burns T, Breathnach S, Cox N, Griffiths C, editors. Rook Textbook of Dermatology. 8th ed. UK: Wiley Blackwell; 2010. p. 56.54.
3. Pissoat L, Megahed M. Disseminated cutaneous leiomyomas. Hautarzt 2012;63:363-5.
4. Collgros H, Iglesias-Sancho M, Tríbó-Boixareu MJ, Creus-Vila L, Umbert-Millet P, Salleras-Redonnet M, et al. Multiple cutaneous and uterine leiomyomatosis or Reed syndrome: A retrospective study of 13 cases. Actas Dermosifiliogr 2015;106:117-25.
5. Kontochristopoulos G, Kouris A, Balamoti E, Vavouli C, Markantoni V, Christofidou E, et al. A case of Reed’s syndrome: An underdiagnosed tumour disorder. Case Rep Dermatol 2014;6:189-93.
6. Malhotra P, Walia H, Singh A, Ramesh V. Leiomyoma cutis: A clinicopathological series of 37 cases. Indian J Dermatol 2010;55:337-41.
7. Damle RP, Dravid NV, Gadre AS, Suryawanshi KH, Rokade CM. Solitary cutaneous pilar leiomyoma: A rare entity with review of literature. Clin Cancer Investig J 2015;4:678-81.
8. Patel VM, Handler MZ, Schwartz RA, Lambert WC. Hereditary leiomyomatosis and renal cell cancer syndrome: An update and review. J Am Acad Dermatol 2017;77:149-58.