A Rare Case of Multiple Cutaneous Leiomyomas Exhibiting Features of Reed Syndrome

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Abstract

Cutaneous leiomyomas are rare benign smooth muscle tumors often associated with Hereditary Leiomyomatosis and Renal Cell Cancer (HLRCC), a genetic syndrome caused by mutations in the fumarate hydratase (FH) gene. These tumors typically present as firm papules or nodules and may be symptomatic, causing pain or cold sensitivity. They are frequently linked to uterine fibroids and other smooth muscle neoplasms, making it essential to recognize them as potential indicators of systemic conditions like Reed's syndrome. This case report describes a 46-year-old woman with multiple hyperpigmented papules and nodules on her back, which had progressively increased in size over seven years. The patient had a past medical history of uterine leiomyomatosis for which she underwent myomectomy. Histopathological examination confirmed the diagnosis of cutaneous leiomyomas, and immunohistochemical studies were performed; the cells stained strongly positive for smooth muscle actin (SMA). The patient's medical history of uterine fibroids and the presence of multiple cutaneous leiomyomas, combined with a family history of uterine fibroids, raised suspicion for Reed's syndrome. Genetic testing for FH mutations was recommended to confirm the diagnosis. Reed's syndrome is a rare genetic disorder characterized by multiple cutaneous and uterine leiomyomas, with an increased risk of other smooth muscle neoplasms such as renal cell carcinoma. This case emphasizes the importance of early recognition, comprehensive clinical evaluation, and genetic testing to guide diagnosis and management, including surveillance for associated malignancies.

Keywords: Leiomyoma; Reed's Syndrome; Painful Skin Lesion; Oman.

Introduction

Cutaneous leiomyomas are rare benign tumors arising from smooth muscle, most commonly the arrector pili muscles in the skin. They typically present as firm, skin-colored to reddish-brown papules or nodules, which may occur singly or in clusters and are often distributed in a dermatomal or linear pattern. These lesions are frequently associated with symptoms such as pain, tenderness, or cold sensitivity.[1,2] While they can appear sporadically, their presence may also indicate Hereditary Leiomyomatosis and Renal Cell Carcinoma (HLRCC), an autosomal dominant syndrome caused by mutations in the fumarate hydratase (FH) gene.[3] HLRCC is clinically significant due to its association with aggressive malignancies, including type 2 papillary renal cell carcinoma, uterine leiomyosarcoma, and other smooth muscle neoplasms.[4,5] The diagnostic and management challenges posed by cutaneous leiomyomas highlight the need for careful clinical evaluation, histopathological confirmation, and genetic testing where appropriate. This case report underscores the unique presentation and broader clinical implications of this rare dermatologic condition.

Case Report

A 46-year-old woman presented to the dermatology department with a cluster of papules and nodules on her back. The lesions had first manifested before 7 years but has doubles on numbers over the last years with slight pain and itching. On clinical examination, multiple hyperpigmented, smooth dermal papules and nodules of varying sizes were observed on the patient's back [Figure 1].

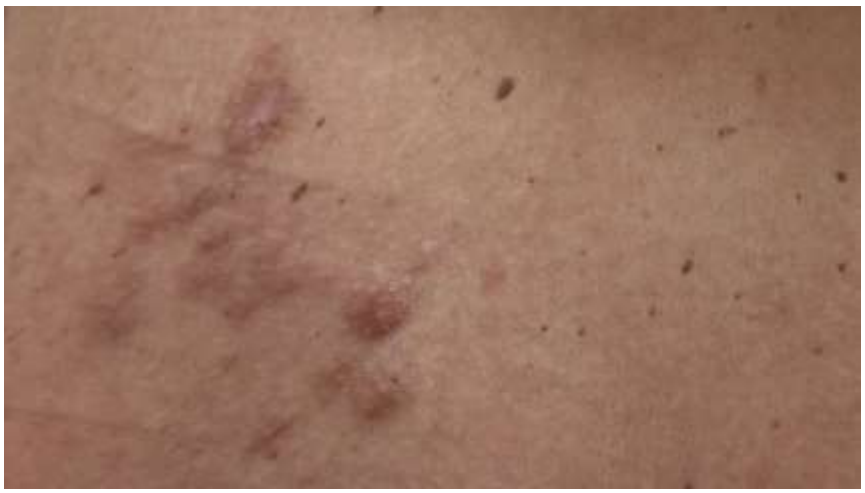

Figure 1: multiple papules on patient's back.

The lesions were generally asymptomatic but occasionally caused slight pain. The patient reported a history of uterine fibroids in her 30s for which she underwent myomectomy. A family history revealed that her 2 sisters had a history of multiple uterine leiomyomatosis.

Complete blood counts, urea, creatinine, electrolytes, liver function tests were all normal. A skin biopsy showed tissue composed of epidermis, dermis and subcutaneous tissue. The dermis shows a nodular lesion with smooth muscle cells arranged in interlacing fascicles. The cells show cigar-shaped nuclei with indistinct nucleoli and eosinophilic cytoplasm. Lymphoid aggregates are noted. There is no evidence of mitotic activity, atypia or necrosis. The overlying epidermis shows mild papillomatosis and pigment incontinence as shown in figure 2.

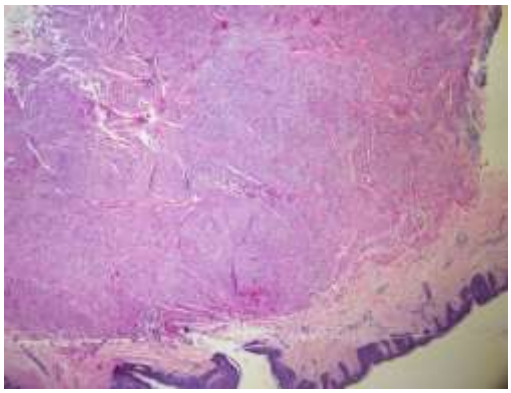

Figure 2: haematoxylin and eosin (H&E) stain, x4 magnification, nodular lesion with smooth muscle bundles in the dermis.

Histopathological examination showed positive for smooth muscle active (SMA) and negative for S100. (figure 3)

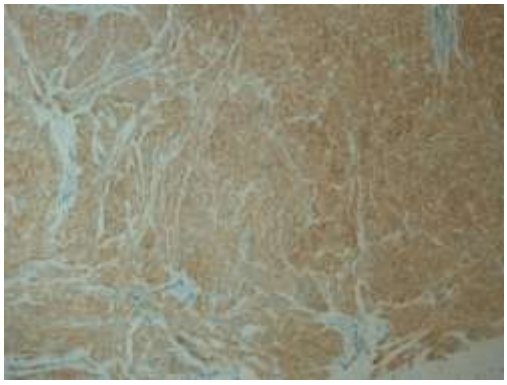

Figure 3: immunohistochemistry (IHC) stain, x10 magnification, SMA positive muscle bundles.

Given the patient's clinical presentation, her surgical and family history along with the histopathological findings, a diagnosis of multiple cutaneous and uterine leiomyomatosis, typical of Reed's syndrome, was established.

The patient was referred for genetic testing to confirm the diagnosis of Reed's syndrome, with particular emphasis on mutations in the fumarate hydratase (FH) gene.

Discussion

Reed's syndrome, or multiple cutaneous and uterine leiomyomatosis (MCUL), is a rare genetic disorder characterized by the presence of multiple smooth muscle tumours, primarily affecting the skin and uterus. This syndrome is caused by mutations in the fumarate hydratase (FH) gene, which encodes the enzyme fumarate hydratase, an important component of the citric acid cycle.[6] In our case, the patient presented with multiple cutaneous leiomyomas on her back, which had progressively increased in size and number over the past several years. This is typical of Reed's syndrome, as cutaneous leiomyomas often manifest in early adulthood and can increase in number with age. The lesions are typically asymptomatic but can be associated with pain or itching, as seen in this patient. The patient also had a significant history of uterine fibroids, which is another common manifestation of the syndrome.

Moreover, she has a family history of uterine fibroids, which further raises the suspicion of Reed's syndrome in this case, given the hereditary nature of the disorder.

The skin lesions in our patient were confirmed as smooth muscle tumours by histopathological examination, which revealed cigar-shaped nuclei and eosinophilic cytoplasm, typical of leiomyomas. Immunohistochemistry for smooth muscle actin (SMA) further confirmed the smooth muscle origin of the lesions, while the absence of S100 staining ruled out a neural origin.

The genetic basis of Reed's syndrome was first described in 2001, when mutations in the FH gene were linked to the condition.[7] In our patient, although genetic testing was pending at the time of writing. the strong clinical and histopathological evidence supports the diagnosis of Reed's syndrome. Genetic testing for mutations in the FH gene is essential to confirm the diagnosis and assess the patient's risk for other associated complications.

There are a few important differential diagnoses to consider when evaluating patients with multiple cutaneous leiomyomas. One important condition to rule out is the Birt-Hogg-Dubé syndrome, which can also present with multiple dermal leiomyomas. However, Birt-Hogg-Dubé syndrome is associated with fibrofolliculomas, pulmonary cysts, and an increased risk of certain types of renal cancer, which were not present in our patient.[7] Another condition to consider is hereditary leiomyomatosis and renal cell cancer (HLRCC) syndrome, which is also associated with uterine and cutaneous leiomyomas, but with an even higher risk of developing renal cell cancer (RCC) at an earlier age.

The treatment of cutaneous leiomyomas is dictated by the number of lesions and the degree of discomfort or cosmetic nuisance. When only a few lesions are present, surgical excision is the gold standard for complete removal, but may have a high rate of recurrence and possibly require skin grafting for larger lesions.[8]

Destructive methods like electrodessication or cryotherapy can be used for smaller lesions, but they may not be more effective than excision and can lead to scarring or recurrence.

Recent treatments such as botulinum toxin injections and carbon dioxide (CO2) laser ablation have shown promising results. Botulinum toxin works by inhibiting pain-related neuropeptides, and CO2 laser ablation helps reduce pain through muscle breakdown myolysis.[9]

Conclusion

This case underscores the significance of recognizing cutaneous leiomyomas as a rare but clinically relevant entity. Their potential association with HLRCC necessitates a multidisciplinary approach to diagnosis and management, including genetic counseling and regular surveillance for systemic malignancies. For clinicians, maintaining a high index of suspicion and relying on histopathological confirmation are vital steps in distinguishing leiomyomas from other dermatological conditions. As our understanding of these rare tumors evolves, sharing individual cases adds to the collective knowledge, guiding improved diagnostic accuracy and management strategies. The case also serves as a reminder of the potential for dermatologic findings to reveal underlying systemic disease, emphasizing the value of a holistic approach to patient care.

Disclosure

The authors of this report have no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this manuscript. A written informed consent was obtained from the patient at the armed forced hospital in Oman for publication and accompanying images of the case report.

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