

Reed's Syndrome: A Rare Systemic Genodermatosis

Reed's Syndrome: Uma Genodermatose Sistémica Rara

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RESUMO

A síndrome de Reed é uma genodermatose rara, autossómica dominante, caracterizada pela presença de múltiplos leiomiomas cutâneos e uterinos, podendo estar associada a carcinoma de células renais e leiomiossarcoma.

Uma mulher de 55 anos foi observada em consulta de rotina. À observação, apresentava múltiplas pápulas e nódulos no tórax e braço esquerdo, assimétricos, irregulares, cor de pele e de superfície lisa, que referia estarem presentes há cerca de duas décadas. A doente tinha antecedentes de miomectomia e hysterectomia. A biópsia de uma pápula torácica revelou um leiomioma. De acordo com os achados clínicos e histológicos e antecedentes cirúrgicos, foi colocada a hipótese diagnóstica de síndrome de Reed, confirmada posteriormente por teste genético. A família da utente foi também referenciada para aconselhamento genético.

O exame sistemático de lesões cutâneas é de grande relevância, pois estas podem ser elementos clínicos orientadores do diagnóstico de doenças sistémicas.

PALAVRAS-CHAVE: Leiomiomatose; Neoplasias da Pele; Neoplasias do Rim; Síndromes Neoplásicas Hereditárias

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Recebido/Received: 2022/05/05 - Aceite/Accepted: 2023/06/27 - Publicado online/Published online: 2023/09/06 - Publicado/Publicated: 2023/09/30
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ABSTRACT

Reed's syndrome is an autosomal dominant rare genodermatosis, characterized by the presence of multiple cutaneous and uterine leiomyomatosis. This syndrome can be associated with renal cell carcinoma and leiomyosarcoma.

A 55-year-old woman presented to routine consultation. Physical examination was notorious for the presence of multiple asymmetrical, irregular, skin-colored, with a smooth surface papules and nodules on her chest and left arm. They had been present for about two decades. The patient's past medical history was significant for myomectomy and hysterectomy. A cutaneous papule's biopsy revealed a leiomyoma. Clinical and histological findings combined with surgical history suggested Reed's syndrome, which was later confirmed by genetic tests. Her family was referred for genetic counseling.

Systematic review of skin lesions is essential, as they can be the diagnostic clue for systemic diseases.

KEYWORDS: Kidney Neoplasms; Leiomyomatosis; Neoplastic Syndromes, Hereditary; Skin Neoplasms

INTRODUCTION

Reed's syndrome is a rare genodermatosis, characterized by the presence of multiple cutaneous and uterine leiomyomatosis (MCUL) in women. This syndrome can be associated with renal cell carcinoma, being labeled as hereditary leiomyomatosis and renal cell carcinoma (HLRCC), and leiomyosarcoma. Both MCUL and HLRCC have an autosomal dominant pattern of inheritance. They result from a germline heterozygous mutation of fumarate hydratase (*FH*) gene on chromosome 1q42.3-q43. It is thought that just a few specific mutations are associated with the development of renal cell cancer. *FH* gene encodes the fumarate enzyme, which converts fumarate to malate in the Krebs cycle and is classified as a tumor suppressor gene.¹

CASE REPORT

A 55-year-old woman presented to routine consultation with her family doctor. The patient had no current diseases and was not taking any medication regularly. The physical examination was normal, except for the presence of multiple papules and nodules on her chest (Fig. 1) and left arm (Fig. 2). They were asymmetrical, irregular, skin-colored, with a smooth surface, and she reported that they were sometimes associated with pruritus and had been present for about two decades, slowly increasing over the years.

The patient's past medical history was significant for myomectomy thirty years ago, and hysterectomy eight years ago, due to uterine leiomyomas. She was unaware of the family history. A papule biopsy from her chest was taken, and the histological examination revealed a leiomyoma. Clinical and histological findings, combined with surgical history, suggested Reed's syndrome. Therefore, a genetic test was conducted.

The result showed a heterozygous variation of *FH* gene, confirming the Reed's syndrome diagnosis.

Given this, the patient underwent tomographic examination, which showed a renal cyst with a 13 mm diameter. No evidence of renal carcinoma was found. Her parents and siblings were also referred for genetic counseling.

DISCUSSION

Reed's syndrome is rare, but it has characteristic clinical expressions that all doctors must be aware of because of its' multisystem involvement. When suspected, genetic testing and counseling should be offered to the patients, and when confirmed, also to their family members.

When a patient presents with cutaneous leiomyomas, it is important to perform a complete history, including family and surgical antecedents, and physical examination. Although not compatible with our patient's history, cutaneous leiomyomas are usually the first manifestation of the disease, with a mean age of 25 years old.² Cutaneous leiomyomas or piloleiomyomas appear as small (0.5-2 cm) firm skin colored papules or nodules. They arise from the arrector pili muscles, which are responsible for making hairs stand on end. The papules and nodules can be asymptomatic or associated with pain and paresthesias.³ They are most frequently located in extensor surfaces of the extremities, but also on the trunk, neck and face. These lesions develop often in clusters, commonly in a segmental distribution, and tend to increase in number and dimension with aging.⁴

On the other hand, the diagnosis' mean age of uterine leiomyomas is 30 years old.² Women can experience several gynecological symptoms such as dysmenorrhea, menstrual irregularities, menorrhagias and fertility problems, which emphasize the importance of an



FIGURE 1. Caption: papules and nodules presented by the patient on her chest.

early diagnosis, allowing a proper counseling to female patients.⁵

Although it is rare, leiomyomas can degenerate into leiomyosarcomas.⁶ Treatment of cutaneous leiomyomas depends on the number, extension, and symptomatology. Camouflage with cosmetics and avoidance of cold may be sufficient for some patients.⁷ For single and small lesions, surgical excision, cryotherapy, carbon dioxide laser ablation and electrocoagulation are an option.^{4,8} For more symptomatic leiomyomas, calcium channel blockers (particularly nifedipine), an alpha-adrenoceptor blocker (phenoxybenzamine) and gabapentin have been used with limited effectiveness.^{7,9-11}

Renal cell carcinoma is the most concerning feature of the heterozygous mutation of *FH* gene. This renal cancer does not occur in all individuals with the disease, but unfortunately, when present, it occurs at an early age (median of 44-year-old) and it is usually aggressive. Papillary type 2 renal cell carcinoma is the most frequent subtype. The patient can be asymptomatic or can complain about lumbar pain and hematuria. Annual renal imaging should be recommended to anticipate the detection and treatment of renal cell carcinoma, and magnetic resonance imaging and/or computerized tomography are the preferred exams.¹² The incidence of benign renal cysts seems to be higher in HLRCC patients (36%), compared to the general population (4.6%-8.2%).¹³

This case emphasizes the importance of systematic review of skin lesions, as they can be the diagnostic clue for systemic diseases. An early diagnosis enables the genetic counseling of both the patient and his family members, through a multidisciplinary approach that allows prompt fertility counseling to female patients and early detection of the underlying malignancies - renal cell carcinoma and leiomyosarcoma.



FIGURE 2. Caption: papules and nodules presented by the patient on her left arm.

The article was submitted for presentation at WONCA Europe Conference 2022 and is awaiting approval.

DECLARAÇÃO DE CONTRIBUIÇÃO/ CONTRIBUTORSHIP STATEMENT

MB: Revisão de literatura, concepção e escrita do artigo

LFS e NMP: Escrita do artigo

GF e MM: Mentoria e escrita do artigo

MB: Literature review, article design and writing

LFS and NMP: Article writing

GF and MM: Mentoring, article writing.

RESPONSABILIDADES ÉTICAS

CONFLITOS DE INTERESSE: Os autores declaram a inexistência de conflitos de interesse na realização do presente trabalho.

FONTES DE FINANCIAMENTO: Não existiram fontes externas de financiamento para a realização deste artigo.

CONFIDENCIALIDADE DOS DADOS: Os autores declaram ter seguido os protocolos da sua instituição acerca da publicação dos dados de doentes.

CONSENTIMENTO: Consentimento do doente para publicação obtido.

PROVENIÊNCIA E REVISÃO POR PARES: Não comissionado; revisão externa por pares.

ETHICAL DISCLOSURES

CONFLICTS OF INTEREST: The authors have no conflicts of interest to declare.

FINANCING SUPPORT: This work has not received any contribution, grant or scholarship.

CONFIDENTIALITY OF DATA: The authors declare that they have followed the protocols of their work center on the publication of data from patients.

PATIENT CONSENT: Consent for publication was obtained.

PROVENANCE AND PEER REVIEW: Not commissioned; externally peer reviewed.

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