

Case presentation

Piloleiomyomas in multiple cutaneous and uterine leiomyoma syndrome (hereditary leiomyomatosis and renal cell cancer or Reed syndrome)

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Abstract

Multiple cutaneous and uterine leiomyoma (MCL), or Reed syndrome is an uncommon condition that includes cutaneous piloleiomyomas and internal neoplasms of the uterus and kidney. Clinical findings include clusters of variably-painful, skin-colored-to-red-brown papules. Genetic testing shows germline mutations in the gene encoding fumarate hydratase. We describe a patient with MCL who presented with subtle cutaneous findings. We believe it is important that dermatologists consider a diagnosis of MCL when presented with patients with small painful dermal papules.

Case synopsis

History: A 44-year-old man presented to the Skin and Cancer Unit in December, 2013, with a two-year history of a papular eruption of the chest, abdomen, and back. The lesions initially presented as pinpoint papules that grew slightly over time. The eruption was largely asymptomatic, with the exception of intermittent pruritus and pain that were exacerbated by pressure and friction. He had no systemic symptoms. He had evaluated seen by an outside dermatologist who had performed several biopsies, but did not provide pharmacologic treatment. There was no family history of similar lesions. He denied fevers, chills, diaphoresis, joint pain, antecedent infections, and medications, which included prescription and over-the-counter pharmaceuticals.

Physical examination: A few, well-demarcated, erythematous, and slightly-translucent papules were present on the chest and back.

Laboratory data: A complete blood count, fasting lipid panel, thyroid function studies, and comprehensive metabolic panels were normal. Human immunodeficiency virus 1/2 antibody was negative. Serologic testing was positive for a mutation in the fumarate hydratase gene. A renal ultrasound was normal. Magnetic resonance imaging of the abdomen demonstrated a 1.5 cm adrenal adenoma and normal-appearing kidneys.

Histopathology: Within the dermis there is a neoplasm that is comprised of spindle cells that are arranged as fascicles. The lesional cells have blunt, rectangular nuclei, eosinophilic cytoplasm, and many have perinuclear vacuoles.



Figures 1,2. Erythematous papules on chest and back

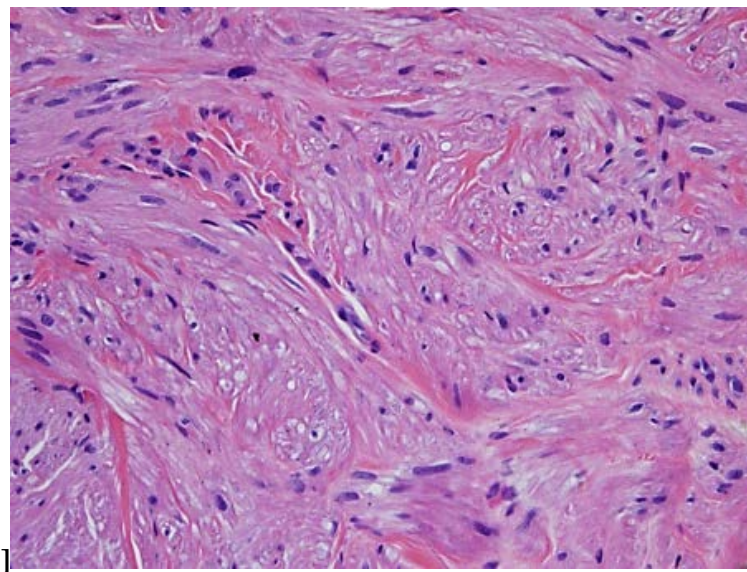


Figure 3. Spindle cell neoplasm with cells showing rectangular nuclei, eosinophilic cytoplasm, and perinuclear vacuoles

Discussion

Diagnosis: Piloleiomyomas in multiple cutaneous and uterine leiomyoma syndrome (hereditary leiomyomatosis and renal cell cancer or Reed syndrome)

Comment: Piloleiomyomas are benign smooth muscle tumors that arise from arrector pili muscles of the pilosebaceous unit. The incidence of such proliferations is unknown, but they are considered to be uncommon tumors. Although multiple piloleiomyomas may occur sporadically, they can be inherited in an autosomal dominant fashion as a component of hereditary leiomyomatosis and renal cell cancer (HLRCC), which is also known as Reed syndrome or multiple cutaneous and uterine leiomyoma syndrome (MCL) [1]. Although germline mutations in the gene encoding fumarate hydratase (FH), which is an enzyme in the Krebs cycle, predispose affected individuals to the development of MCL, how such mutations translate into smooth muscle tumors is unknown [1, 2],

The cutaneous hallmarks of MCL include piloleiomyomas that appear during the second to fourth decade. Lesions are typically small, grouped, skin-to-red-brown dermal papules, which measure 0.2 to 2cm in diameter and are located on the trunk and extremities [3]. Whereas lesions may be asymptomatic, they also may be associated with pain, which is either spontaneous or precipitated by cold or trauma [4, 5]. Simple excision, ablation, or laser therapy typically is curative. However, in MCL, piloleiomyomas are commonly associated with internal neoplasms of the uterus and kidney. Uterine leiomyomas affect over 90% of women with MCL. Such tumors may result in menorrhagia and pelvic pain. More importantly, renal-cell carcinomas have been found in 10 to 16% of families with MCL [6]. Tumors are most commonly type II papillary renal-cell carcinomas that present

early and behave aggressively. Metastases have been noted in greater than 50% of affected patients [1]. Rarely, uterine and cutaneous piloleiomyomas or leiomyomas may transform into leiomyosarcomas [7].

For patients with multiple cutaneous piloleiomyomas, there are no firm screening guidelines. However, screening recommendations include history and physical examination (including pelvic examination in women), abdominal and pelvic ultrasound, and genetic testing for mutations in the FH gene [1]. For those with confirmed MLC, annual physical examination (including pelvic examination in women) and every other year abdominal and pelvic imaging are recommended. In addition, owing to the inheritance pattern of MLC, genetic counseling, molecular genetic testing of asymptomatic at-risk individuals as well as physical examination of first-degree family members with abdominal and pelvic imaging as indicated are recommended [6]. One group has recommended renal ultrasound and magnetic resonance imaging at the age of 20, which is followed by semi-annual ultrasound and annual MRI in all carriers of FH germline mutations [8].

In approaching patients with suspected cutaneous piloleiomyomas, one must consider other dermal nodules in a differential diagnosis. Such entities include adenexal tumors, dermatofibromas, and epidermal inclusion cysts. A clustering of papules, especially those of red-brown color or the presence of pain, may lead toward the diagnosis of piloleiomyoma.

Our patient adds to a small literature base that describes the presentation of multiple cutaneous and uterine leiomyoma syndrome. This case is notable in that it may give clinicians pause and allow them to expand their differential diagnosis when approaching a patient with innocuous-appearing papules of the trunk and extremities.

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