CLINICAL VIGNETTE

Cutaneous Findings in Hereditary Leiomyomatosis and Renal Cell Cancer

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Background

Hereditary leiomyomatosis and renal cell cancer (HLRCC) is a rare genetic condition, marked by cutaneous and uterine leiomyomas with an increased risk of aggressive papillary renal cell carcinoma (RCC).[1] The syndrome is caused by mutations in the fumarate hydratase (FH) gene and is transmitted in an autosomal dominant pattern.[2] The cutaneous lesions are often asymptomatic, though occasionally painful. Cutaneous lesions are typically present on the trunk, though a variety of distributions along the limbs has been reported, as well as occasionally on the face. However, not all patients will have all of the clinical features. Cutaneous leiomyomas have been reported to affect 76–100% of affected individuals, and the risk of developing renal tumors is about 10–16%.[1,3] We present a case of a patient who presented with cutaneous leiomyomas and a history of uterine leiomyomas, diagnosed with HLRCC upon confirmatory genetic testing.

Report

A 54-year-old female with a history of myomectomy for uterine leiomyomas presented for evaluation of scattered papules and plaques along the back, shoulders, and upper legs. The lesions were occasionally sensitive but generally asymptomatic. The patient was afebrile with no history of recent illness or travel, and review of systems was otherwise negative. The patient's sister also had a history of uterine and cutaneous leiomyomas.

Physical exam revealed scattered red-brown papules and plaques on the back, shoulders, legs, and one along the frontal hairline. 4 mm punch biopsies taken of the left shoulder and left leg confirmed presence of cutaneous leiomyomas. Genetic testing revealed the patient is heterozygous for a mutation in the FH gene, consistent with a diagnosis of HLRCC. The patient was encouraged to undergo annual skin checks and yearly abdominal MRIs to monitor for development of renal cell carcinoma.

Discussion

The discovery of the link between HLRCC and the fumarate hydratase gene is relatively recent, occurring in 2002.[4] Reported rates of positive FH mutations in HLRCC patients have ranged from 75–100%.[5] Prior to the discovery of the association with renal tumors the condition was called Reed's syndrome, also known as multiple cutaneous and uterine leiomyomatosis syndrome. However, HLRCC has fallen into favor given the unknown risk of developing RCC in all affected patients.[1] The majority of renal tumors in HLRCC patients are classified as type 2 papillary renal cancer based off of architectural and histopathological findings, although other tumor types have been reported.[1]

Given the autosomal dominant transmission pattern and high penetrance of this syndrome, genetic counselling is recommended for at-risk relatives. There is no current consensus on clinical surveillance, but it is recommended that affected patients undergo regular annual skin checks to assess the extent of cutaneous lesions. Female patients are recommended to receive annual gynecologic consultation for monitoring of uterine leiomyoma for growth or possible development of leiomyosarcoma. All HLRCC patients are also often recommended to undergo yearly abdominal MRI for monitoring of renal lesions, to avoid accumulating higher-dose radiation over time from yearly CT scans.[1]

While the mainstay of treatment is excision for symptomatic leiomyomas and detected renal tumors, anti-VEGF and tyrosine kinase inhibitor therapies are beginning to be tested, with positive early results.[1] This case highlights a classic case of HLRCC with typical cutaneous manifestations, to raise awareness of this condition and promote prompt surveillance for underlying renal tumors.

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Submitted July 11, 2017