Recognizing Reed Syndrome Case Report and Discussion
Megan Furniss, DO, Greg Delost DO, Michael Mahon, DO

LEARNING OBJECTIVES
Reed Syndrome is a genodermatosis characterized by benign leiomyomas of the skin and uterus. The presentation of the disorder can be subtle, and yet be a herald of risk of aggressive papillary renal cell carcinoma. It is therefore important that providers recognize leiomyomatosis and have awareness of this association.

CASE SUMMARY
A 58-year-old Caucasian woman presented to our dermatology clinic with a complaint of tender, mildly pruritic bumps on her bilateral flanks which erupted 12 years ago after her fourth pregnancy. Further questioning revealed a history of uterine fibromatosis, which necessitated hysterectomy with resultant removal of 42 uterine fibroids. Review of her records from a clinic visit in 2002 revealed that a similar lesion had been biopsied and diagnosed as a leiomyoma.

On exam the patient had clusters of several skin-colored to pink dermal nodules on the bilateral anterior flanks which were mildly tender to touch. Skin surface changes were absent. Two skin biopsies were taken; both results were consistent with leiomyomas.

Based on this combination of multiple cutaneous and uterine leiomyomas, the patient was presumptively diagnosed with leiomyomatosis cutis et uteri, also known as Reed syndrome, or hereditary leiomyomatosis and renal cell cancer syndrome (HLRCC).

The treatment plan was to obtain appropriate screening for renal pathology, given the high-risk for aggressive renal cell carcinomas in these patients. The patient was sent for a renal US, CT abdomen/pelvis, and labs including a CBC, CMP, and UA. The work-up to date has been negative for internal pathology.

Definitive genetic testing is under consideration.

DISCUSSION OF REED SYNDROME
Reed Syndrome is an autosomal dominantly inherited genodermatosis caused by a germline mutation in the fumarate hydratase gene. The cutaneous lesions of RS are solitary or multiple cutaneous leiomyomas, appearing as firm and painful skin-colored or pink to brown papules or nodules up to 2 cm in diameter. With an incidence of 85%, cutaneous leiomyomas are mainly found on the trunk and extremities, but can also affect the face. Because cutaneous leiomyomas are rare in the general population, their presence should elicit suspicion of underlying HLRCC with further investigation warranted.

The initial cohort study, consisting of two European families with HLRCC, found papillary type II renal tumors in 6 of 19 individuals (32%). A much larger North American cohort of 95 individuals from 35 families identified a 14% prevalence (13 of 95 patients) of renal tumors in the FH mutation positive carriers. Extrarenal manifestations of HLRCC are quite common with uterine leiomyomas being the most common. In the North American cohort study, 98% of women with cutaneous leiomyomas also had uterine leiomyomas. Furthermore, more than 90% of these women underwent myomectomy or hysterectomy with approximately half of the hysterectomies occurring by the age of thirty.

Compared to other hereditary renal tumor syndromes, such as von Hippel-Lindau disease, hereditary papillary renal carcinoma, and Birt-Hogg-Dubé syndrome, renal tumors in patients with HLRCC syndrome are significantly more aggressive, often with early metastasis, despite small primary tumor size. The proposed mechanism of carcinogenesis is that FH is a tumor suppressor, as loss-of-heterozygosity disease models in HLRCC display loss of the wild type allele in cutaneous, uterine, and renal tumors.

WORKUP/ MANAGEMENT
Biopsies of leiomyomas show interlacing fascicles of bland cells with brightly eosinophilic cytoplasm and blunt-ended, cigar-shaped nuclei centered in the reticular dermis, and an absence of mitoses.

Removal of painful or changing lesions to detect malignant transformation to leiomyosarcoma. Specific guidelines for management do not exist, however current recommendations are:

• Genetic testing by PCR (available through the NIH), or by histopathological staining for the fumarate hydratase defect is imperative
• Referral to gynecology and genetic counselling
• Referral to nephrology for serial monitoring for renal malignancy with labs, CT abdomen/pelvis
• Screening of first degree relatives for the gene defect and renal malignancy

CONCLUSIONS
Recognition of leiomyomatosis presenting to a dermatology clinic is imperative to correctly diagnose and screen Reed Syndrome patients, who are at a high risk of aggressive renal cell carcinoma.

REFERENCES