Cutaneous and Uterine Leiomyomas

To the Editor: We read with great interest the medical image feature by Seranno and Ruiz-Villaverde on a woman with cutaneous and uterine leiomyomas published in the March 2015 issue of Mayo Clinic Proceedings.1 As the authors correctly point out, the molecular defect in this syndrome is a mutation of one allele of the fumarate hydratase gene. However, this syndrome is now classified as hereditary leiomyomatosis and renal cell cancer syndrome (Online Mendelian Inheritance in Man #150800).2 Rather than Reed Stream syndrome, it highlights the more serious aspects of the disease.

The papillary renal cell cancer is an aggressive form of the disease that tends to present at an early age and can be metastatic at the time of diagnosis even when the tumor is less than 1 cm.2 Likewise, women with hereditary leiomyomatosis and renal cell cancer syndrome tend to be younger at age of presentation and to have more numerous and larger uterine leiomyomas than women with the nonsyndromic form of this disease.2 Moreover, they tend to have abnormal histologic findings including cellular and atypical leiomyomas and may have a heightened risk of uterine sarcomas.2 3 These characteristics are important both because (1) contemporary data suggest that cellular leiomyomas may evolve into uterine sarcomas and (2) there is currently a focus on the risk of dissemination of sarcomas by minimally invasive hysterectomies or myomectomies for uterine fibroids.3 Genetic counseling is highly recommended for this family given the serious nature of the autosomal dominant disease.

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In reply—Cutaneous and Uterine Leiomyomas

We appreciate the comments from Drs Stewart and Morton regarding our medical image feature on a woman with cutaneous and uterine leiomyomas published in the March 2015 issue of Mayo Clinic Proceedings.1 We recognize that this syndrome is now classified as hereditary leiomyomatosis and renal cell cancer syndrome (Online Mendelian Inheritance in Man #150800). Some authors have described it as a different entity altogether when multiple cutaneous uterine leiomyomas are associated with aggressive renal cancer, also known as hereditary leiomyomatosis and renal cell carcinoma (OMIM #605839).2 3 Although more than 18 mutations in the fumarate hydratase (FH) gene have been described,4 the mechanisms by which FH mutations cause tumor predisposition is unknown. Fumarate hydratase is an enzyme of the Krebs cycle and plays an important role in intermediary metabolism.

As Stewart and Morton pointed out, the patients who present with uterine myomas usually do so at a younger age, with the myomas being larger and more numerous than those diagnosed in the general population. This was the reason that led to an early hysterectomy before the age of 30 years in the patient in our report.5 Histopathologic study of extirpated myomas did not reveal any sign of malignant disease, but we were unable to review whether high cellularity and hyaline necrosis were present because the hysterectomy was performed in another hospital 30 years previously. We performed abdominal ultrasonography to examine for renal cell cancer, and it showed a simple cyst of 6 to 7 cm in the upper pole of the right kidney. Genetic study was not available, so we could not determine whether 1p deletion was present. These 2 characteristics would have helped us to clarify if this patient was at risk of development of a uterine sarcoma.6 7 In addition, genetic counseling was also provided to our patient, and her family was studied. She has only one child, a son who has no evidence of cutaneous leiomyomas.

It is unclear which patients should be screened for renal cancer, at what age, by what means, and how frequently. Some type 2 papillary or collecting duct renal cell carcinomas cannot be identified by ultrasonography and may therefore require computed tomography or magnetic resonance imaging.