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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). Rather than Reed syndrome or hypertension and chronic disease, 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 cancer syndrome (OMIM #605839)2,3 may have a heighted risk of uterine sarcomas.4,1 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). 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, patients who present with uterine myomomas 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.2 Histopathologic study of excirpated myomomas 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 lp deletion was present. These 2 characteristics would have helped us to clarify if this patient was at risk of development of a uterine sarcoma.5,6 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 for adequate screening. It is also extremely difficult to determine whether earlier detection provides an improved outcome.

According to Alam et al., an aggressive strategy of screening all individuals with the FH mutation from their early teens might be considered. Less aggressive options would include screening only those FH mutation carriers whose families have either a history of renal cancer or FH mutations previously associated with renal cancer. Finally, the option of no screening at all may be considered. 


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