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Post-transplant diagnosis of hereditary leiomyomatosis and renal cell carcinoma syndrome in a kidney donor

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A 58-year-old woman developed multiple, clustered, pink, painless, papules on her upper extremities, back and flank (Figure 1A–C). Her past medical history was notable for multiple uterine leiomyomata, follicular thyroid carcinoma and cutaneous basal cell carcinomas. The patient had donated her left kidney one year after the skin lesions developed. Pertinent family history included uterine leiomyomata in her mother, uterine leiomyomata and two miscarriages in her maternal grandmother, and a maternal cousin with uterine cancer. A biopsy of a representative skin lesion demonstrated clustered fascicles of benign, spindle-shaped smooth muscle cells within the

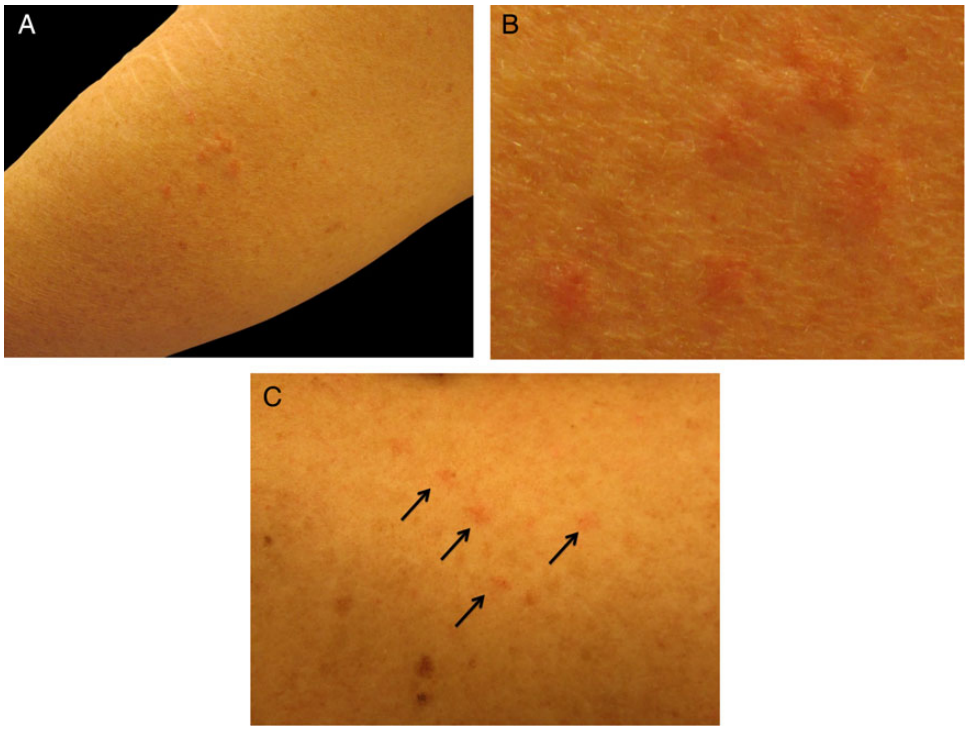

Fig. 1. Clinical photograph. (**A**) Multiple, clustered, pink to brown-colored painless papules present on the extensor surface of her left upper extremity. One of the representative lesions was biopsied. (**B**) Higher magnification imaging illustrates another collection of agminated, pink to flesh-colored flat-topped papules with irregular borders. (**C**) Additional faintly pink to flesh-colored, flat-topped papules with irregular borders present on the flank highlight the varying morphologies of these clinical lesions (arrows).

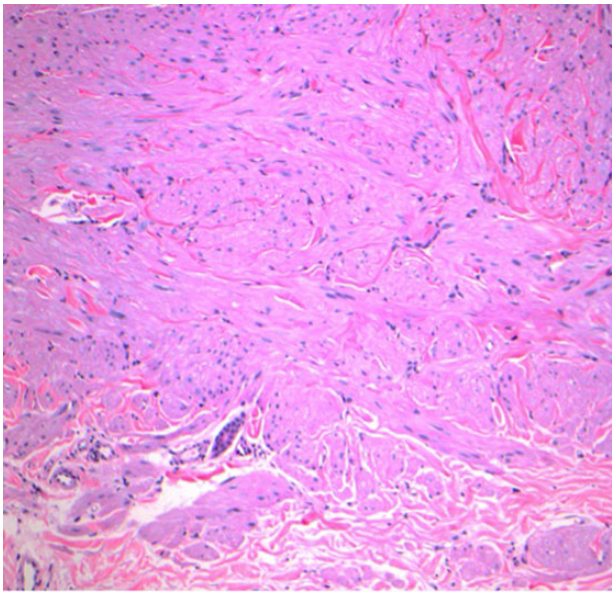

Fig. 2. Skin histopathology. Clustered fascicles of benign, spindle-shaped cells showing smooth muscle differentiation on hematoxylin and eosin (H&E) stain (×10 magnification).

dermis, consistent with the diagnosis of cutaneous leiomyoma (Figure 2). Based on these findings, the patient was referred for genetic testing and counseling given suspicion for hereditary leiomyomatosis and renal cell carcinoma (HLRCC). She was found to harbor a germline missense mutation (Glycine397Arginine) in the fumarate hydratase (FH) gene on chromosome one, confirming this diagnosis. Further investigation revealed the same mutation in the patient's mother but the family history was negative for renal cell carcinoma (RCC). Given the risk of internal malignancy with this condition, routine surveillance of her remaining kidney with alternating ultrasound and MRI every six months was initiated and has remained negative to date. In addition, the recipient of the patient's transplanted kidney was notified of her donor's diagnosis and also continues to undergo imaging surveillance.

HLRCC is an autosomal dominant condition characterized by the development of multiple cutaneous and uterine leiomyomata as well as a predisposition for RCC. This condition is caused by a germline mutation in a single copy of the FH gene [1]. Up to 6% of individuals from families affected by germline FH mutations develop RCC [1]. In addition, studies suggest that the RCCs arising in HLRCC may behave more aggressively than those arising in other RCC predisposition syndromes [2]. The scenario encountered in our case is notable in that the donor patient's hereditary predisposition for RCC was identified only after having donated her kidney, despite the cutaneous manifestations of her condition developing 1 year prior to the donation. The added risk to the recipient of developing a *de novo* malignancy in the transplanted kidney due to a donor-derived germline predisposition is unknown; there have been no such reported cases. Given the rarity of familial cancer syndromes, routine genetic screening of donors or their organs for germline mutations is not currently performed. However, it is known that the overall incidence of *de novo* malignancies after kidney transplantation ranges from 6–11%, with cutaneous squamous and basal cell carcinomas, thyroid carcinomas and malignancies of the native kidney among the most common [3, 4]. Taken together, our case emphasizes the importance of a thorough physical examination and an awareness of the dermatologic manifestations of hereditary cancer predisposition syndromes.

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Conflict of interest statement. None declared.

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