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Letter to Editor

Could fumarate hydratase germline mutation in cutaneous leiomyomas predict Hereditary Leiomyoma and Renal Cell Cancer (HLRCC)?

Keywords:
Hereditary leiomyomatosis and renal cell cancer (HLRCC)
Cutaneous leiomyoma(CL)
Tumor susceptibility genes

Dear Editor,

Hereditary Leiomyoma and Renal Cell Cancer (HLRCC) is an autosomal dominant syndrome associated with heterozygous pathogenic germline variants of the fumarate hydratase (FH) gene. It is characterized with cutaneous and/or uterine leiomyomas and an increased risk of developing aggressive renal cell carcinoma (RCC). Most HLRCCs are identified due to multiple cutaneous leiomyomas (CL) or large uterine smooth muscle tumors (USMT). So far, there are few reports about HLRCC only presented as single CL as it is usually ignored.[1] Here, we report a case of single CL with fumarate hydratase germline mutation, we ask if a potential diagnosis of HLRCC could established and an intensive follow up should be taken for the case?

The man presented to our clinic with a bean sized skin color neoplasm on his right lower extremity. The tumor has been found over 20 years and there were no subjective symptoms until the tumor increased in size recently. The tumor was a firm well circumscribed 1 × 1 cm^2 sized nodule with no adhesion to the surrounding tissues and no tenderness on palpation (Fig. 1 A). Therefore, an impression of cutaneous fibroma was primarily made and a surgical resection was employed. The histopathology showed cutaneous leiomyoma with FH staining negative (Fig. 1B–E), so the diagnosis of the FH deficient CL was established. Due to the close correlation between FH deficient CL and HLRCC, an enhanced CT scan of the kidneys was employed, which revealed multiple cystic lesions in both kidneys and small stones in his left kidney (Fig. 1 F). There was no abnormal finding of blood chemistry detected. The family history found that his sister had uterine fibroids and took a fibroid surgery 30 years ago but a complete pathological examination was lack then. The tumor susceptibility gene testing of PBMCs showed a p. A316D mutation in the FH gene.

The FH gene mutation would result in FH inactivation, which might be responsible for the susceptibility to HLRCC.[2] So, a proposal of single FH- deficient CL with high risk of HLRCC was initiated. HLRCC is a very rare and extremely life-threatening with a mortality rate of 74% due to metastasis.[3] The lifetime renal cancer risk for FH mutation carriers is estimated to be 15%.[4] HLRCC only presented as single CL is usually disregarded and misdiagnosed which might be more nimbler and vicious. Remarkably, the kidney cysts in the case might be precancerous since FH mutation carriers with renal cysts tend to develop kidney cancer more frequently than those without cysts.[5] Hence, we propose that FH gene mutation in CL with renal cysts may pose a dangerous risk of developing HLRCC.

We suggest the vigilance for the disease and an imperative pathological biopsy plus gene screening for CL patients are the key to get early diagnosis and interventions for HLRCC. Now the patient is under careful follow-up to monitor his renal cysts.

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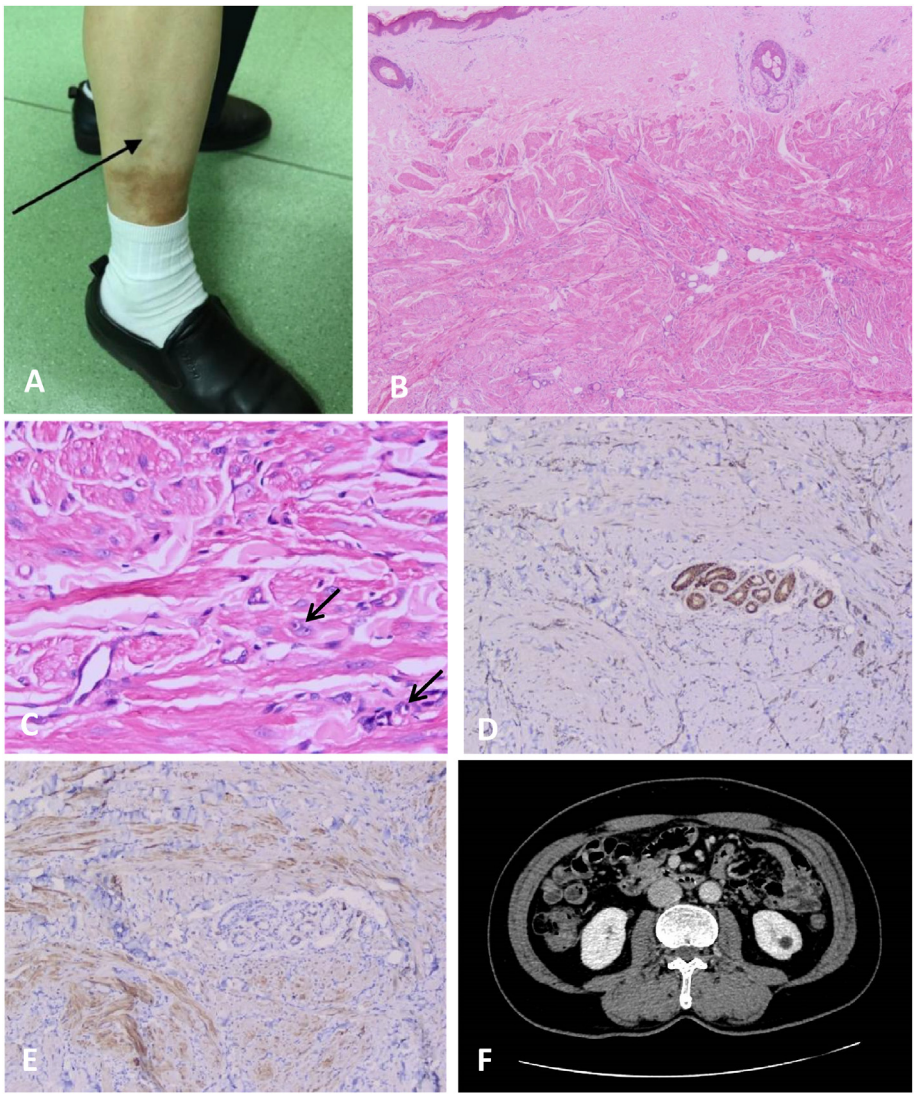

Fig. 1. A, The tumor is located on the lateral aspect of the right lower leg. B–C, Histopathological examination revealed the tumor cells were fusiform, with abundant eosinophilic cytoplasm and perinuclear vacuoles (B × 100,C × 400). D-E, Immunohistochemical staining demonstrated FH staining was negative, H-caldesmon (+) (D-E × 200). F, Enhanced computed tomography (CT) scan of the patient's kidneys.

Ethical approval

Institutional review board approval was received from The Second Hospital affiliated to Guangdong Medical University.

Disclosure of competing interest

The authors report no conflict of interest related to this manuscript.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.asjsur.2023.07.144.

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