Newly Emerging Hereditary Kidney Cancer: BHD Syndrome and HLRCC

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Summary

- Birt-Hogg-Dubé (BHD) syndrome and Hereditary Leiomyomatosis and Renal Cell Cancer (HLRCC) are rare hereditary kidney cancers.
- We collected BHD families (n=189) and HLRCC families (n=5) and investigated gene mutations and clinicopathologic features, focusing on renal neoplasms.
- HLRCC are highly aggressive, and all patients with RCC have poor prognoses.
- Most of BHD-RCCs (75/90) are chromophobe RCC or hybrid tumors: however, they have distinctively different chromosomal state from those of sporadic counterparts.

Introduction

We investigate clinicopathologic features of rare familial kidney cancers; BHD and HLRCC.

Birt-Hogg-Dubé syndrome (BHD)

Caused by germline mutation of \(FLCN\) (17p11.2)

Hereditary Leiomyomatosis and RCC (HLRCC)

Caused by germline mutation of \(FH\) (1q43)

Morbidities of renal cell carcinoma (RCC) and related diseases in BHD & HLRCC

- Most BHD-RCCs are slow growing but multiple and bilateral.
- HLRCCs develop in aggressive single mass.

Histopathology of BHD-RCCs

- Distinctively different from sporadic counterparts

Germline mutation hot spots in Japanese BHD families

Most families have \(FLCN\) mutations at exon 11, 12 or 13

Histopathology of BHD-RCCs

Most tumors are derived from distal nephron

Chromosomal characteristics of BHD-RCCs

Distinctively different from sporadic counterparts

High mortality rates of young adults with HLRCC

Family histories of uterine/skin leiomyomas are often overlooked.

 HLRC-RCC-associated type 2 papillary RCCs are negative for FH in IHC and WB.

We provide Japanese BHD/HLRCC patients with the latest information about familial kidney cancers. We open BHD/HLRCC clinic and organize family association every year. We hope that our activities will help familial kidney cancer patients and reduce cancer death.

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