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Original contribution

Pathologic spectrum of cysts in end-stage kidneys: possible precursors to renal neoplasia☆

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Summary Acquired cystic disease (ACD) is common in patients with end-stage renal disease. Given the significant increased risk of renal cell carcinoma (RCC) in these patients, we characterized the pathologic spectrum of cysts in end-stage kidneys to determine the possible relationship with coincidental neoplasms. Twenty-one native end-stage kidneys contained multiple cysts (0.1-4 cm), which could be categorized into 3 groups based on the cytoplasm of the predominant cell type: clear, eosinophilic, or foamy. Clear cell cysts showed strong staining with carbonic anhydrase IX (CA9) in a cup-shaped manner. Of 7 kidneys with CA9-positive clear cell cysts, 3 had at least 2 foci of RCC (0.5-8 cm), which all demonstrated the morphologic features and immunoprofile of clear cell papillary RCC. Eight kidneys contained foamy cysts, and 4 of these contained ACD-associated RCC, but 1 papillary RCC was also encountered. Six kidneys had eosinophilic cysts, which were negative for CA9, and 3 of these were associated with papillary RCC. Clear cell cysts, although few in number, are common in end-stage nephrectomy specimens. These cysts were present in all kidneys with clear cell papillary RCC and a few kidneys without an obvious mass. In specimens with ACD-associated RCC or papillary RCC, cysts lined by epithelial cells with predominantly eosinophilic or foamy cytoplasm were identified. These data support the idea that the cysts in end-stage kidneys could represent the earliest precursor lesion of renal neoplasia.

1. Introduction

Acquired cystic disease (ACD) of the kidney is a well-known complication of the uremic state in the setting of end-stage renal disease (ESRD) [1]. Patients with ACD have 100 times the risk of developing malignant renal neoplasms compared with the general population [2]. The carcinomas in patients with ACD are smaller, often bilateral, multifocal, and lower stage [3]. The incidence of both benign and malignant renal neoplasms in patients with ACD ranges from 20% to 33% [4]. Although only 18% of these neoplasms are renal cell carcinomas (RCCs) affecting 6% of patients with ACD [1,5], they develop 20 years earlier than sporadic RCC [6].

The cysts in ACD can involve either the proximal or the distal nephron segments [7], but their morphologic spectrum has not been well characterized. Given the common occurrence of both cysts and neoplasms, the present study focused on the pathologic spectrum of cysts in ESRD to determine their possible relationship with a renal neoplasm if present.

☆ This study was previously presented in abstract form at the 2010 United States and Canadian Academy of Pathology annual meeting, which was held in Washington, DC.

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2. Materials and methods

2.1. Patients

The University of Chicago Medical Center pathology archives were searched for native nephrectomy specimens from patients with ESRD. Twenty-one native nephrectomy specimens from 17 patients with ESRD were identified, and all except for 1 specimen had pathologic findings consistent with ACD. Patients ranged in age from 23 to 77 years and consisted of 7 women and 10 men. The clinicopathological data are summarized in Table 1. Patients with polycystic kidney disease or hereditary forms of RCC, such as von Hippel-Lindau–associated neoplasia, were excluded from this study. This study was approved by The University of Chicago Medical Center institutional review board.

2.2. Immunohistochemistry

The specimens were evaluated by light microscopy with an emphasis on the cysts and cystic lesions. Standard immunohistochemistry was performed for carbonic anhydrase IX (CA9; NCL-L-CA9; Leica Biosystems, Richmond, VA), racemase (P405S, CPK200 AK, BK, CK; Biocare Medical, Concord, CA), cytokeratin 7 (CK7; OV-TL 12/30; Dako, Carpinteria, CA), and CD10 (NCL-CD10-270; Leica Biosystems) on any cysts lined by epithelial cells with clear, foamy, or eosinophilic cytoplasm.

3. Results

3.1. Characterization of epithelial cells lining cysts

Twenty kidneys generally contained "numerous" or "multiple" cysts, which measured from 0.1 to 4 cm in greatest diameter during the initial gross descriptions. Therefore, the number of cysts for each kidney was determined from the glass slides without using a microscope. These data are detailed in Table 2. Based on the epithelial cell lining, the predominant cyst type could be categorized into 3 groups: (1) clear cells with polygonal to columnar shape, clear cytoplasm, and vesicular nuclei that often have a suprabasal location with subnuclear vacuole (n = 7); (2) foamy cells with abundant vacuolated cytoplasm and small nuclei (n = 8); and (3) eosinophilic cells with flat cuboidal to polygonal shape and abundant eosinophilic cytoplasm and small nuclei (n = 6; Fig. 1A-H). Multiple cyst types were often encountered within the same specimen. Epithelial lining cells with eosinophilic and foamy cytoplasm were often present within the same cyst. However, the cysts lined by cells with optically clear cytoplasm did not coincide with the other cell types within a given cyst.

Clear cysts ranged from 1 to 17 mm in greatest diameter, foamy cysts ranged from 1 to 15 mm, and eosinophilic cysts ranged from 1 to 25 mm. Three (38%) of the kidneys with clear cysts had a diameter greater than 5 mm. Clear cell cysts showed architectural variation, as some were lined with a

Table 1 Clinicopathological data

Specimen	Age/Sex	Dialysis time before nephrectomy	Indication for nephrectomy	Kidney size (cm)	Kidney weight (g)
1	59/M	>5 y	Unknown	7 × 4.6 × 3.2	80
2	62/F	5 y	Renal mass	8.5 × 4.5 × 3.5	91
3L	60/M	6 y	Renal mass	NA	NA
3R			Renal mass	NA	NA
4	53/F	Functioning allograft	Renal mass	6.5 × 3.5 × 2.4	62
5	38/M	1 y	Renal mass	7.8 × 4.3 × 3.5	NA
6	77/M	2 y	Renal mass	9.5 × 5.7 × 5	NA
7L	49/F	Unknown	Renal mass	NA	NA
7R			Renal mass	NA	NA
8	71/F	7 y	Renal mass	7.1 × 4.6 × 3.4	NA
9L	46/M	>15 y with 2 failed allografts	Renal mass	6 × 4 × 2.5	54
9R			Renal mass	6.2 × 3.8 × 3	NA
10	55/F	Unknown	Renal mass	5 × 3.8 × 3	22
11	58/F	>15 y	Renal mass	10 × 5.7 × 5	NA
12	60/M	Functioning allograft	Renal mass	9.5 × 5.2 × 2	NA
13	65/M	Functioning allograft	Renal mass	14 × 7 × 7	NA
14L	50/M	Functioning allograft	Renal mass	6.3 × 3.9 × 3	NA
14R			Renal mass	10 × 4.5 × 3.3	NA
15	23/F	6 y	Native kidney removed for allograft	8.5 × 5 × 3.5	96
16	59/M	Functioning allograft	Unknown	NA—morselated	NA
17	50/M	1.5 y	History of urothelial carcinoma	12.7 × 6.9 × 4	NA

Abbreviations: L, left; R, right; M, male; F, female; NA, not available.