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Renal Tumors in Postmortem Material

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Renal tumors include several categories, the most frequent being clear cell renal cell carcinoma, papillary renal cell carcinoma, chromophobe carcinoma, oncocytoma, adenoma and angiomyolipoma. The aim of the study was to analyze the incidence of renal tumors in autopsy material. Among 3512 autopsies performed in our institution in the last decade, we found 97 post mortem examinations in which 108 renal tumors were detected. The most frequent diagnosis was adenoma (53 cases, 49.1%) and, among cancers, clear cell carcinoma (20 cases, 21.1%) followed by papillary carcinoma (17 cases, 15.5%). Less frequent lesions were angiomyolipoma (4 cases), oncocytoma (4 cases), unclassified renal cell carcinoma (3 cases), medullary fibroma (5 cases) leiomyoma (1 case) and urothelial carcinoma (1 case). The adenomas were significantly more frequent in cases of kidneys with chronic fibrosis. When comparing the present series to surgical material from a similar period, of note is that 44% of renal carcinomas in the autopsy series were papillary, but only 9.4% were papillary in the surgical material.

Introduction

Renal tumors consist of several categories. The principal variants of renal cell carcinoma (RCC) are clear cell, papillary and chromophobe RCC. Urothelial carcinomas derived from the pyelocaliceal mucosa form a separate group. Benign lesions include renal adenomas and oncocytomas. The only frequent mesenchymal lesion is angiomyolipoma. Although several surgical series are available, a limited number of studies have been done on unselected autopsy materials. These may be expected to disclose other features than surgical series, in particular to include a large number of incidental, clinically silent lesions [2, 6, 9, 12, 17, 25, 35].

The aim of the study was to analyze the incidence rate of particular tumor types in autopsy material and to compare them to other features of the patients.

Material and Methods

The autopsy files of our department for the years 1997-2007 were screened for information on renal tumors detected. In cases where such lesions were found, the slides and tissue blocks were located. In all the cases the material was formalin-fixed and routinely processed, and paraffin-wax embedded. From the tissue blocks, 4um sections were obtained and hematoxilin-eosin stained. The slides were reviewed by both authors, using a multihead microscope, and a consensus diagnosis was reached. The diagnoses were based on the WHO classification [9].

For statistical analysis, the χ^2 test, t-Student test, Mann-Whitney U test and Kruskall-Wallis ANOVA were used when appropriate. All statistical analyses were performed with STATISTICA version 7.1 (StatSoft Inc, USA) and Excel 2003 (Microsoft Corp, USA). The significance level was set to 0.05.

Results

In the period under study, 3512 post-mortem examinations were performed in our institution. In 97 cases, a total of 108 renal tumors were found. The mean age of the patients was 67.3 years (range 33 to 95, SD 13.2). There were 34 females and 63 males. The mean age for males was 63.6 and for females 74.1 years. This difference is statistically significant ($p<<0.01$). The principal diseases in patients under study are shown in Table 1.

TABLE 1
Main cause of death in our autopsy series

	N	%
Cardiovascular	42	43.3
Non-renal cancer	19	19.6
Abdominal, surgical	11	11.3
Infection	8	8.2
Renal cancer	7	7.2
Traumatic	4	4.1
Chronic neurological disease	3	3.1
Cryptogenic bone marrow failure	1	1.0
Chronic renal failure	1	1.0
Chronic respiratory disease	1	1.0

N – number of cases

TABLE 2
Histologic types of renal tumors

	N	%
Adenoma	53	49.1
Clear Cell RCC	20	21.1
Papillary RCC	17	15.5
Oncocytoma	4	3.7
Angiomyolipoma	4	3.7
Renal cell carcinoma, unclassified	3	2.8
Fibroma	5	2.1
Leiomyoma	1	0.9
Urothelial carcinoma	1	0.9

N – number of cases

The most frequently seen tumor type was adenoma (53 tumors, 49.1%) and, among cancers, clear cell (conventional) carcinoma (20 tumors, 18.9%). The histological types are shown in Table 2. The "unclassified" category includes, unlike in the surgical material, cases with extensive autolysis, hampering the exact classification.

In 11 cases, more than one tumor was seen. Of these second lesions, eight were adenomas and three fibromas. In 88 cases, the tumor was undiagnosed prior to autopsy. The lesion was identified in one of 17 (5.9) papillary carcinomas, one of four (25%) oncocytomas, six of 20 (30%) clear cell carcinomas, the one urothelial carcinoma (100%), but none of the other lesions. The difference in frequency of incidental post-mortem carcinoma detection between histological diagnoses was statistically significant ($p<0.01$). In 52 cases, important non-neoplastic renal lesions were found (Table 3). In the majority of cases (40, 41.2%), they consisted in chronic scaring, including benign nephrosclerosis and chronic pyelonephritis, often in combination. In four cases (4.1%), suppurative pyelonephritis was present. Of some interest is the single case of crescentic glomerulonephritis, seen in a case of clear cell RCC, as glomerular disease are in some instances linked etiologically to cancer. Examining the relationship of non-neoplastic renal disease to renal tumor type, it was worth stressing that adenomas were frequently seen in kidneys with chronic scaring (25 of 45 cases). This relationship is known from previous reports. No significant pattern was seen for other tumor categories. Also examining the cause of death versus renal tumor type showed no significant relationship.

TABLE 3
Non-neoplastic renal lesions

	N	%
Chronic renal disease	40	41.2
Acute pyelonephritis	4	4.1
Renal infarcts	3	3.1
Nephrolithiasis	2	2.1
Hypoplastic kidney (ipsilateral to the tumor)	1	1.0
Hypoplastic kidney (contralateral to the tumor)	1	1.0
Crescentic glomerulonephritis	1	1.0
None	45	46.4

N – number of cases

In 30 cases, extrarenal tumors were detected as well. The diagnoses are presented in Table 4. Of 20 clear cell carcinomas, four (20%) were accompanied by extrarenal tumors, of 17 papillary carcinomas, six (35.2%) occurred concomitantly with extrarenal tumors, 17 (37.8%) of adenomas were accompanied by extrarenal tumors, as well as one oncocytoma and two fibromas. However, these differences were not statistically significant.

TABLE 4
Extrarenal tumors by site and histological type

	N
Pulmonary squamous cell carcinoma	5
Pulmonary small cell carcinoma	3
Colorectal adenocarcinoma	2
Intestinal adenomas (multiple)	2
Pulmonary adenocarcinoma	2
Uterine leiomyomas (multiple)	2
Non-Hodgkin lymphoma	2
Adenocarcinoma of the gallbladder	1
Adrenocortical adenoma	1
Cardiac liposarcoma	1
Cervical squamous cell carcinoma	1
Duodenal lipoma	1
Esophageal squamous cell carcinoma	1
Gastric leiomyoma	1
Gastric lipoma	1
Hepatic hemangioma	1
Laryngeal neurofibroma	1
Pancreatic adenocarcinoma	1
Prostatic adenocarcinoma	1

N – number of cases

TABLE 5
Comparison of the incidence by tumor types in autopsy and surgical material

	surgical	autopsy
Clear Cell RCC	71.72%	18.87%
Papillary RCC	7.46%	15.09%
Chromophobe RCC	5.27%	-
Renal cell carcinoma, unclassified *)	3.08%	2.83%
Oncocytoma	2.83%	3.77%
Adenoma	-	49.06%
Urothelial carcinoma	6.81%	0.94%
Angiomyolipoma	2.57%	3.77%
Leiomyoma	0.13%	0.94%
Leiomyosarcoma	0.13%	-
Fibroma	-	4.72%

RCC stands for renal cell carcinoma
*) note that in surgical series, this class include tumors with uncertain features, as papillary tumors with clear cells; in autopsy material, the autolytic changes are the major factor responsible for diagnostic uncertainty.

We decided to compare the histologic type frequency to surgical pathology records of our department. The set contained 778 tumors; among them, a very large majority was again clear cell carcinomas, but this was an even more obviously dominant type (Table 5). The incidence of papillary carcinoma was twice as high in the autopsy as compared to the surgical material. Limiting the analysis to lesions frequent in both sets (i. e. clear cell RCC and papillary carcinoma) strengthened this relationship, yielding the incidence of papillary RCC of 44% in the autopsy versus 9.4% in the surgical series. This difference was statistically highly significant ($p<0.001$).

Discussion

Traditional classification of renal tumors distinguished several entities, basing on both cytological details and growth pattern [32]. The relationship between these entities was unclear as the link to the histogenesis. This situation was modified with the introduction of the new WHO classification [9]. In this system, the main categories are conventional (clear cell) carcinoma (CCRCC), chromophobe renal cell carcinoma (ChRCC, collecting duct carcinoma (ColRCC) and papillary carcinoma (PapRCC); some cases do not fit into these groups and remain unclassified. Commonly seen benign tumors include oncocytoma and adenoma. Mesenchymal tumors are rare, including mainly angiomyolipomas and medulary fibromas. Some of the lesions listed above are seen predominantly in autopsy material or are detected incidentally in nephrectomy specimens, namely renal adenomas and medullary fibromas [10, 27, 29, 30]. Amin et al. [3] showed that renal cancers greatly differ in 5-year survival rates, with as much as 100% for chromophobe carcinoma, 86% for papillary carcinoma, 76% for clear cell carcinoma and 24% for unclassified carcinoma. Li et al. [19] analyzed DNA ploidy in various RCC types by flow cytometry. They found a diploid pattern in all oncocytomas, hypodiploid pattern in most chromophobe RCC; most of conventional and papillary RCC were also DNA-diploid.

In our series, many incidentally detected renal tumors have papillary architecture. Early reports (e.g. [21]) already stressed differences of PapRCC from the bulk of RCC, such as lower stage at presentation, hypovascularity, extensive necrosis and more favorable prognosis [4, 11, 22, 24]. As the traditional definition of PapRCC required at least 50% of the lesion to be composed of papillae, tumors in which papillae were fused, the so called solid variant, were described in details only by Renshaw et al. [28]. Such tumors share the very same characteristics of classic PapRCC. Cytogenetically, trisomy of chromosomes 7 and 17 was shown to be characteristic for PapRCC [5, 18]. In the same study, the DNA-ploidy pattern was diploid for 2/3 of low grade tumors, but only for 1/4 of high grade carcinomas. In a series of 41 cases, Henke found trisomies of chromosomes 7 and 17 in 38 [13]. Additionally, other trisomies (12, 16, 20) were noted in this study, and these were correlated with histologic criteria of malignancy.

PapRCC is much more frequent in end stage kidney disease than in general population, the difference being 10-fold in one study [14]. These authors noted no difference in sex, age and tumor size between papillary and non-papillary tumors. However, a longer dialysis period was seen in papillary carcinoma patients Wang et al. [33] found that more than 18% of papillary adenomas are related to acquired cystic kidney disease and end stage kidney disease. In our material, this was even more striking. In a case of a renal allograft, DeLong et al. [7] observed as many as 29 separate foci of PapRCC. Some cases of hereditary PapRCC were related to c-met germline mutation. The same gene may be involved in some of sporadic PapRCC. Cases associated with this mutation were described as low grade type 1 tumors, were frequently multifocal or accompanied by papillary adenomas [20]. Generally, PapRCC may be multifocal in as many as 1/4 of cases (17% in our series). According to Mejean et al. [23], there is no relationship between mutifocality and any prognostic factors. Indeed, multifocal tumors were said to exhibit the very same behavior. A subclassification of PapRCC was proposed by Delahunt and Eble [8]. Type 1 tumors were composed of papillae lined by small cells with pale cytoplasm and regular, low grade nuclei. The less frequent type 2 tumors

were formed of papillae lined by larger cells with abundant, pinkish cytoplasm. The nuclei were higher grade and often pseudostratified.

Renal adenomas are tiny lesions composed of papillary or tubular growth of uniform, small cells. The relationship between renal papillary adenoma and PapRCC is unclear. Wang et al. [33] found papillary adenomas in 7% of nephrectomy specimens. Forty-seven per cent of these accompanied PapRCC. Adenomas accompanying PapRCC were more frequently multiple. The authors believe that renal adenoma is a PapRCC precursor. Multifocal PapRCC seem to have discordant patterns of loss of heterozygosity (LOH), supporting their independent origin [15], in contrast to multifocal clear cell RCC [16]. Another case that could add to the histogenesis of some PapRCC was described by Al-Saleem et al. [1]. Their case was an oncocytoma with areas of papillary differentiation. These areas showed CK7 reactivity and chromosome 7 and 17 trisomy. It was interpreted as an oncocytoma progressing to PapRCC.

A poor prognosis for unclassified RCC (UnRCC) was evident in the work of Zisman et al. [36]. These authors found UnRCC to constitute around 3% of RCC. These tumors tended to be larger, with more advanced local extension and more frequent metastatic disease. Nephrectomy was often non-radical or not attempted. Immunotherapy seemed to be of benefit, but nephrectomy alone was not an effective treatment modality. As commented in the "Results" section, the features of UnRCC in surgical and autopsy material may be altogether different.

During the past two decades, the incidence of RCC has increased by approximately 2% per year [31]. Wunderlich et al. [35] reported a 15 to 20% increase in the incidence of RCC. They believed that it is only in part due to better detection, but also reflects a true incidence increase, as an increase in the rate of autopsy-detected RCC was seen. The reported incidence of RCC at autopsy was 1.55% to 1.77% on the basis of over 23,000 autopsies. In [34], 260 RCC were reported in 14,793 post-mortem examinations. Of these, 13.85% were multifocal (12% unilateral, 88% bilateral). Six of multifocal cases were adenomas, 15 carcinomas, and in ten, both benign and malignant tumors were present. Reis et al. [26] analyzed the occurrence of renal tumors and tumor-like lesions in a 500-case autopsy series from forensic material, noting that 195 were cysts, 89 fibromas and 20 adenomas. Others were classified as lipomas, leiomyomas, fibromyolipomas and capsular fibromas. Hajdu et al. [12] analyzed autopsy records of 29 years with over 15,000 autopsies in the files. They found the M:F ratio of 2.5:1 and the average age of 67 years. One half of the cases were at M1 stage at autopsy, with the lung, lymph nodes, liver and contralateral kidney as leading locations. In 50% of cases, RCC was the main cause of death. Alanen et al. [2] reported 112 renal tumors in a series of 8,489 autopsies. Among 7,970 autopsies, Kihira et al. [17] found 51 RCCs (0.65%). The M:F ratio was 4.6: 1 and the average age 66.3. One half of the cases were not clinically suspected. The incidental tumors were significantly smaller (2.6cm) than symptomatic (7.3cm); 86% of incidental cases, but only 52% of symptomatic ones were clear cell. The authors used an older categorization method for classifying non clear cell RCCs, thus, the comparison of their incidence to that observed in more recent findings is not possible.

In Dall'Oglio et al. series [6], 51% of RCCs were symptomatic and 49% were incidentally detected during imaging studies done for other reasons. Small size (<4cm) was the predominant feature of incidentally detected tumors (51%) as compared to symptomatic ones (20%). Large tumors (>10cm) were usually more frequently symptomatic. The symptomatic tumors had also a significantly worse prognosis. Porena et al. [25] compared incidentally detected and symptomatic cases of RCC. They showed that incidental cases constituted roughly 1/2 of all cases, and tended to be significantly less advanced.

In conclusion, we observed renal tumors in 2.76% of unselected anatomopathological post mortem examinations. The most frequent tumor types were adenoma, clear cell carcinoma and papillary carcinoma. In particular, the incidence of papillary carcinoma was far greater than in surgical material.

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