ORIGINAL ARTICLE

PATTERN OF MALIGNANT RENAL TUMOURS USING 2004 WHO CLASSIFICATION OF RENAL TUMOURS ON RADICAL NEPHRECTOMY

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Objective: To determine the type of malignant renal tumours subjected to radical nephrectomy at a tertiary care urology unit using the 2004 WHO classification for renal tumours. **Methods:** It was an observational study conducted at Department of Urology, AFIU Rawalpindi, from October 2008 to September 2010. The study included 92 patients with malignant renal tumours of both genders aged above 15 years. The histopathological types and grades were recorded along with the gross tumour presentation. The data was entered in structured proforma and analysed for descriptive statistics using SPSS-14. **Results:** Over the span of 24 months study, 92 cases of malignant renal tumours were subjected to radical nephrectomy. The age was 16–82 (57.23±14.61) Years and male to female ratio was 2.1:1. The lesions were mostly unifocal (96.7%) and 58.6% affecting the right side. The commonest malignant renal tumour encountered was the conventional clear cell renal carcinoma (78.2%). The other tumours in descending order were the transitional cell carcinoma (7.6%), papillary (chromphilic) renal cell carcinoma (6.5%), renal cell carcinoma unclassified (3.2%), chromophobe renal cell carcinoma (2.1%), Wilm's tumour and oncocytoma (1.7%). T1 lesions were found in 42 cases (45.6%), T2 lesions in 25 cases (27.1%), T3a lesions in 17 cases (18.4%) each, while 8 cases (8.6%) had T3b lesions. Four cases had high and 3 had low grade lesions in transitional cell carcinoma. Wilm's tumour had favourable prognosis, 1 case had oncocytoma limited to kidney. Among the rest, 26 (28.2%) were G1, 35 (38%) were G2, 16 (17.3%) were G3, and 6 (6.5) were G4. **Conclusion:** The commonest type of the malignant renal neoplasm remains the clear cell (conventional) renal cell carcinoma. The lesions from T1 to T3 are amenable to radical nephrectomy and may not include the ipsilateral adrenalectomy as well. The grade may range from G1 to G4.

Keywords: Clear cell carcinoma, Radical nephrectomy, Transitional cell carcinoma

INTRODUCTION

The malignant renal neoplasms constitute the primary and the secondary lesions of the kidney. The operable cases of primary malignant renal tumours require surgical treatment, nothing short of radical nephrectomy. The classical radical nephrectomy[1] entails *en bloc* removal of the kidney and its enveloping fascia (Gerota's fascia) including the ipsilateral adrenal, proximal one half of the ureter and lymph nodes up to the area of transaction of the renal vessels. However, some surgeons believe that the adrenal gland should not be removed because of the low probability of ipsilateral adrenal metastasis and the morbidity associated with adrenalectomy. Lymph nodes may be involved in 10–25% of patients. Approximately 5% of patients with renal cell carcinoma have inferior vena caval involvement.

Renal cell carcinoma is the commonest type of malignant renal tumours. The age-adjusted incidence of renal cell carcinoma has been rising by 3% per year. According to the American Cancer Society, in 2007 there were 51,590 cases (31,990 in males and 19,600 in females) of malignant tumours of the kidney diagnosed in the United States with 12,890 deaths (8,080 in males and 4,810 in females); renal cell carcinoma accounted for 80% of this incidence and mortality.[2] Number of deaths worldwide from kidney cancer exceeded 100,000 in 2001. Renal cell carcinoma is the eighth or ninth leading cause of cancer death in the United States. Cheville *et al*[3] classified the renal cell carcinoma following the 1997 Union Internationale Contre le Cancer and American Joint Committee on cancer guidelines. There were 83.2% patients with clear cell, 11.3% with papillary, 4.3% with chromophobe, 0.3% with collecting duct, 0.3% with purely sarcomatoid RCC and no underlying histologic subtype, and 0.7% with RCC, not otherwise specified. Cancer-specific survival rates at 5 years for patients with clear cell, papillary, and chromophobe RCC were 68.9%, 87.4%, and 86.7%, respectively. In 2004 a comprehensive histological classification of the tumours of the kidney was introduced by WHO.[4] This includes the benign as well as the malignant neoplasms of the kidney, comprising of the renal cell tumours, metanephric tumours, nephroblastic tumours, mesenchymal tumours, mixed mesenchymal and epithelial tumours, neuroendocrine tumours, haemopoietic/lymphoid tumours, germ cell tumours and metastatic tumours. The diverse nature of the tumours signifies the renal architectural complexity. The aim of

conducting this study was to ascertain the pattern of the histological types of malignant renal tumours found in our patients, undergoing radical nephrectomy using the 2004 WHO Classification of the renal tumours.

The disease has been reported in younger people who belong to family clusters. It is more common in people of Northern European ancestry (Scandinavians) and North Americans than in those of Asian or African descent. In the United States, its incidence has been equivalent among whites and African Americans, but incidence among African Americans is increasing rapidly. Special attention should be focused on black Americans since their incidence rate recently increased significantly surpassing that in white Americans.[5]

MATERIAL AND METHODS

This descriptive/observational study was carried out from October 2008 to September 2010 at the Department of Urology, Armed Forces Institute of Urology, Rawalpindi. A total of 92 cases presenting to the urology outdoors with a pre-operative suspicion of malignant renal tumours subjected to radical nephrectomy were included in the study. All these patients were evaluated in detail, prior to the surgical intervention. A complete blood picture, urinalysis, serum urea, electrolytes, creatinine, liver function tests, serology for hepatitis B and C, ultrasound KUB/ abdomen, chest radiograph and CT Scan Abdomen and Pelvis (contrast enhanced) were contemplated.

The patients of suspicious renal masses of either sex and above 15 years of age were included in the study. Inoperable cases (T4 lesions, metastatic lesions) were excluded from our study. Patient's age, gender, site, focality and size of the tumour were recorded. After pre-operative assessment informed written consent was taken and radical nephrectomy was performed under general anaesthesia through a transperitoneal approach. A drain was placed and wound was closed in layers. The specimen was preserved in formalin and sent for histopathology. The histopathological type and grade of the tumour was recorded.

RESULTS

A total of 92 cases were included in the study. The age distribution was 16–82 years (57.23±14.61) with the highest number of cases (44.6%) recorded in the sixth and seventh decade (50–69 years). The male to female ratio was 2.1:1. Fifty-four (58.6%) tumours were on the right side and 38 (41.3%) on the left with a right to left ratio of 1.4:1. The majority of tumours were unifocal (96.7%) and only 3 cases (3.2%) showed multifocality. The maximum diameter of the tumour ranged from 1.5 Cm to 42 Cm (6.75±5.72). The diameter of 42 Cm was seen in a case of Wilm's tumour in a 16 years old male. The upper pole was involved in 29 cases (31.5%), middle pole in 25 cases (27.1%) and lower pole in 29 cases (31.5%). The whole kidney involvement was seen in 9 cases (9.7%).

The commonest malignant renal tumour encountered was the clear cell (conventional) carcinoma in 72 cases (78.2%). Among these cases of clear cell carcinoma, two had sarcomatoid differentiation, three with extensive necrosis, two with chronic granulomatous inflammation and one with granular cell change. Transitional cell carcinoma was noted in 7 cases (7.6%), and papillary renal cell carcinoma in 6 cases (6.5%). Renal cell carcinoma – unclassified was seen in 3 cases (3.2%), out of which two were cases of sarcomatoid carcinoma. Two cases (2.1%) of chromophobe renal cell carcinoma and one (1.08%) each of Wilm's tumour and oncocytoma were noted (Table-1). One case of papillary renal cell carcinoma had a concomitant benign cystic teratoma of the ovary which was also excised in the same sitting.

Considering the findings of the ultrasound, CT Scan and histopathology, T1 lesions were found in 42 cases (45.6%), T2 lesions in 25 cases (27.1%), T3a lesions in 17 cases (18.4%) each, while 8 cases (8.6%) had T3b lesions. Amongst the 42 cases of T1 lesions, 10 were confirmed T1 on ultrasound and CT Scan, however on histopathology they showed invasion of the renal capsule but the perinephric fat was not involved, so they were also kept in T1 lesions. On histopathology 10 cases showed lymphovascular invasion. Lymph nodes were seen in 11 cases with only two showing lymph node metastases. Adrenal gland was evident in only 9 cases and none of them showed any element of involvement of the adrenal gland.

Among the 7 cases of transitional cell carcinoma 4 had high grade and 3 had low grade lesions. However the Wilm's tumour had a histopathological grade of favourable prognosis. One case had oncocytoma which was limited to the kidney. The rest of the 83 tumours showed 26 cases (28.2%) of G1 grade, 35 cases (38%) of G2 grade, 16 cases (17.3%) of G3 grade and 6 cases (6.5%) of G4 grade.

Table-1: Types of malignant renal tumours (n=92)

Histological types	Number	Percentage
Clear cell (conventional) renal cell carcinoma	72	78.2
Transitional cell carcinoma	7	7.6
Papillary (chromophilic) renal cell carcinoma	6	6.5
Renal cell carcinoma - unclassified	3	3.2
Chromophobe renal cell carcinoma	2	2.1
Wilm's tumour	1	1.08
Oncocytoma	1	1.08

DISCUSSION

The malignant renal neoplasms constitute the primary and the secondary tumours of the kidney. Approximately 85% of primary malignant renal tumours develop in the renal parenchyma and nearly all

of these are renal cell carcinomas.[5] Renal cell carcinoma accounts for ~3% of human malignancies and its incidence appears to be rising.[6] It is diagnosed in ~150,000 people each year worldwide and 78,000 die from the disease.[6] It is most commonly seen in the 5th and 6th decade and has a male to female ratio of 2:1.[1] In our study the malignant renal tumours were mostly seen in the 6th and 7th decade (44.6%) and the male to female ratio was 2.1:1.

Renal cell carcinomas originate from the proximal tubular epithelial cells as evidenced by electron microscopy[7] and immunohistochemical analysis.[8] The cytological features are given priority compared to the histological growth forms for classification of renal cell carcinomas.[9] According to the 2004 WHO Classification of the tumours of kidney[4], they are classified into the following types: clear cell (conventional) renal cell carcinoma, multilocular clear cell renal cell carcinoma, papillary (chromophilic) renal cell carcinoma, chromophobe renal cell carcinoma, carcinoma of the collecting ducts of Bellini, renal medullary carcinoma, Xp11 translocation carcinoma, carcinoma associated with neuroblastoma, mucinous tubular and spindle cell carcinoma, renal cell carcinoma (unclassified), papillary adenoma and oncocytoma. However the histological growth forms constitute the compact, acinar, tubulopapillary, cystic. All these types of renal cell cancer may show sarcomatoid differentiation. However ones showing significant sarcomatoid change, can be included in the unclassified type of renal cell carcinoma. The sarcomatoid type may have a worst outlook.

Over 75% are clear cell carcinomas, named after the characteristics they display when looking at them under the microscope. The descending order of prevalence includes papillary (chromophilic) (10–15%), chromophobic (5%), oncocytic (5%)[10] and collecting duct renal cell carcinomas are the rarest. Hereditary renal cell carcinoma syndromes are estimated at <3% but have major clinical and scientific implications.[11,12] However it does not appear that the various types of renal cell carcinomas differ in presentation or prognosis. In our study the conventional clear cell renal carcinoma (78.2%) was the commonest, the other tumours were the transitional cell carcinoma (7.6%), papillary (chromphilic) renal cell carcinoma (6.5%), renal cell carcinoma-unclassified (3.2%), chromophobe renal cell carcinoma (2.1%), Wilm's tumour and oncocytoma (1.08%).

Papillary renal cell carcinomas also called chromophilic renal cell carcinoma and represent about 10% of all renal cell tumours; with a clear excess in male patients (male to female ratio: 5 to 1).[13,14] We had 6.5% (6 cases) of papillary renal cell carcinoma with five out of six cases in males. Renal cortical adenomas are also frequently associated with papillary renal cell carcinoma in the same kidney, suggesting the possibility of transformation from adenoma to carcinoma. Multiple, bilateral renal tumours are seen in the hereditary papillary renal cell carcinoma which is autosomal dominant.

Chromophobe renal cell carcinoma is a distinct type of renal cell carcinoma possibly originating from the intercalated cells of the collecting tubules. It comprises approximately 5% of all renal tumours.[15,16] In our study we had only two cases (2.1%) of this tumour. Rare example of composite oncocytoma/chromophobe renal cell carcinoma have been described leading to the hypothesis that the two tumours may be related. Chromophobe renal cell carcinoma has a tendency to grow very slowly in vitro in comparison to all other types of renal tumours. It is listed as a rare disease by the Office of Rare Diseases (ORD) of the National Institute of Health (NIH). Metastases often only occur late in the course of the disease and surgical removal usually leads to a good prognosis. When compared to stage for stage, chromophobe renal cell carcinomas have the same prognosis as other renal cell carcinomas.[17] Tumours with larger size and sarcomatoid change are known to have a worse prognosis.[17,18]

Collecting duct carcinoma of Bellini is a rare type of renal cell carcinoma. It affects younger patients, and is associated with poor prognosis due to the aggressive regional and distant spread.[19–22] Unclassified renal cell carcinoma is associated with distinct and highly aggressive biological behaviour, and poor clinical outcome.[23–25] de Peralta-Venturina M *et al*[26] reported that the incidence of sarcomatoid differentiation was 8% in conventional (clear cell) renal carcinoma, 3% in papillary renal carcinoma, 9% in chromophobe renal carcinoma, 29% in collecting duct carcinoma, and 11% in unclassified renal cell carcinoma. Cheville JC *et al*[27] evaluated the renal cell carcinoma with sarcomatoid component and found that these all tumours had a nuclear grade 4, highlighting the grave prognosis of it.[28,29] In our study we had no case of collecting duct carcinoma, however sarcomatoid change with clear cell carcinoma was seen in 2 cases (2.1%) and renal cell carcinoma-unclassified (sarcomatoid) renal cell carcinoma in 2 cases (2.1%) as well.

The renal cell carcinomas are vascular tumours that tend to spread either by direct invasion through the renal capsule into the perinephric fat and adjacent visceral structures or by direct extension into the renal vein.[1] The metastatic lesions can be found in lung, liver, bone, ipsilateral adjacent lymph nodes, adrenal gland, brain, opposite kidney and subcutaneous tissue. Although there still is no agreement as to which grading system should be used, the most common system is the one proposed by Fuhrman *et al*.[30] The Fuhrman grading has become commonly used by the pathologists of North America.[31,32] The system uses four grades based

on nuclear size and irregularity and nucleolar prominence. The system is most effective in predicting metastases (50% of high grade tumours within 5 years). Grade 1 (G1) tumours have small, round nuclei with inconspicuous nucleoli visible at ×400; grade 2 (G2) contain round to slightly irregular nuclei with mildly enlarged nucleoli visible at ×200; grade 3 (G3) have round to irregular nuclei with prominent nucleoli visible at ×100; grade 4 (G4) contain enlarged pleomorphic or giant cells.[30] The importance of nuclear grading in renal cell carcinoma is well documented. In 1997, an international consensus conference on renal cell carcinoma sponsored by the Union Internationale Contre le Cancer (UICC) and the American Joint Committee on Cancer (AJCC) outlined recommendations for the grading of renal cell carcinoma. In our study we had 28.2% cases of G1 grade and 38% cases of G2.

Apart from the renal cell carcinoma, many other primary malignant renal tumours have been encountered. Over 90% of cancers that develop in the renal pelvis are called transitional cell carcinomas (TCC). About 7–8% kidney cancers diagnosed in the UK are TCC. In our study we found 7.6% cases of TCC. They are also named because they develop from cells that line the renal pelvis, ureter and urinary bladder. However these carcinomas of the renal pelvis and the ureter are rare and account for only 4% of all urothelial tumours. The male to female ratio is 2–4:1. The grading of these is similar to that of the bladder tumours. Squamous cell carcinomas are also found in the renal pelvis, accounting for 10% of the renal pelvic cancers. Such tumours are commonly identified in patients with a history of chronic inflammation from infection or calculous disease. Adenocarcinoma arising from the upper urinary tract including renal pelvis is very rare. The primary sarcomas of the kidney are also rare, with a reported incidence ranging from 1–3% of all malignant renal neoplasms.[33,34]

CONCLUSION

The commonest type of the malignant renal neoplasm remains the clear cell (conventional) renal cell carcinoma. The lesions from T1 to T3 are amenable to radical nephrectomy and may not include the ipsilateral adrenalectomy as well. The grade may range from G1 to G4 which is evident on the histopathology of the specimen of radical nephrectomy.

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