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EXPERIENCE WITH RENAL CELL CARCINOMA- A SINGLE CENTRE STUDY FROM KHYBER PAKHTUNKHWA

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ABSTRACT

Objective: To analyze the clinical characteristics, management and outcome of renal cell carcinoma (RCC) and its variants in patients treated at CMH Peshawar, from Aug 2011 to Aug 2014.

Study Design: Retrospective descriptive.

Place and Duration of Study: Combined Military Hospital (CMH) Peshawar, from Aug 2011 to Aug 2014.

Material and Methods: All patients who underwent nephrectomy for renal masses at our institution between Aug 2011 and Aug 2014 were included in the study. The demographic distribution, symptoms, tumour characteristics, operative findings and histopathology reports were extracted from the hospital records and analysed via SPSS version 20.0.

Results: Among 27 patients male to female ratio was 1.25:1. Mean age was 55.5 ± 11.7 years. Flank pain was the commonest symptom reported. Mean maximum diameter of the tumour was 13.6 ± 4.6 cm. All the tumours were malignant and most common histopathological type was conventional/clear cell RCC. All patients were treated by radical nephrectomy through transperitoneal approach. One patient developed post operative thrombosis of inferior vena cava. Two patients developed metastatic deposit during follow up.

Conclusion: Renal tumours in the study population of Khyber Pakhtunkhwa at our centre presented late with large sizes, and incidental diagnosis is rare. Health education and availability of advanced diagnostic facilities will improve outcomes.

Keywords: Nephrectomy, Renal cell carcinoma, Renal tumours.

INTRODUCTION

Improvements in imaging modalities have radically changed evaluation of renal masses. Intravenous urography (IVU) and ultra-sonography are being replaced by CT scan and MRI[1]. Such advancements have also increased the capturing of incidentalomas and frequently more mitotic lesions of kidney are being diagnosed and treated at early stages[2]. In Pakistan however, these imaging modalities are not readily available everywhere and their high cost prevents their liberal use, so late presentations of RCC are still the rule. This study is retrospective evaluation of the patients diagnosed and treated for renal masses at Combined Military Hospital, Peshawar for a period of three years, from Aug 2011 to Aug 2014.

PATIENTS AND METHODS

This retrospective descriptive study was conducted at urology department of CMH Peshawar. Data were extracted retrospectively from hospital records for all the patients presenting to and operated at the urology department during the study period i.e. August 2011 to August 2014. All the 27 patients who had undergone nephrectomy for renal mass during the study period were included in the study by non-probability consecutive sampling method. Patients undergoing nephrectomy for other conditions were excluded from the study. As a routine all these patients had undergone ultrasonography and contrast enhanced CT scan of abdomen and pelvis. Urinalysis, haemogram and assessment of renal and liver biochemical

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functions were also carried out. Patient's demographic and clinical data including age, gender, and durationof symptoms, tumour size, laterality and palpability of tumour were recorded from clinical records and the histopathology findings, including the gross and microscopic findings, were obtained from pathology reports. World Health Organization (2004) classificationof adult renal tumours was employed for the pathological classification of tumours[3]. Fuhrman nuclear grading system was used for RCC, while TNM staging system was applied for assessing the extent of spread[4,5]. Statistical analysis was performed by SPSS software (the Statistical Package for the Social Sciences, Version 20.0, SPSS Inc, Chicago, Illinois, USA). Descriptive statistics i.e. mean ± SD for numeric variables like age was calculated, while frequency and percentages were used for categorical variables to describe the data.

RESULTS

All 27 patients with renal masses were included in the study. 12 (44.4%) patients were females while 15 (55.6%) were males. Mean age at presentation was 55.5 ± 11.7 years. The commonest symptom reported was flank pain by 17 (62.9%) patients. None of the patient had any para-neoplastic syndrome but 7 (25.9%) patients were anaemic. Only 4 (14.8%) patients were completely asymptomatic and were diagnosed incidentally (table-I).

In one third of patients (33.33%) left kidney was involved. No bilateral tumour was encountered. Most common site was at upper pole in 12 (44.44%) patients. Renal vein and vena cava invasion was found in only one case. Mean operation time was 131 ± 21 minutes. Accessory renal arteries were found in 3 (11.1%) patients. Blood was transfused in 15 patients. Mean tumour volume was 1124 ± 1448.2 cm^3. The smallest tumour encountered had maximum diameter of 5 cm whereas the largest one measured 28 cm. Mean tumour volume in incidentally diagnosed patients was 2033.25 cm^3.

Table-I: Demographics and symptomatology of patients under study.

Age (mean) years	**55.56 ± 11.67 (range 35-75)**
Male to female ratio	1.25 : 1 (15 : 12)
Co-morbids	Frequency (percentage)
Diabetes mellitus	2 (7.4%)
Hypertension	6 (22.2%)
Smokers	2 (7.4%)
Symptoms	
Haematuria	16 (59.25%)
Flank pain	17 (62.97%)
Fever	2 (7.4%)
Palpable mass	10 (37%)
Classical triad (haematuria + Flankpain + palpable mass)	4 (14.8%)
Incidental diagnosis	4 (14.8%)

All the cases were renal cell carcinomas with 59.2% being conventional/clear cell RCC and 22.2% being papillary RCC. One case each of collecting duct carcinoma and RCC with oncocytic features was encountered. Table-I and II summarise the results (table-II).

Peroperatively one patient had para-aortic lymphadenopathy and radical nephrectomy could not be performed, so simple nephrectomy was done. Post operatively one patient in whom tumour was removed from the inferior vena cava (IVC), developed thrombosis of IVC and was put on warfarin therapy that resulted in clearance of IVC thrombus in 3 months. All the other patients had a smooth post operative course.

At three months follow up one patient (3.7%) developed metastasis in liver and died 8 months after operation. Another patient developed a metastatic deposit in mandible and at operation site 16 months after operation and was alive at the time of submission of this manuscript 19 months post operation. She was having Sunitinib therapy for the metastatic lesions. In the patient in which simple nephrectomy was performed enlarging lymph nodes produced severe pain 6 months after surgery. One more patient developed recurrence in the ipsilateral adrenal gland 2 years after her surgery. She was having a Fuhrman grade-4 tumor.

Table-II: Operative findings and tumour characteristics by histopathology.

Operation time (min)	**131.2 ± 21.5 (range 80-180)**
Tumor location	Frequency (percentage)
Upper pole	12 (44.44%)
Lower pole	6 (22.22%)
Middle portion	4 (14.8%)
Whole kidney	5 (18.52%)
Tumor size	
Mean tumor volume (cm^3)	1124 ± 1442.8 (range 75-7448)
Mean maximum tumor size (cm)	13.6 ± 4.6 (range 5-28)
Tumor thrombus in renal vein or IVC	1 (3.7%)
Accessory renal arteries	3 (11.1%)
Histopathology	
Renal cell carcinoma (conventional)	16(59.2%)
Papillary renal cell carcinoma	6 (22.2%)
Chromophobe RCC	2 (7.4%)
Collecting duct carcinoma	1 (3.7%)
Clear cell with oncocytic features	1(3.7%)
Clear cell with sarcomatoid features	1 (3.7%)
Fuhrman grade of RCC	
Grade I	3 (11.1%)
Grade II	16 (59.2%)
Grade III	3 (11.1%)
Grade IV	5 (18.5%)

DISCUSSION

Renal tumours comprise a diverse spectrum of neoplastic lesions with patterns that are relatively distinct for children and adults[6]. Renal cell carcinoma (RCC) represents 2-3% of all visceral malignant tumors in adults and 85% of all primary malignant kidney tumors[6,7]. Renal tumours in adults are increasing in incidence throughout the world, probably as a result of detection by wide spread use of cross sectional imaging modalities and ultrasonography[6,8,9]. In our study the mean age of presentation was 55 years which is slightly younger as compared with previously published studies, which show a higher age ranging 52 to 68.3 years[9,10]. The reason for this is not clear. Gender distribution of renal tumours (female to male 1: 1.25) is also slightly more equal than reported previously in local and international studies[2,6,16].

The classical triad of loin pain, hematuria with a palpable mass presents only in 10% of RCC though individually these symptoms may occur in up to 40% of cases[2,12]. The symptom most commonly reported by our patients was flank pain (62%) and the classical triad was present in 4 patients. Other authors have reported hematuria to be the commonest initial symptom which was

found in 59% of our patients[2]. Over time ratio of incidentally diagnosed renal cancers is increasing as is those of smaller tumor size at diagnosis and organ confined disease[7]. Some centres report incidental diagnosis of renal cell carcinoma in upto 72% of recently diagnosed patients[7]. In our series incidental diagnosis was made in only 14.8% patients, the reason being sparse availability of modern radiological investigations and late presentation to doctors due to financial constraints of common man. Interestingly the patient with one of the largest tumor measuring 28cm in maximum diameter was completely asymptomatic. Diabetes Mellitus and hyperlipedemia are common in patients with RCC. In some series 14%-35% of the patients of RCC suffered from Diabetes Mellitus at a frequency 5 times that found in the general population[2]. Only 7.4% of our patients were diabetic. Cigarette smoking has been proposed as a risk factor for RCC. However, in a retrospective study of smokers in the US with RCC the greatest increase in risk was among those men smoking pipes and/or cigars[9,2]. Overall 7.4% of patients in our study were smokers and both were males, the incidence being quite less than other reported data from Pakistan[2]. The reason may be that in Khyber Pakhtunkhwa province the trend of smoking cigarettes is replaced by chewing tobacco (niswar).

When a renal mass lesion is encountered the challenge is to distinguish solid renal masses from the more common benign renal cysts. The distinction between solid and cystic component is easily made by sonograms but accurate pathological nature of a solid or mixed density mass cannot be ascertained before surgery and histopathologic evaluation[6]. Contrast enhanced CT scans come in handy for further non-invasive evaluation of renal masses. Any renal mass that enhances with intravenous administration of contrast material on CT scanning by more than 15 hounsfield units (HU) should be considered a renal cell carcinoma (RCC) until proved otherwise[1,2]. Fine-needle aspiration or biopsy has traditionally been of limited value in the evaluation of renal masses due to high incidence of false-negative biopsy findings in patients with renal malignant neoplasms and the difficulty differentiating renal oncocytoma from eosinophilic variants of RCC[2]. The prognosis of RCC is related to tumor stage. CT and MRI are accurate in the staging local spread of RCC and are the examinations of choice in preoperative assessment[2]. Smelka et al demonstrated that MRI was more accurate than CT for the evaluation of tumour extension into the renal vein and inferior vena cava; a finding of great surgical significance as surgical approach will be altered[2,13].

Although not of much clinical significance, in the present study, 2/3rd of all tumours occurred in right kidney. The experience of other authors is more in favour of equal distribution among the sides. 30% of patients with RCC already have metastasis at the time of diagnosis and metastasis occurs in about 30% to 50% after surgical treatment[7,14]. None of our patients had metastatic disease at time of diagnosis but two (7%) developed metastasis during follow up. The smaller percentage in our study may be due to short time of follow up.

Aggressive surgical management with a hope of cure is currently the standard treatment for RCC patients even with tumor thrombus extending to the RV and IVC[6,11]. Preoperative or postoperative irradiation has not been shown definitely to enhance survival and is no longer used routinely[2]. With evolving technology open radical nephrectomy is rapidly being replaced with laparoscopic nephrectomy in developed world and number of nephron sparing nephrectomies is also on the rise, given the smaller size of tumor at diagnosis[7]. Nephron sparing surgery (NSS) is recommended for tumor less than 4cm and in cases of solitary kidney, bilateral tumors or tumor in a transplanted kidney. In our series all patients underwent transperitoneal radical nephrectomy with pedicle first approach. Adrenal gland was preserved in all cases. None of our patients was candidate for NSS due to larger tumor sizes. Per-operatively accessory renal arteries were found in 3 (11%)

cases. Anatomic variations in the renal vasculature are common, occurring in 25% to 40% of kidneys,most common being supernumerary renal arteries, with up to five arteries reported[1,15].

In our study, the mean maximum dimension of RCC was 13.6 ± 4.6 cm. This is much higher than overall mean size of RCC in a local study and symptomatic RCCs even from India[6,16]. The mean overall size of the primary tumour is markedly lower in western studies, where majority of RCCs are now detected as incidental finding[17,18]. In our study, Fuhrman's nuclear grade 2 was the most common, seen in 59.2% of RCC. Fuhrman's grade I/II are found in about two third of cases of RCC worldwide[6,7,17].

Regarding pathologic staging of RCC according to 1997 revised TNM staging system, it is observed that almost all of our cases (96.3%) presented at an advanced stage (pT2 or above) as compared with studies from the developed world and India. In India 80% tumors were pT2 or above in 2004 depicting a dire need in Pakistan to improve health education of masses and enhancing availability of better diagnostic and treatment facilities[16].

CONCLUSION

Majority of renal tumours in adults in our setting were malignant. Benign neoplasms were rare. Conventional/clear cell RCC was the most frequent histologic type. Most malignant tumours of kidney in our population were of large size and presented at advanced stage. Surgery remained the only curative treatment. Prognosis can be much improved with health education of population and ample provision of latest investigative modalities to diagnose the tumors at early stage.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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