Afr. J. Med. med. Sci. (2013) 42, 239-243

Renal cell carcinoma in Ibadan: a 5-year clinicopathologic review

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Abstract

Background: To review all the cases of the patients with renal cell carcinoma seen during the study period and to determine the pattern of presentation, number of operable cases, histological types and outcome of treatment.

Materials and Methods: The data of the patients with renal cell carcinoma was retrieved from the Urology division audit book, theatre record books and case files from the health records department and pathology register in the department of pathology. The parameters studied were age, gender, pattern of presentation, number of patients who had surgery, histology types and the outcome of treatment.

Results: In total, there were 69 patients with renal cell carcinoma that accounted for 59.5% of all renal masses seen. The male to female ratio was 1:1. Their age ranged from 16 to 88 with a mean of 48 years and median of 50 years. The main clinical feature was loin swelling (100%) and others were loin pain (29%), hematuria (18.8%), weight loss (4%) and paraneoplastic syndrome (anaemia without haematuria) was seen in 2.9%. Ten percent of the cases had the classical triad of hematuria, loin pain and loin swelling. All cases were unilateral disease and 15 (21.7%) had metastasis at presentation. The pre-operative tests were abdominal ultrasound (94%), intravenous urography (45%) and CT-Scan (11.6%). Twenty eight patients (40.6%) had surgery of which 5 were unresectable. 37 of the patients (53.6%) were subsequently lost to follow-up. The 28 operative specimens were histologically confirmed and 85.7% were clear cell carcinoma. The 23 patients whose tumours were resected have remained symptom free, some up to 5 years. However the five patients with unresectable tumours died between 3 to 6 months of exploratory surgery.

Conclusion: The patients with resectable tumour could remain disease free for a significant period afterwards despite late presentation. However, there is a high loss to follow-up rate.

Keywords: *Renal cell carcinoma, resectable, late presentation, histology*

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Résumé

Contexte: Passer en revue tous les cas des patients avec insuffisance rénale carcinome baso-cellulaire vu au cours de la période à l'étude de déterminer le modèle de présentation, le nombre de cas exploitable, types histologiques et résultats du traitement.

Méthodes: Les données des patients avec insuffisance rénale carcinome baso-cellulaire a été récupéré de la division Urologie audit livre, théâtre registres et fichiers des dossiers du service des archives médicales et à la pathologie s'inscrire dans le département de pathologie. Les paramètres étudiés étaient l'âge, le sexe, le motif de la présentation, le nombre de patients qui ont subi une intervention chirurgicale, l'histologie types et au résultat du traitement.

Résultats: Au total, il y avait 69 patients avec insuffisance rénale carcinome baso-cellulaire qui représentaient 59,5 % de toutes les masses rénale vu. Le rapport entre hommes et femmes était de 1:1. Leur âge variait de 16 à 88 avec une moyenne de 48 ans et la médiane de 50 ans. La principale fonctionnalité clinique était aloyau enflure (100 %) et d'autres ont été aloyau douleur (29 %), hématurie (18.8 %), une perte de poids (4 %) et syndromes neurologiques paranéoplasiques syndrome (anaémie sans hématurie) a été observée dans 2,9 %. Dix pour cent des cas avait la triade classique d'hématurie, aloyau douleur et aloyau enflure. Tous les cas étaient unilatérales maladie et 15 (21,7 %) avaient les métastases à la présentation. Le pré-opératoires essais étaient échographie abdominale (94 %), intraveineuse urographie par rm (45 %) et CT-Scan (11.6 %). Vingt-huit patients (40,6 %) avaient une chirurgie dont 5 étaient non résécables. 37 Des patients (53,6 %) ont été perdus par la suite de suivre. Les 28 coopératives spécimens ont été confirmée histologiquement et 85,7 % étaient claires carcinome baso-cellulaire. Les 23 patients dont les tumeurs étaient spécimen tumoral prélevé (corrélé sont restés indemnes, certains jusqu'à 5 ans. Cependant les cinq patients avec tumeurs non résécables sont décédés entre 3 à 6 mois de chirurgies exploratoires.

Conclusion: Les patients avec resectable tumour pourrait rester exempte de maladie pour une période significative après malgré présentation tardive. Toutefois, il existe une forte perte de taux de suivi.

Introduction

Renal cell carcinoma is the third most common urological malignancy after prostate cancer and urothelial carcinoma [1]. The incidence of kidney cancer is 11.8 per 100,000 population in developed country and 2.5 per 100,000 populations in developing countries [2]. In developed countries more than 50% are discovered incidentally, unlike in the Sub-Saharan African countries where majority of the patients present in an advanced stage of the disease [3-6]. The symptomatic patients often present with hematuria, loin pain or loin swelling and occasionally with paraneoplastic syndrome [4-7]. Computed tomography of the abdomen or magnetic resonance imaging are essential in the staging and planning of surgery [8,9].

Renal cell carcinoma is best treated by surgical removal either as nephron sparing nephrectomy or radical nephrectomy. The challenge in its management is in the advanced and metastatic disease [1,4]. Recent advances in molecular genetics and cancer biology have shown that inhibition of vascular endothelial growth factors and mammalian receptors cells has beneficial effects on patients with advanced and metastatic renal cell tumours [2].Worldwide, the commonest histologic type is clear cell adenocarcinoma although papillary type was found to be the commonest in Ibadan in a previous study [2,10]. This may be due to the observation that the patients in the previous study in Ibadan were in their 4th decade and clear cell renal cancer is common at or above the 6th decade of life. We therefore reviewed all the recent consecutive cases of renal tumour from July 2007 to June 2012 seen at a single tertiary hospital in Ibadan in South Western Nigeria to determine the clinical presentation, investigative modalities, histological types and the outcome of surgery.

Materials and methods

All the patients with clinical, radiological and histological diagnosis of renal cell carcinoma seen from July 2007 to June 2012 were included in the study. The data of the age, gender, pattern of clinical presentation, outcome of treatment and follow up was obtained from the Urology division audit book and the case files from the health records department. The number of patients who had surgery was retrieved from the theatre record books while the details of the histological type were retrieved from the cancer registry in pathology department. Patients with secondary metastasis to the kidney and urothelial carcinoma of the renal pelvis were excluded from the study. These data were analysed using mean, standard deviation of mean, median and percentage. The data were presented in tables.

Results

From the various record books sixty-nine patients with clinical, radiological and histological diagnosis of renal cell carcinoma were seen and this represented 59.5% of all renal masses seen over the study period. The other renal masses were due to cystic kidney diseases, pelvi-ureteric junction obstruction and hydronephrosis. The age ranged from 16 to 88 with a mean of 48 years ± 14.6years SD and median age was 50 years.

In Table 1, there were 36 females and 33 males with a female to male ration of 1:1. The peak age was in the 6th decade for both genders.

Table 1: Demography of patients with renal cell carcinoma

Age range (years)	frequency of RCC	male	female
< 20	3		3
21 – 30	8	3	5
31 – 40	11	5	6
41 – 50	15	9	6
51 – 60	20	10	10
61 – 70	9	4	5
71 – 80	2	1	1
81 – 90	1		

RCC renal cell carcinoma

As shown in Table 2, the clinical features were loin swelling (100%), loin pain (29%), hematuria (18.8%), and weight loss (4%) and paraneoplastic syndrome (anaemia without hematuria) was seen in 2.9%.

Tables 2: Clinical presentation of renal cell carcinoma

Clinical presentation	No. of patient (%)
Loin swelling	69 (100)
Loin pain	20 (29)
Hematuria	13 (18.8)
Weight loss	5 (4)
Anaemia without hematuria	2 (2.9)
Classical triad	7 (10)
Localized disease	54 (78.3)
Metastatic disease	15 (21.7)

Data in figure and percentages in parenthesis

All cases were unilateral disease and Table 3 shows that 15 of the tumours had metastasized

confirmed clinically, by abdominal ultrasound, radiograph of the chest, spine and upper limbs, CT scan and intra-operative findings. The commonest sites of metastases were liver in 5 (33.3%), lymph nodes 4 (supraclavicular in 1(6.7%), and renal hilum in 3 (20%), and lungs 3 (20%). Other common sites for metastases were the spine, humerus and peritoneum (as ascites) each 1 (6.7%).

Table 3: Sites of metastases of renal cell carcinoma

Metastatic sites	number (%)
Liver	5(33.3)
Lungs	3(20.0)
Renal hilum lymph node	3(20.0)
Left supraclavicular lymph node	1(6.7)
Spine (paraparesis)	1(6.7)
Left humerus	1(6.7)
Peritoneal (ascites)	1(6.7)

Data in figure and percentages in parenthesis

Table 4: The histological types of adult renal malignancy

Histological type	number (%)
Clear cell (conventional)	24 (85.7)
Papillary (chromophilic)	1 (3.6)
Chromophobic	1 (3.6)
Undifferentiated	2 (7.1)
Total	28 (100)

Data in figure and percentages in parenthesis

The pre-operative investigations done were abdominal ultrasound (94%), intravenous urography (45%) and CT- scan (11.6%). All the surgically resected tumours and biopsy specimens were histologically confirmed as renal. Some 24 (86%) of the tumours were clear cell renal carcinoma while one each were chromophilic (papillary) and chromophobic were 3.6% respectively as shown in Table 4. There were no histology reports on some of the cases because they were lost to follow up during the period of evaluation.

As shown in Table 5, twenty-eight patients (40.6%) had surgery of which 5 tumours were unresectable. Some 37 (53.6%) patients were lost to follow-up. Four patients had palliative treatment. This was done with intramuscular weekly Depo-Provera in 2 patients, chemotherapy =with Vincristine, Adriamycin and Cyclophosphamide in one patient and radiotherapy in 1 patient. The 23 patients whose tumours were resected had a 5 year mean survival time of 31±17.4 (SD) at the end of study period. However the five patients with unresectable tumours died between 3 to 6 months of surgery.

Discussion

In a previous study in Ibadan, the peak age for renal cell carcinoma was in the 4th decade. However, in the current study the peak age is in the 6th decade which is comparable to similar studies in some other parts of Nigeria as well as in Western Europe [2,4.10,11,12]. The older peak age in our study is a reflection of the increase in clear cell type of renal cell carcinoma compared to the previous younger peak age in Ibadan where the predominant histological type was papillary renal cell carcinoma [2,10].

The male to female sex ratio in Ibadan has remained equal despite the differences in histologic types of papillary renal cell carcinoma and clear cell renal carcinoma [10]. The exact reason for this gender equality in Ibadan is not known. This is perhaps due to the sample size. In other studies in Nigeria with predominant clear cell carcinoma as histologic type, gender ratio had varied from predominant male to predominant female [4,5,6,12].

Table 5: Outcome of treatment

Intervention	Number of patient (%)	outcome (%)
Operated	*28 (40.6)*	
Resectable tumour	23	mean survival time 31± 17.4(SD) months (100)
Unresectable tumour	5	died 3-6 months after surgery (100)
Palliative	*4(5.8)*	
Depo-provera (i.m weekly)	2	died at 2-3 months (100)
Chemotherapy VAC	1	died at a month
Radiotherapy	1	died at 2 months
Lost to follow up	37 (53.6)	variable (unaccountable)

VAC: vincristine Adriamycin cyclophosphamide, i.m intramuscular

The classical triad of flank pain, flank mass and hematuria to diagnose renal cell carcinoma is now very rare in Europe and USA because majority of the patients are diagnosed incidentally during investigations for other abdominal pathologies [2,3]. In this study, 10% of our patients presented with the classical triad although this is quite low compared to 43.2% and 67% in the previous studies from the Eastern and Western parts of Nigeria where the commonest histologic type remains clear cell carcinoma [4,7].

The majority of our patients presented with loin swelling similar to that of some other studies in our environment [2,3,4,6,13]. There is therefore a need to engage a policy that would enhance the early diagnosis of potentially lethal intra-abdominal malignancies, including renal cell carcinoma. It may involve routine abdominal ultrasonography during pre-employment medical assessment or during recruitment into military and paramilitary services.

The proportion of patients with metastatic renal tumour in this study is comparable to that seen in other parts of the world [14]. The common sites of metastasis in decreasing order include the lung parenchyma (69%), bone (43%), liver (34%), lymph nodes (22%), and brain (7%) [15]. However, in this study, we found the liver to be the commonest site of metastasis followed by the lungs, renal hilar lymph nodes and less frequently the bone, peritoneum and left supraclavicular lymph node. The liver metastases were seen intra-operatively during exploration of intra-abdominal organs at laparotomy and thereafter confirmed histologically as renal cell origin. The other metastatic sites were diagnosed clinically either on physical examination or radiographs of the chest, spine and the limbs.

Our standard pre- and post-operative investigations for evaluating renal cell carcinoma are abdominal ultrasound, computed tomography (CT scan) and magnetic resonance imaging (MRI) of the abdomen. These investigations allow proper staging, panning of operative approaches, decision to operate or not, choice of appropriate treatment options and the post-operative monitoring of the patient [8,9,16,17]. In the present study. CT-scan was the least common investigation used because only few of the patients could afford it.

Renal cell carcinoma has a poor prognosis when the patients present late, but in this study despite this late presentation, all the patients whose tumours were resected were symptom free at 5 years [2]. It is hoped that the CT scan and MRI which are available in our centre, would be utilized more often in the future to ensure proper patient evaluation.With the improvement in the use of CT scan, it is now possible to plan the extent of patient's pre-operative evaluation and surgery [8]. Renal cell carcinoma is best treated by surgical removal of the tumour [2]. RCC is chemo-resistant and radio-resistant and these had been the trend in the past particularly in the patient with metastatic disease. Despite this fact, various combination of immunotherapy and chemotherapy have been tested with some survival benefit [18-22]. In this study 4 (5.8%) of the patients opted for weekly 250mg Depo-Provera, chemotherapy combination of Vincristine, Adriamycin and Cyclophosphamide, and radiotherapy. The outcome of these treatments was overall very poor.

Recent advances in molecular biology with the discovery of vascular endothelial growth factor (VEGF) and mammalian target of rapamycin (mTOR) inhibitor have improved the prognosis for patients with metastatic renal cell carcinoma. Targeted therapies with sorafenib, sunitinib, bevacizumab, and temsirolimus have been shown to achieve stable disease or progression-free survival of patients with metastatic renal cell carcinoma [23,24]. The use of targeted therapies is desirable in our patients but the limiting factor remains the cost.

In conclusion, the patients with resectable tumour can remain symptom free for a significant period afterwards despite late presentation. CT scan should be encouraged in all the patients as a minimum investigative modality. Significant proportions of our patients were lost to follow-up.

Acknowledgements

Professor L.I. Okeke and Professor E.O. Olapade-Olaopa, for allowing us access to the information of their patients with renal cell carcinoma.

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Received: 10/04/13
Accepted: 29/07/13