Clinocopathological Features of Renal Cell Carcinoma seen at a Radiotherapy Centre in Ibadan, Nigeria

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ABSTRACT

Renal cell carcinoma (RCC) is a rare but lethal disease that accounts for about 2-3% of all adult malignancies. Reports from developing countries indicate a rising incidence while studies in our environment are sparse. The aim of this study is to determine the prevalence, pattern of presentation and outcome of treatment of patients with RCC seen at the Radiotherapy Clinic of the University College Hospital Ibadan.

A 25 year retrospective study of patients treated for RCC was conducted. Case file records were retrieved and information on patients' socio demographic data, presentation pattern, histology, treatment received and outcome of treatment were extracted.

A total of twenty four (24) patients were seen within this period. A higher percentage of patients were female (62.5%) while males accounted for only 37.5%. The mean patient age was 42.9 years. Hematuria, loin pain and flank mass accounted for 80%, 37.5% and 28% of the presenting complaints respectively. Only 12.5% of patients presented with the classic triad of hematuria, loin pain and flank mass. Majority of the patients (62.5%) presented with advanced metastatic diseases. The commonest site of metastasis was the spine (29.2%). About two-third (67%) of patients had surgery. All patients had radiotherapy; 50% to the primary sites, 37.5% to metastatic sites and 12.5% to both metastatic and primary sites. All patients who presented with metastasis had chemotherapy. Only 4 patients (17%) were disease-free at the end of the first year post treatment while only 1 was reported dead. The rest were either lost to follow-up (42%) or referred for palliative care (25%) as a result of disease progression.

Renal cell carcinoma is a rare malignancy in Nigeria and patients often present late. Physicians working in this region needs to have high index of suspicion to diagnose the disease early as the outcome of treatment in late cases is poor.

INTRODUCTION

Renal cell carcinoma (RCC) was first described by Koenig in 1826 [1]. It accounts for about 2- 3% of all adult malignancies [2] and 90- 95% of all malignancies arising from the kidney [3]. It is usually characterized by lack of early warning signs, diverse clinical manifestations and relative resistance to radiation and chemotherapy.

Most cases occur in people between 50-70yrs with a mean age of 64yrs [4]. However, it has been described in children as young as 6 months and younger patients who belong to family clusters.

Globally, about 270,000 cases are diagnosed and 116,000 people die from the disease annually [3].

Renal cell carcinoma is slightly more common in males with a male to female ratio of 1.6:1 [5]. It is also more common in urban dwellers than people living in rural areas.

Renal cell carcinoma is more common in people of Scandinavian descent and North Americans than in Asians or Africans. However, in the USA, it is slightly more common among blacks, (21.3 versus

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19.2 per 100,000 population in men and 10.3 versus 9.9 per 100,000 populations in women) [6]. It is the 10th leading cause of cancer death in males in the USA.

Until recently, the incidence of renal cell carcinoma has risen 2% annually worldwide [3]. The American cancer society estimated in 2010 that there would be 58,240 cases of renal cell carcinoma with 13,040 deaths from kidney cancer, the vast majority being RCC [6]. In contrast to this, the incidence in Scandinavian countries has decreased or stabilized over the past decade [7]. This is perhaps due the reduction in tobacco smoking in men. Also, the mortality rate has declined in Europe. Mortality rate per 100,000 in male population fell from 4.8 between 1990-1999 to 4.1 per 100,000 between 2000 and 2004. In women, mortality rate fell from 2.1 per 100,000 to 1.8 per 100,000.

In sub-Saharan Africa, renal cell carcinoma is relatively rare. In a study conducted at the Korlebu Teaching Hospital in Ghana in 2004, Klufio showed that RCC accounted for 10.4% of all urogenital malignancies seen in the hospital [8]. This is in contrast to a more recent study done by Tijani et al in Lagos, Nigeria where RCC accounted for only 3.7% of all urogenital malignancies seen between January 2000 and December 2010 [9]. Another 20-year retrospective study done at the University of Benin Teaching Hospital by Olu-Edo et. al. showed that renal cell carcinoma accounted for 87% of all malignant adult renal tumours seen within that period [10].

A number of environmental, cellular, hormonal and genetic factors have been implicated as possible factors in the development of renal cell carcinoma. These include cigarette smoking which is said to account for about 30% of renal cell carcinoma in men and 24% in women. Smoking is said to double the risk of developing disease and is related to number of pack-years [11].

Other factors include obesity which has a linear relationship with renal cell carcinoma, particularly in women [12], [13] Hypertension, [14] analgesic abuse especially phenacetin and non-aspirin NSAIDS, long term exposure to high levels of trichloroethylene, [15] leather tanners, asbestos, cadmium, petroleum tar and the radiology contrast, thorotrast.

About 35-47% of patients on long term dialysis will develop renal cysts and about 5.8% of them will develop renal cell carcinoma. These patients have a risk of developing renal cell carcinoma that is as high as 30% more than the risk of the general population. Renal cell carcinoma can also occur in renal transplant patients who develop acquired renal cystic disease [16].

Other rarer causes include family history, Von-Hippel LIndau syndrome, hereditary papillary renal cell carcinoma, hereditary leiomyomatosis renal cell carcinoma and Birt-Hogg Dub syndrome.

In this retrospective study, we present the review of cases of renal cell carcinoma seen at the Department of Radiation Oncology, University College Hospital in Ibadan.

PATIENT AND METHOD

This is a retrospective study of all cases of renal cell carcinoma seen in our department over a 25-year period, between 1987 and 2011. The Department act as a major referral centre for cancer treatment in southern Nigeria and parts of West Africa.

The charts of all cases of renal cell carcinoma sent to us for review and management between 1987 and 2011 were retrieved and reviewed. Data extraction forms were used to retrieve relevant data, including the socio-demographic data, presentation pattern, treatment received, histological pattern etc.

SPSS statistical package version 16 for Windows® was used to analyze the data which are then presented in tables and percentages.

RESULTS

A total of 24 cases were seen over this period. This represents less than 1% of all cancer cases seen in the Department over this period. There were 15 females, and 9 males representing 62.5% and 37.5% respectively. Male to female ratio (M: F) is 0.6 to 1 (1:1.7), showing a moderate female preponderance in the series.

Figure 1 is the pie chart of the age group of the patients in the series. The oldest patient seen was 70 years while the youngest was 12 with a mean age of 42.9 years. The disease appears evenly distributed between the ages probably because of the few number of cases. However, there were more cases in the 51-60 years age group compared to others. Three cases were seen below 20 years.

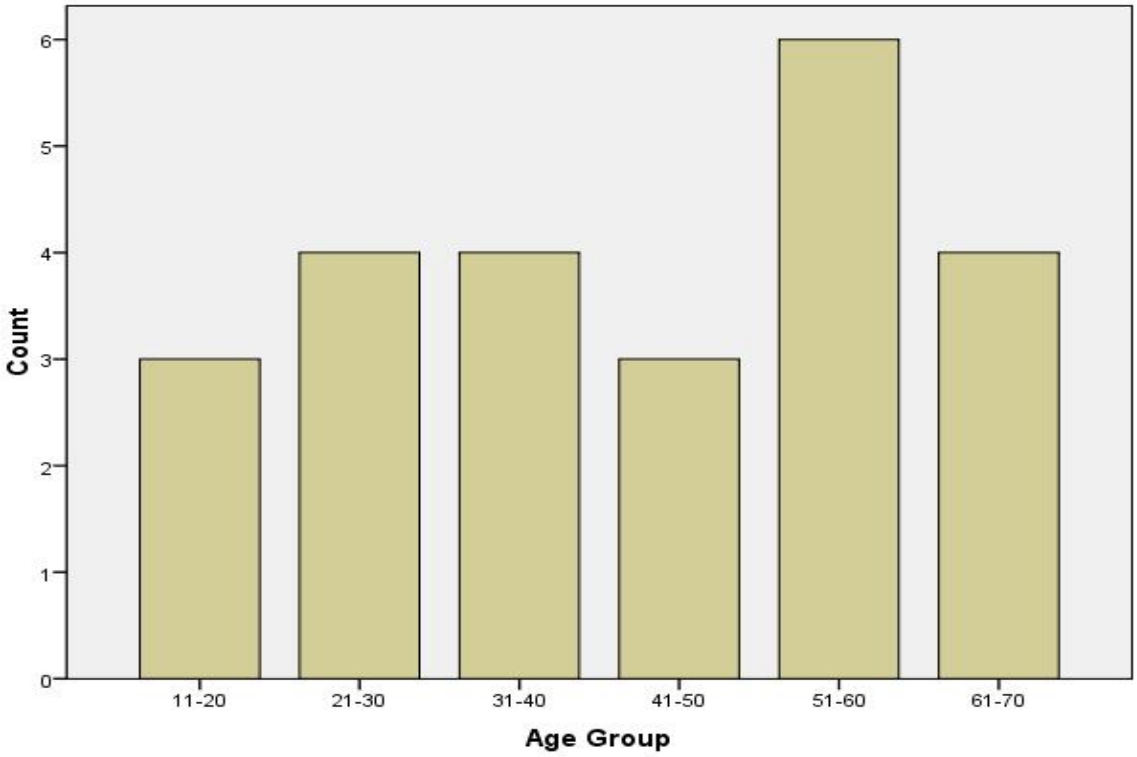

Fig.1: Age grouping of the cohort

Table 1: Clinical presentation

	Frequency	Valid Percent
Hematuria Only	4	18.2
Loin pain Only	2	9.1
Flank mass Only	3	13.6
Triad	2	9.1
Hematuria, loin pain	3	13.6
Unspecified	8	36.4
Total	**22**	**100.0**

PRESENTATION

Of the 24 cases, we had record of the sides of affectation in 21 cases with 10 patients (47.6%) presenting with disease in the right kidneys while 11 cases (52.4%) were in the left kidneys. We were unable to determine the affected kidneys in 3 cases from the available records. These were cases who presented with advanced diseases and received palliative treatment to metastatic sites only and none to the primary sites.

Sixteen patients have their presenting symptoms properly documented. Only two of these patients (12.5%) presented with the classical triad of hematuria, flank tenderness and flank mass. A total of 8 patients (50%) presented with hematuria, 6 (37.5%) with loin pains and 4 (25%) with flank mass. Taken by symptoms 4 patients (25%) presented with hematuria, 2 (12.5%) with flank tenderness and 3 (18.8%) with flank mass as their only presenting complaints. The presenting complaints in 8 patients were not specified.

Fifteen (15) of the patients had metastases at presentation. The metastatic sites are as indicated in Table 2.

TREATMENT

Treatment comprised of a combination of radical nephrectomy, chemotherapy and radiation therapy. Sixteen patients (67%) had surgery, but two patients had unresectable disease while the remaining 14 had radical nephrectomy. The remaining patients were not considered for surgery because their diseases were advanced at presentation. All the patients received radiation treatment either to the tumour bed or the metastatic sites.

Table 2: Metastatic sites

Metastatic Site	Frequency	Percent
Bone Only	3	12.5
Spine Only	7	29.2
Bone and Spine	2	8.3
Liver	1	4.2
Lungs	2	8.3
No Metatasis	9	37.5
Total	**24**	**100.0**

Twelve patients (50%) received radiation to the primary disease or the tumour bed while 9 (37.5%) received radiation to the metastatic sites only. Three patients (12.5%) received treatments to both the primary and the metastatic sites.

All the 15 patients with metastases received adjuvant chemotherapy.

OUTCOME AND FOLLOW-UP

Ten patients (about 42%) were lost to follow up within the first year of treatment. 6 patients (25%) were referred for palliative care as their disease progressed while 1 patient (about 4%) was reported dead. Three patients (12%) presented with recurrence within the same one-year period post treatment. Two were local recurrences, while the other one presented with distant metastases. The other four patients (17%) were free of disease at one year review.

DISCUSSION

Renal cell carcinoma is a rare malignancy in Nigeria. Though it is more common among the blacks in North America, the overall incidence in the Americans is much higher than in Africans and the Asia. Figures from ASCO in 2011 showed that it accounts for over 50,000 new cases in the USA and 15,000 cases in Germany each year [17]. Figures among the African population varies widely even within the same geographical region. In a 1985 series by Lawani et al working in Nigeria renal cell carcinoma accounts for 21% of urogenital tumours seen by them [18]. This is a bit high compared with only 10.4% by Klufio et al from Ghana [8]. Some other studies done in Lagos by Tijani *et. al* in 2012 showed that it accounted for only 3.7% of all urogenital malignancies [9]. The reason for this still remains unclear and different theories have been postulated. One of them is that since many patients in our society present late and are not fit for surgery, they might have escaped tissue diagnosis alltogether [9].

In this study only 24 cases were seen in our department between 1987 and 2011. This confirms the fact that renal cell carcinoma in our environment is rare. In a 47 year study by Odubanjo et al between 1960 and 2007, only 159 cases of renal cell carcinoma were seen [19]. Similarly, in a ten year study by Badmus et al in Ife only 18 cases of malignant adult renal cell tumours were seen with renal cell carcinoma accounting for the majority of cases [20].

In this study, renal cell carcinoma was more common in females than in males (M: F ratio of 1:1.7). This is contrary to reports in most literature which indicate a male preponderance [5]. Studies done in Benin by Olu-Edo et al showed a slight male preponderance of 1.2:1 [10] and studies by Aghaji et al in Enugu showed a M:F ratio of 3.3:1. However, our findings correlate with some studies done in our immediate environment. Studies done by K.H. Tijani et al in Lagos showed a M: F ratio of 1:1.7. The peak age of incidence in this study was in the 5th decade with a mean age of 50.4 years. This is also similar to findings in our environment but in contrast to reports from literature for Caucasians, this figure is one decade earlier [4]. It therefore appears that renal cell carcinoma occurs in a much younger age group in this environment. The explanation for this remains unclear although a school of thought is that because the average life expectancy is about 48 years, many people do not live long enough to develop the disease

[9] therefore giving an apparent shorter median age of presentation.

The left kidney was the commonest side affected accounting for 52.4% of cases while the right kidney accounted for 47.6%. This is in contrast to a study done in Ibadan by Odubanjo et al where the right kidney was more commonly affected (58.6%) [19]. However, studies in Ife by Badmus et al show that the left side was more affected than the right (44.4%:55.5%; R: L) [20].

In this study, 50% of patients presented with hematuria, 37.5% with loin pain and 25% with flank mass, while the classic triad was seen in only 12.5%. This correlates with literature from developed countries where hematuria is the commonest symptom and the classic triad accounts for less than 10% of patients presenting symptoms [21]. It however contrasts some literature in our environment. In a study by Tijani et al in March 2012 hematuria only accounted for 36% of patients' complaints and loin pain and mass were twice as common [9]. Similarly, a 10 year study by Badmus et al in 2008 found loin pain and mass more common [20].

The commonest histological type of RCC observed in this study was clear cell carcinoma followed by papillary RCC (12.5%). This correlates with previous studies done in the USA where it accounts for about 75-80% of all RCC [22]. This also correlates with studies done by Tijani et. al. in Lagos where clear cell carcinoma accounted for 60% of cases seen [9].

Whereas most patients in developed countries are diagnosed early due to the increasing use of medical imaging for other diseases, many patients in this study presented with Robson's stage 4 (62.5%). This is similar to findings in our environment where many people present to several quacks and medicine men before presenting to a specialist [18, 19, 20]. The commonest site of metastases was the spine (29.2%), followed by bone (12.5%), lungs (8.3%) and liver (4.2%). This is different from Caucasian literature where the commonest site of metastases is the lungs (75%) followed by soft tissue (36%) and bone (20%) [23].

Renal cell carcinoma is relatively resistant to chemoradiation therapy and the mainstay of treatment still remains surgery. In this study, 67% of all patients had surgery; 58% had radical nephrectomy while 9% of the patients had unresectable tumours at surgery. No patient had an ablative procedure or partial nephrectomy. This might be attributed to the late presentation of most of the patients.

All patients had radiotherapy. About 50% had radiotherapy to the primary site or tumour bed while 37.5% of the patients had radiotherapy to the metastatic site only. About 12.5% of patients in this study had radiotherapy to both sites. All patients with metastatic disease received some form of systemic therapy with chemotherapy or hormonal therapy. Most chemotherapy given was Adriamycin based with only 2 patients receiving Gemcitabine based chemotherapy. The most common form of hormonal therapy given was progesterone.

Renal cell carcinoma still remains a fatal disease and even developed countries still record a high death toll because of its aggressive growth pattern, high rate of early metastases and lack of curative therapy in advanced cases [24]. It is said to be the 7th leading cause of death in the USA. Other studies also show that since 1971 there has been a 2 fold increase in mortality from renal cell carcinoma.

Treatment outcome and follow-up were very poor in this study. 42% of patients were lost to follow-up, 25% referred for palliative care as their disease progressed, 12% of the patients presented with recurrence within the first year of follow-up and 4% of patients were reported dead. This is not surprising and it reflects the lack of good follow-up support in our environment and the late stage of presentation of many of the patients which is the most important prognostic factor. Studies have shown that the 5 year survival rate for stage 4 disease is 4.6% and median survival rate for patients with metastatic disease is only 1.1 years [25]. Since many of the patients presented with metastatic disease (62.5%), it might be safe to assume that the majority of patients in this study might actually be dead.

CONCLUSION

Renal cell carcinoma is quite rare in our environment and often present late. Hematuria remains a leading symptom and only a small percentage of the patients will present with the classic triad. The physicians working in this environment therefore requires to be vigilant especially as hematuria of renal cell carcinoma might simply be confused with other common ailments like shcistosomiasis. The health

workers therefore need to have high index of suspicion while dealing with a patient with hematuria.

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