PATTERN OF PRESENTATION OF RENAL CELL CARCINOMA AT INSTITUTE OF KIDNEY DISEASES, PESHAWAR

Muhammad Naeem[1], Muhammad Kamran Khan[2], Hazrat Ullah[3], Muhammad Imran Khan[4], Izhar Ahmad[5], Alamgir Khan[6]

[1-6] Department Of Urology and Renal Transplantation Institute of Kidney Diseases Hayatabad Medical Complex Peshawar - Pakistan.

Address for correspondence:
Dr. Muhammad Naeem
Assistant Professor,
Department of Urology and Renal Transplantation,
Institute of Kidney Diseases,
Hayatabad Medical Complex
Peshawar-Pakistan.
E-mail: mnaeem04@yahoo.com

Date Received:
February 05, 2014
Date Revised:
June 29, 2014
Date Accepted:
June 30, 2014

ABSTRACT

Objective: To study the pattern of presentation of patients with renal cell carcinoma.

Methodology: This descriptive study was conducted at Institute of Kidney Diseases, Hayatabad Medical Complex Peshawar-Pakistan from January to December 2012. All patients who were diagnosed as renal masses on ultrasound were admitted. Detailed history and physical examination was performed on all patients. Relevant investigations were done on all patients.

Results: A total of 65 patients with renal cell carcinoma were included in the study. Patients presented with flank pain (n=30, 46%); hematuria (n=14, 22%); flank mass (n=2, 3%); both hematuria and flank pain (n=3, 5%); incidental tumors (n=10, 15%); and with metastasis (n=6, 9%). The tumors were located on right side in 39 (60%) cases and 26 (40%) on left side with 80% of the tumors involving the upper pole of the kidney. Twenty six patients (40%) were cigarettes smokers. No patient was found to have positive family history of renal cell carcinoma or any other cancer in the close family. Fifty nine patients with renal tumors underwent radical nephrectomy and histopathology was done of every specimen. In six patients of renal tumor with metastasis, needle biopsy was taken. The histopathology of the specimen showed that 61 (94%) were clear cell type and 4 (6%) were papillary cell carcinoma.

Conclusion: Renal cell carcinoma presents with a variety of symptoms. It can also present incidentally during investigation for non-specific symptoms. Ultrasonography is encouraged for nonspecific abdominal symptoms to detect renal cell carcinoma at earlier stage.

Key Words: Renal cell carcinoma, Hematuria, Flank pain, Flank mass, Incidental tumors, Metastasis.

This article may be cited as: **Naeem M, Khan MK, Ullah H, Khan MI, Ahmad I, Khan A. Pattern of presentation of renal cell carcinoma at institute of kidney diseases, Peshawar. J Postgrad Med Inst 2014; 28(3):292-6.**

INTRODUCTION

Renal cell carcinoma (RCC) represents 2-3% of all cancers[1]. Renal cell carcinoma is the commonest solid lesion within the kidney and represents 90% of all kidney malignancy[2]. There is a 1.5:1 predominance of men over women, with peak incidence occurring between 60 and 70 years of age[3-7]. Risk factors include lifestyle factors such as smoking, obesity. Patients who have a first-degree relative with kidney cancer are also associated with an increased risk of RCC[8, 9].

Many renal masses are asymptomatic and non-palpable until the late stages of the disease[10]. Currently, more than 50% of RCCs are detected incidentally by using imaging to investigate a variety of non-specific symptom complexes[11-13]. The classic triad of flank pain, gross hematuria, and palpable abdominal mass constitute only 6-10% cases[14, 15]. A few patients present with symptoms due to metastatic disease, such as bone pain or persistent cough[16].

The most commonly assessed laboratory parameters are serum creatinine, glomerular filtration rate, haemoglobin, erythrocyte sedimentation rate, alkaline phosphatase, lactate dehydrogenase (LDH), and serum corrected calcium[17, 18]. Most renal tumors are diagnosed by abdominal ultrasound or CT performed for various reasons. Imaging must be performed both before and after administration of intravenous contrast material to demonstrate enhancement. A change of 20 HU or greater is a strong evidence of enhancement[19]. There

is a consensus that most bone and brain metastases are symptomatic at diagnosis so that a routine bone or brain CT scan is not generally indicated [20, 21]. However, if indicated by clinical or laboratory signs and symptoms, other diagnostic procedures may be used, such as a bone scan, brain CT or MRI[22, 23].

Renal cell cancer is treatable disease if it is diagnosed in early stage (T1, T2). Most of these patients are non-symptomatic in early stage of the disease. These patients can only be diagnosed by imaging like ultrasound which is easily accessible, every where available, and cheap also. If the ultrasound is done on every patient presenting with specific and non specific symptoms in urology outpatient department, we can catch the Renal Cell Carcinoma in early stages (T1, T2). This study was thus conducted to report pattern of presentation of renal cell carcinoma at institute of kidney diseases, Peshawar - Pakistan.

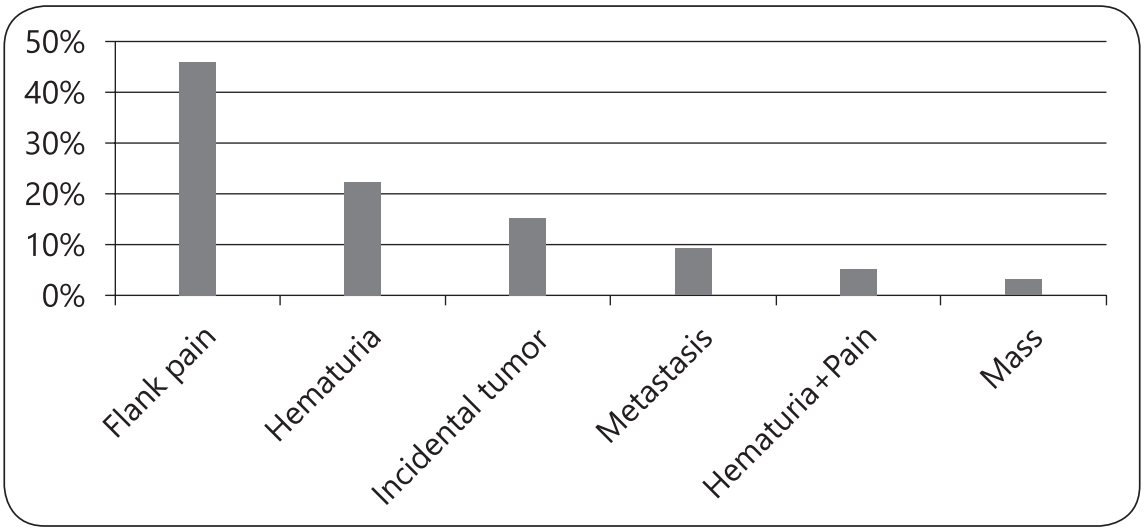
METHODOLOGY

This descriptive study was conducted at institute of kidney diseases Hayatabad Medical Complex Peshawar from January to December 2012. All patients who were included in the study presented to Out Patient Department or Emergency department of Institute of Kidney Diseases with flank pain, hematuria and renal mass. These were further investigated with routine laboratory investigation and imaging. The patients who were diagnosed as having renal tumors were included in the study. The data collection was done through consecutive sampling technique. Ultrasounds were done on all patients in the Out Patient Department. All patients with renal masses were admitted in the urology ward. Detailed history including symptoms, smoking history, family history and occupational history was taken and physical examination was performed on all patients. Investigations including urine analysis, complete blood counts, renal function tests, alkaline phosphatase, Lactate Dehydrogenase, serum electrolytes including serum calcium, x-ray chest and computerized tomography with intravenous contrast were done on all patients. After preoperative preparation, 59 patients with renal tumors underwent radical nephrectomy and excision biopsy of each was sent for histopathology. All these patients underwent uneventful surgery. In 6 patients who presented with metastatic tumors which were non operable had only biopsy done to get the histopathology and were referred to oncologist for further treatment. All the data was collected on a predesigned proforma.

RESULTS

In our study, 65 patients were identified as having renal masses. This included 60 male (93%) and 5 female (7%) patients. The mean age of the sample was 49.2±20 years. Most of our patients were in their 5th decade of life. Most patients presented with flank pain (n=30, 46%), followed by hematuria (n=14, 22%) [Figure 1]. Only 10 (15%) patients were identified as having incidental tumors and 6 (9%) patients presented with metastasis. The tumors were located on right side in 39 (60%) cases and left side in 26 (40%) cases, with 52 (80%) tumors involving the upper pole and 13 (20%) tumors involving the lower pole of the kidney on computerized tomography. Among them 26 (40 %) patients had positive history of cigarettes smoking. No patients were found to have positive family history of renal cell carcinoma or any other cancer in the family. All the tu-

Figure 1: Presentation fo renal tumor



mors came out to be renal cell carcinoma, with 61 (94%) patients diagnosed as clear cell type and 4 (6%) patients as papillary cell carcinoma.

DISCUSSION

Renal cell carcinoma is a common urological malignancy presenting with variety of symptoms like hematuria (50-60%), flank pain (40%), palpable mass (30%) and both hematuria and flank pain (in less than 10% cases) as reported by Motzer et al[24]. According to Greenberg et al, Renal cell carcinoma presents with hematuria (40%), flank pain (40%), palpable mass (25%), weight loss (33%), fever (20%), Hypertension (20%), metastasis (30%) and in 10% cases as classic triad of haematuria, flank pain and flank mass[25]. In our study the renal mass presentation was flank pain (46%), hematuria (22%), flank mass (3%), (hematuria and flank pain) 5% incidental tumors 15%, and metastasis (9%). It can present with Para neoplastic manifestations including hypercalcemia, polycythemia, hepatic dysfunction and amyloidosis in 20% of cases[24, 26-28]. Renal cell carcinoma can also present with atypical symptoms like hoarseness and calverial metastasis[29, 30], cardiac metastasis[31], monoarthritis[32], pancreatitis[33], life threatening poly neuropathy[34], polymyalgia rheumatica[35] and gastrointestinal bleeding[36]. Hypercalcemia is the most common paraneoplastic complication of renal cell carcinoma, and approximately 17% of all patients with renal cell carcinoma develop hypercalcemia during the course of their disease[37-39]. Of patients with known malignancy who develop hypercalcemia, the most common malignancies are of lung and kidney[40, 41]. It can present with loco regional and distant metastasis in up to 25% of cases. In our study we found 9% patients presented with metastasis with raised alkaline phosphatase and LDH.

Symptomatic presentation correlates with aggressive histology and advanced disease. The mode of presentation can independently predict an adverse patient outcome. Indicators of symptomatic presentations include flank pain, flank mass, varicocele, constitutional symptoms. Para neoplastic syndromes and bone pain are related to metastatic disease[42]. Preoperative clinical variables may be used instead of the pathologic stage to determine the risk of recurrence[43]. In our study we also found that the symptomatic patients like pain, hematuria and associated paraneoplastic syndrome patients were of high stage tumor patients.

Today, most tumors are diagnosed incidentally[44]. Due to increased use of noninvasive radiological modalities like ultrasound and computerized tomography, there is increased frequency of detecting incidental renal cell carcinoma accounting of 25-40% cases in developed countries. The incidental tumors are usually smaller in size and are of lower stage (T1, T2) as compared to symptomatic tumors and are more amenable to nephron sparing surgery with less postoperative morbidity and better survival outcome. In our study the frequency of incidental renal tumors were (15%) which were detected through ultrasonography and CT scan advised for non specific complaints.

Our results do not match the presentation pattern of renal cell carcinoma seen in other studies. Most of our patients were in the 5th decade although patients in their sixties and seventies with renal cell carcinoma were also seen. Patients in our study are younger as compared to the other studies[24]. There is very low incidence of incidental tumors in this study. Most of our patients were symptomatic and flank pain was the most common presenting symptom as opposed to Greenberg et al, where hematuria was the most common presenting complaint[25]. Reasons for these discrepancies may be due to that most of our patients were referred patients. Because of low level of education and lack of health awareness among the people in this region they usually ignore the warning signs like an episode of hematuria and present late to the hospital after they develop other symptoms like flank pain. Another reason for low number of incidental tumors in our study may have been the non availability of expert sonologist and radiological facilities in our peripheral catchment areas for our tertiary care kidney center. The male to female ratio for the renal cell carcinoma is 1.5:1[3] but in our study this ratio is 10:1. This may be because of less number of female patients presenting to the hospital because of cultural trends and lack of health awareness amongst the females in this region.

CONCLUSION

Renal cell carcinoma presents with a variety of symptoms like flank pain, hematuria and renal mass. It can also present incidentally during the investigation for non-specific symptoms. Symptomatic tumors are usually at advanced stage whereas the incidental tumors are smaller and of lower stage (T1, T2). In our study, relatively younger population was noted to have RCC. We therefore recommend that more use of Ultrasonography in non specific abdominal complaints should be encouraged so that we may be able to start picking up incidental early stage renal tumors.

REFERENCES

1. European Network of Cancer Registries. Eurocim version 4.0. European incidence database V2.3, 730 entity dictionary. Lyon: European Network of Cancer Registries; 2001.
2. Kovacs G, Akhtar M, Beckwith BJ, Bugert P, Cooper CS,

Delahunt B, et al. The Heidelberg classification of renal cell tumours. J Pathol 1997;183:131-3.

3. Lipworth L, Tarone RE, McLaughlin JK. The epidemiology of renal cell carcinoma. J Urol 2006;176:2353-8.

4. International Agency for Research on Cancer (IARC). WHO IARC monographs evaluation of carcinogenic risks to humans. Lyon: IARC; 2004.

5. Bergstrom A, Hsieh CC, Lindblad P, Lu CM, Cook NR, Wolk A. Obesity and renal cell cancer--a quantitative review. Br J Cancer 2001;85:984-90.

6. Pischon T, Lahmann PH, Boeing H, Tjønneland A, Halkjaer J, Overvad K, et al. Body size and risk of renal cell carcinoma in the European Prospective Investigation into Cancer and Nutrition (EPIC). Int J Cancer 2006;118:728-38.

7. Weikert S, Boeing H, Pischon T, Weikert C, Olsen A, Tjonneland A, et al. Blood pressure and risk of renal cell carcinoma in the European prospective investigation into cancer and nutrition. Am J Epidemiol 2008;167:438-46.

8. Clague J, Lin J, Cassidy A, Matin S, Tannir NM, Tamboli P, et al. Family history and risk of renal cell carcinoma: results from a case-control study and systematic meta-analysis. Cancer Epidemiol Biomarkers Prev 2009 ;18:801-7.

9. Gudbjartsson T, Jónasdóttir TJ, Thoroddsen A, Einarsson GV, Jonsdottir GM, Kristjansson K, et al. A population-based familial aggregation analysisindicates genetic contribution in a majority of renal cell carcinomas. Int J Cancer 2002;100:476-9.

10. Novick AC, Bukowski RM, Campbell SC. Renal tumours. In: Wein AJ, Kavoussi LR, Novick AC, Partin AV, Peters CA, editors. Campbell-Walsh urology. Philadelphia: WB Saunders; 2007. p. 1565-638.

11. Kutikov A, Fossett LK, Ramchandani P, Tomaszewski JE, Siegelman ES, Banner MP, et al. Incidence of benign pathologic findings at partial nephrectomy for solitary renal mass presumed to be renal cell carcinoma on preoperative imaging. Urology 2006;68:737-40.

12. Remzi M, Ozsoy M, Klingler HC, Susani M, Waldert M, Seitz C, et al. Are small renal tumors harmless? Analysis of histopathological features according to tumors 4 cm or less in diameter. J Urol 2006;176:896-9.

13. Kane CJ, Mallin K, Ritchey J, Cooperberg MR, Carroll PR. Renal cell cancer stage migration: analysis of the National Cancer Data Base. Cancer 2008;113:78-83.

14. Lee CT, Katz J, Fearn PA, Russo P. Mode of presentation of renal cell carcinoma provides prognostic information. Urol Oncol 2002;7:135-40.

15. Patard JJ, Leray E, Rodriguez A, Rioux-Leclercq N, Guillé F, Lobel B. Correlation between symptom graduation, tumor characteristic sand survival in renal cell carcinoma. Eur Urol 2003;44:226-32.

16. Kim HL, Belldegrun AS, Freitas DG, Bui MH, Han KR, Dorey FJ, et al. Paraneoplastic signs and symptoms of renal cell carcinoma: implications for prognosis. J Urol 2003;170:1742-6.

17. Sufrin G, Chasan S, Golio A, Murphy GP. Paraneoplastic and serologic syndromes of renal adenocarcinoma. Semin Urol 1989;7:158-71.

18. Motzer RJ, Bacik J, Murphy BA, Russo P, Mazumdar M. Interferon-alfa as a comparative treatment for clinical trials of new therapies against advanced renal cell carcinoma. J Clin Oncol 2002;20:289-96.

19. Israel GM, Bosniak MA. Pitfalls in renal mass evaluation and how to avoid them. Radiographics 2008;28:325-38.

20. Kabala JE, Gillatt DA, Persad RA, Penry JB, Gingell JC, Chadwick D. Magnetic resonance imaging in the staging of renal cellcarcinoma. Br J Radiol 1991;64:683-9.

21. Gupta NP, Ansari MS, Khaitan A, Sivaramakrishna MS, Hemal AK, Dogra PN, et al. Impact of imaging and thrombus level in management of renalcell carcinoma extending to veins. Urol Int 2004;72:129-34.

22. Hendriksson C, Haraldsson G, Aldenborg F, Lindberg S, Pettersson S. Skeletal metastases in 102 patients evaluated before surgery for renal cell carcinoma. Scand J Urol Nephrol 1992;26:363-6.

23. Seaman E, Goluboff ET, Ross S, Sawczuk IS. Association of radionuclide bone scan and serum alkaline phosphates in patients with metastatic renal cell carcinoma. Urology 1996;48:692-5.

24. Motzer R, Bander N, Nanus D. Renal-cell carcinoma. N Engl J Med 1996;335:865.

25. Greenberg RE, Cooper J, Krigel RL, Richter RM, Kessler H, Petersen RO. Hoarseness: a unique clinical presentation of renal cell carcinoma. Urology 1992;40:159-61.

26. Cohen H, McGovern F. Renal cell carcinoma. N Engl J Med 2005;353:2477-90.

27. Gold P, Fefer A, Thompson J. Paraneoplastic manifestations of renal cell carcinoma. Semin Urol Oncol 1996;14:216-22.

28. Ziya K, Can O. Clinical aspects of renal cell carcinoma. EAU Update Series 2003;1:89-196.

29. Luciani Lorezo L, Castari Roberto, Tallarigo Carlo. Incidental renalcell carcinoma- age and stage characterization and clinical implications: a study of 1092 patients (1982-1997). Urology 2000;56:58-63.

30. Bussani R, De-giorgio F, Abbate A, Silvestri F. Cardiac metastasis. J Clin Pathol 2007;60:2734.

31. Chakravarty KK, Webley M. Monarthritis: an unusual presentation of renal cell carcinoma. Ann Rheum Dis 1992;51:681-2.

32. Nabi G, Chowdhary A. Renal cell carcinoma presenting as acute pancreatitis. Urol Int 2002;68:202-3.

33. Roy M, May E, Jabbari B. Life-threatening polyneuropathy heraldingrenal cell carcinoma. Mil Med 2002:167:986-9.

34. Sidhom O, Basalaevm, Sigal L. Renal cell carcinoma presenting aspolymyalgia rheumatica. Resolution after nephrectomy. Arch InternMed 1993;153:2043-5.

35. Klasuner J, Rozin R, Lelcuck S, Ilie B. Renal cell carcinoma presenting as acute pancreatitis and GI bleeding. J Surg Oncol 1983;22:265-8.

36. Chasan S, Pothel L, Huben R. Management and prognostic significance of hypocalcaemia in renal cell carcinoma. Urology 1989;33:167-70.

37. Fahn H, Lee Y, Chen M, Huang J, Chen K, Chang L. The incidence and prognostic significance of humoralhypercalcemia in renal cell carcinoma. J Urol. 1991;145:248-50.

38. Papworth K, Grankvist K, Ljungberg B, Rasmuson T. Parathyroid hormone-related protein and serum calcium in patient with renal cellcarcinoma. Tumour Biol 2005;2:201-6.

39. Lee CT, Yang CC, Lam KK, Kung CT, Tsai CJ, Chen HC. Hypercalcemia in the emergency department. Am J Med Sci 2006;331:119-23.

40. Vassilopoulou-Sellin R, Newman B, Taylor S, Guinee V. Incidence of hypercalcemia in patients with malignancy referred to a comprehensive cancer center. Cancer 1993;71:1309-12.

41. Yaycioglu O, Roberts WW, Chan T, Epstein JI, Marshall FF, Kavoussi LR. Prognostic assessment non metastatic renal cell carcinoma: a clinical lybased model. Urology 2001;58:141-5.

42. Ficarra V, Prayer-Galetti T, Novella G, Bratti E, Maffei N, Dal Bianco M, et al. Incidental detection beyond pathological factors as prognostic predictor of renal cell carcinoma. Eur Urol 2003;43:663-9.

43. Lee Cheryl T, Katz Jared, Fearn Paul A, Russo Paul. Mode of presentation of renal cell carcinoma: provides prognostic information. Urol Oncol 2000;7:135-40.

44. Anmar N, Jason J, Rekha G, David B, Richard N. Multilocular cystic renal cell carcinoma: a series of12 cases and a review of literature. Urology 2002;60:421-7.

CONTRIBUTORS

MN planned the study, did data analysis and wrote the manuscript. MKK, HU, MIK, IA and AK helped in data collection and manuscript writing. All authors contributed significantly to the final manuscript.