Scholars Journal of Applied Medical Sciences (SJAMS) **ISSN 2320-6691 (Online)**
Sch. J. App. Med. Sci., 2016; 4(3A):669-673 **ISSN 2347-954X (Print)**
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(An International Publisher for Academic and Scientific Resources)
www.saspublishers.com DOI: 10.36347/sjams.2016.v04i03.008

Original Research Article

Incidence of Renal Cell Carcinoma among Patients with Kidney Tumours with Reference to the Expression of Ck7 & Vimentin

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Abstract: Kidney tumour may be benign or malignant, exact diagnosis of which is necessary for proper treatment. Immunohistochemistry may be needed for correct diagnosis of few discordant cases. In methodology the study was done on 45 patients with kidney tumour who underwent radical nephrectomy. Histopathological examination and immunohistochemistry with CK7 and Vimentin was done on their nephrectomy specimen. In results Among 45 cases, 39 were renal cell carcinoma, three angiomyolipoma, two oncocytoma and one cystic nephroma. Clear cell renal cell carcinoma was the commonest tumor with 72% cases, followed by papillary RCC 21% and chromophobe RCC 5%. CK7 was positive in 14.2% clear cell RCC, 87.5% papillary RCC and 100% chromophobe RCC and was negative in oncocytoma. Vimentin was positive in 100% clear cell RCC and papillary RCC. It was negative for oncocytoma and chromophobe RCC. P-values for both the cases are significant. The concusion was RCC is the most common malignant kidney tumour among which clear cell carcinoma is the commonest subtype. Histopathological diagnosis is sufficient but CK7 and Vimentin can be used as adjunct or to conclude few discordant cases.
Keywords: Renal cell carcinoma, Cytokeratin7, Vimentin.

INTRODUCTION:

Kidney tumours benign or malignant have their own characteristic features, knowledge of which is necessary for proper treatment. Kidney tumours are malignant in more than 80% of cases among which 90% malignancies are Renal Cell Carcinoma (RCC) [1]. RCC is third most common cancer of genito-urinary tract and most lethal urologic cancer, accounting for approximately two percent of all cancer deaths [2]. Approximately one third of the patient with RCC present with metastasis and many patients develop metastasis after surgical resection. Traditionally RCC is known to be resistant to chemotherapy. However, there has been tremendous development in effective molecular targeted therapies in past few years for specific types of RCC with well defined histology and molecular abnormalities. Therefore, accurate histological diagnosis and classification is increasingly important [3].

Clear cell RCC is overwhelmingly the most common type of renal cancer accounting for 70% of cases [4]. Papillary RCC comprises approximately 10% of RCC in large surgical series [5]. Chromophobe RCC is one of its rare subtypes, with an overall incidence of 5% [6]. Histological diagnosis of renal neoplasm is usually straight forward by routine light microscopy. However, immune markers may be essential in several contexts, including differentiating renal and non-renal neoplasm, sub-typing of renal cell carcinoma and diagnosing rare types of renal neoplasm of metastatic RCC in small biopsy specimen [7].

CK7 is positive in most papillary RCC, collecting duct RCC, urothelial carcinoma and Chromophobe carcinoma and negative for clear cell RCC so it can be helpful in differentiating: 1) Clear Cell RCC and Clear Cell Papillary RCC, 2) Clear Cell RCC and Chromophobe RCC and 3) Chromophobe RCC eosinophilic variant & oncocytoma [8].

Vimentin, as a broad mesenchymal marker is expressed in 87-100% of clear cell RCC and papillary RCC, whereas it is negative in chromophobe RCC and

oncocytoma. So it is also a helpful marker for differentiating clear cell RCC and chromophobe RCC for a renal neoplasm with eosinophilic cells [9].

MATERIALS & METHODS:

It was a prospective and observational study. The study was done on 45 patients who attended the urology department of a tertiary care hospital with radiologically evident kidney tumour and underwent radical nephrectomy from January 2014 to June 2015. We selected all the patients having age more than 12 years. Patients with metastasis to kidney were excluded from our study.

The data regarding patient particulars, history, complaints and radiological reports were collected with the help of a proforma. Then patients underwent nephrectomy. The specimens of nephrectomy were collected. Histopathology examinations and immunohistochemistry were done in the Department of Pathology. Histopathology blocks and slides were prepared following standard method. H&E staining was done and examined under light microscope. Immunohistochemistry was done with immune markers CK7 and Vimentin and their expression were also studied under light microscope. Urothelial tumour was taken as positive control for CK7 and leiomyoma was taken as positive control for Vimentin.

RESULTS:

In this study a total of 45 cases of kidney tumour were selected for histopathological examination and immunohistochemical study. Age of patients ranged from 18 to 80 years, the average being 48.7 years (arithmetic mean). The peak incidence was in the fourth and fifth decades and the male to female ratio of 3:2.

Among 45 patients, 39 patients had histopathologically confirmed renal cell carcinoma and only six patients had benign tumours. Highest occurrence was that of Clear Cell RCC accounting for 28 cases followed by Papillary RCC accounting for eight cases, Chromophobe RCC accounting for two cases and Multilocular Clear Cell RCC accounting for one case. Among the benign tumours there were three cases of Angiomyolipoma, two cases of Oncocytoma and one Cystic nephroma. (Fig.1).Two cases of Clear Cell RCCs showed extensive sarcomatoid changes with relatively poorly identified clear cell areas. One Papillary RCC also exhibited sarcomatoid changes at places. One Oncocytoma showed few areas resembling hybrid tumours.

According to Furhmann nuclear grading, 3% of the tumors were grade 1, 49% grade 2, 32% grade 3 and 16% grade 4; among 37 cases of Clear Cell RCC and Papillary RCC. Multilocular Cystic Clear Cell RCC was the only tumor showing grade 1 nuclear features.

The IHC study was done for CK7 and Vimentin and the positivity was recorded with respect to positive and negative control mentioned previously. Then stastical analysis was done to find the association of the immuno expression of CK7 and Vimentin with different types of renal cell carcinoma.

CK7 was positive in 14.2% Clear Cell RCC, 87.5% Papillary RCC and 100% Chromophobe RCC. Oncocytoma was negative for CK7. P-value was 0.00014 which is significant (Table1). Vimentin was positive in 100% Clear Cell RCC and Papillary RCC. It was negative for Oncocytoma and Chromophobe RCC. Vimentin showed strong positivity in those cases having sarcomatoid changes. P-value is <0.00001 i.e. also significant (Table2).

Table 1: Immuno-expression of CK7 in different types of RCC and Oncocytoma

CK7	CRCC	PRCC	ChRCC	Oncocytoma	Total	Chi-square	P-value
Positive	4	7	2	0	13	20.3826	0.000141
Negative	24	1	0	2	27		
Total	28	8	2	2	40		

Table 2: Immuno-expression of Vimentin in different types of RCC and Oncocytoma

Vimentin	CRCC	PRCC	ChRCC	Oncocytoma	Total	Chi-square	P-value
Positive	28	8	0	0	36	40	<0.00001
Negative	0	0	2	2	4		
Total	28	8	2	2	40		

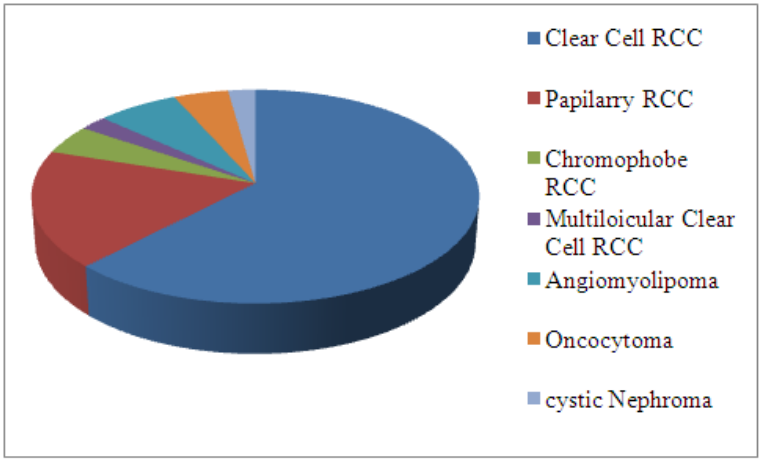

Fig-1: Pie chart showing the variants of Kidney Tumor

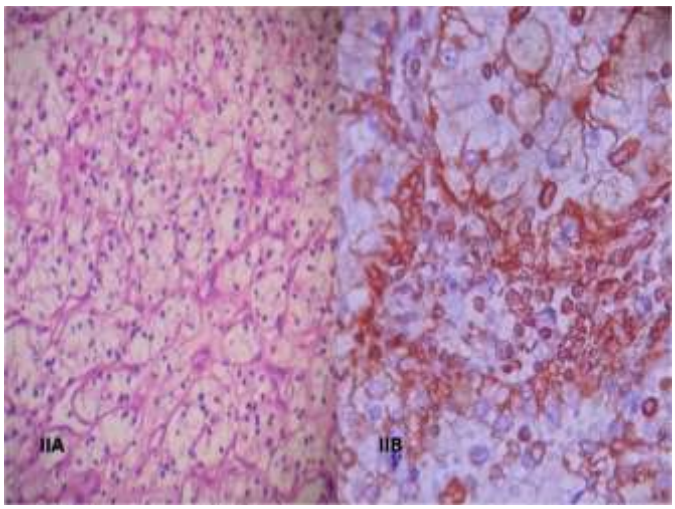

Fig-2: Clear cell RCC: H&E (A), Positive Vimentin expression (B) (100X)

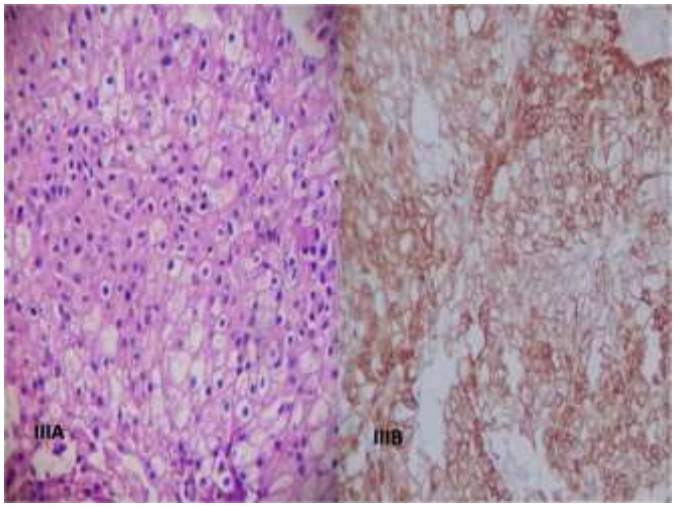

Fig-3: Chromophobe RCC: H&E (A), Positive CK7 expression (B) (100X)

DISCUSSION

Adult renal neoplasms are a heterogeneous group with varying prognosis and outcome. Classification of renal cell carcinoma is important for the treatment and prognostic point of view as well as for understanding of histogenesis. Histological assessment remains the mainstay of RCC classification while immunohistochemistry serves as adjuncts to the histologic analysis.

On histopathological examination, we diagnosed 87% renal cell carcinoma among all radiologically evident kidney tumours in our study. Dzelaludin Junuzovic *et al.;* reported 92% renal cell carcinoma in their study [1]. Clear cell renal cell carcinoma was the commonest tumor with 72% cases followed by papillary RCC 20% and chromophobe RCC 5% in our study. Dinesh Pradhan *et al.;* reported 74.8% Clear Cell RCC, 12.2% Papillary RCC, 7.9% Chromophobe RCC [8]. In our study, sarcomatoid changes were noted in three cases, among which the principal morphology was almost completely replaced in two. RCC with sarcomatoid features is not currently recognized as a specific type of renal parenchymal carcinoma by WHO or by other classifications of renal neoplasia published subsequent to the Heidelberg renal tumor consensus meeting of 1996. This is mainly because of the observation that sarcomatoid areas can be found in all histologic subtypes of RCC. Despite this, reporting of sarcomatoid change is recommended as an indicator of a poor prognosis, with potential treatment implications [10].

We got most of the RCC cases among patients in their fourth and fifth decades. Benign tumours were more common in younger age groups. Three cases of angiomyolipoma were less than 40 years of age and all were females, whereas RCC showed a male predominance.

In our study there were 3% grade 1 tumor, 49% grade 2 cases, 32% grade 3 and 16% grade 4 RCC cases among 37 cases of Clear Cell RCC and Papillary RCC among 37 cases of RCC. Chromophobe RCC cases were not graded. Multilocular Cystic Clear Cell RCC was the only tumor showing grade 1 nuclear features.

Aurora Alexa *et al.;* reported CK7 positivity in 42.5% Clear Cell RCC, 87.5% Papillary RCC and 100% Chromophobe RCC [11]. Lorenzo Memeo *et al.;* showed CK7 positivity in 5% Clear Cell RCC, 95% Papillary RCC, 100% Chromophobe RCC and 4% Oncocytoma [12]. Our study also showed almost similar result in case of Papillary RCC and Chromophobe RCC but intermediate result was obtained for Clear Cell RCC Ryan Carr *et al.;* reported Vimentin positivity in 100% Clear Cell RCC and Papillary RCC and 20% Chromophobe RCC. Our study also showed 100% Vimentin positivity in Clear Cell RCC, Papillary RCC and tumours having sarcomatoid changes.

Straightforward histopathological diagnosis by light microscopy was done in almost all cases of our study. However in one case of oncocytoma, showing few areas resembling a hybrid tumour, there was confusion with Chromophobe RCC. Ck7 negativity confirmed the case as Oncocytoma. CK7 and Vimentin in different cases of our study showed significant p-value.

CONCLUSION:

Renal cell carcinoma is the most common malignant kidney tumour among which clear cell carcinoma is the commonest subtype. Renal cell carcinoma is more common in older age groups with male predominance. Sub typing and grading is necessary for prognostication and appropriate therapy. Histopathological examination is sufficient for diagnosis of most of the cases. But an immune marker like CK7 is very helpful to conclude few confusing cases. Though Vimentin shows positive result in more cases, it is not as helpful in differentiating cases having apparently same histopathological features.

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