International Journal of Medical and Pharmaceutical Research

Online ISSN-2958-3683 | Print ISSN-2958-3675
Frequency: Bi-Monthly
Website: https://ijmpr.in/

Original Article

Clear Cell Renal Cell Carcinoma with Osseous Metaplasia: Clinico-Pathological Analysis

Dr Tazeen Jeelani[1], Dr Zafirah[2], Dr Jubran Amain[*3], Dr Aiffa Aiman[4], Dr Rukhsana Akhter[5], Dr Shazieya Akhtar[6], Dr Ghulam Mustafa[7], Dr Narender[8], Dr Mohd Iqbal[9]

[1]Assistant professor, Department of pathology, Sher-i-kashmir institute of medical sciences soura, Srinagar J&K.
[2]Assistant professor, Department of pathology, Sher-i-kashmir institute of medical sciences soura, Srinagar J&K.
[3]Assistant professor, Department of pathology, Govt. Medical college Anantnag J&K.
[4]Associate professor, Department of pathology, Sher-i-kashmir institute of medical sciences soura, Srinagar J&K.
[5]Associate professor, Department of pathology, Sher-i-kashmir institute of medical sciences soura, Srinagar J&K.
[6]Senior resident, Department of pathology, Sher-i-kashmir institute of medical sciences soura, Srinagar J&K.
[7]Senior resident, Department of pathology, Sher-i-kashmir institute of medical sciences soura, Srinagar J&K.
[8]Postgraduate scholar. Department of pathology, Sher-i-kashmir institute of medical sciences soura, Srinagar J&K
[9]professor, Department of pathology, Sher-i-kashmir institute of medical sciences soura, Srinagar J&K.

Corresponding Author:

Dr. Jubran Amain
Assistant professor, Department of pathology, Govt. Medical college Anantnag J&K.

Received: 12-03-2026
Accepted: 05-04-2026
Published: 16-04-2026

ABSTRACT

Introduction: Clear cell renal cell carcinoma (ccRCC) is the most common subtype of renal malignancy, accounting for approximately 70–80 % of all RCC cases. Osseous metaplasia in RCC has been documented in the literature primarily through case reports and small case series. The exact mechanisms underlying osseous metaplasia in ccRCC remain speculative. Proposed hypotheses include: Ischemia and Necrosis, Bone Morphogenetic Proteins and Pre-Existing Calcifications. **Material and methods:** Ten year retrospective data was analysed from the archival section of the department spanning from January 2016 to December 2025. The histopathological spectrum of renal tumours was analysed. Inclusion criteria: All radical, simple and partial nephrectomy specimens were included in the study. **Results**: A total of 988 specimens were received in the department. Out of which 752 were found to have neoplastic etiology. Out of 752 neoplastic cases 608 (80.8%) were that of clear cell RCC. 8 cases of ccRCC showed areas of metaplastic bone formation. Median age was 48.5 years, and mean age was approximately 52 years. All the eight cases had well circumscribed mass, that measured from 1.8 to 5.0 cm in maximum diameter. **Conclusion**: Renal cell carcinoma with osseous metaplasia is a is a rare finding. It has a favourable prognosis with limitation of tumor spread.

Keywords: *RCC, metaplasia, bone morphogenetic protein, calcification.*

INTRODUCTION

Clear cell renal cell carcinoma (ccRCC) is the most common subtype of renal malignancy, accounting for approximately 70–80 % of all RCC cases. Calcification is a known radiologic and histopathologic feature in RCC however, osseous metaplasia, defined as true bone formation in non-skeletal tissue, is an exceedingly rare phenomenon (1). Osseous metaplasia in RCC has been documented in the literature primarily through case reports and small case series. Fewer than 20–30 cases of RCC with bone formation have been described overall (2). Albrecht (1905) described the earliest recorded calcified RCC, although osseous metaplasia was demonstrated later (3). The exact mechanisms underlying osseous metaplasia in ccRCC remain speculative. Proposed hypotheses include:

Ischemia and Necrosis: Local tissue ischemia and necrosis may induce differentiation of stromal cells into osteogenic lineages, leading to bone formation within the tumor (4).

Bone Morphogenetic Proteins (BMPs) : Expression of osteogenic factors such as Bone Morphogenetic Protein-2 (BMP-2) has been suggested as a possible driver of osteoblastic differentiation in tumor stroma.

Pre-Existing Calcifications: Calcified foci are common in RCC; some researchers propose that ossification arises secondarily from extensive calcification and chronic inflammation (5).

MATERIAL AND METHODS:

Study was conducted in the department of pathology sher-i- Kashmir institute of medical sciences. Ten year retrospective data was analysed from the archival section of the department spanning from January 2016 to December 2025. The histopathological spectrum of renal tumours was analysed. Inclusion criteria: All radical, simple and partial nephrectomy specimens were included in the study. Exclusion criteria: Non neoplastic renal lesions were excluded from the study. All the relevant information such as age, clinical features, radiological findings, and tumour markers were analysed along with Gross and microscopic findings, including the histopathological patterns, were reviewed and recorded. 3-5 um thick sections were taken and slides were prepared and Stained with Hematoxylin & Eosin and the cases were reviewed.

RESULTS:

A total of 988 specimens were received in the department during a period of ten years, from January 2016 to December 2025, Out of which 752 were found to have neoplastic etiology. Out of 752 neoplastic cases 608 (80.8%) were that of clear cell RCC. 8 cases of ccRCC showed areas of metaplastic bone formation (fig1&2).

Clinic-pathological findings of all the 8 cases are listed in Table-1.

Table 1. Clinico-pathologic findings

Case No.	Age(yrs)	Sex	Tumor Size (cm)	Fuhrman/WHO Grade	Stage	ESRD
1	48	F	2.5	G1	pT1N0	No
2	68	M	1.8	G1	pT1N0	No
3	42	M	5.0	G1	pT1N0	No
4	48	M	3.0	G1	pT1 Nx	No
5	65	F	2.8	G1	pT1 N0	No
6	44	M	3.0	G2	pT1 N0	No
7	57	M	4.2	G2	pT1 Nx	No
8	49	M	3.5	G2	pT1 Nx	No

ESRD= end stage renal disease, M= male, F=female

Median age was 48.5 years, and mean age was approximately 52 years. All the eight patients had no prior history of renal disease. Three patients had symptoms related to the tumor, while as in five patients tumor was detected incidentally. All the patients, had Computerized Tomography (CT scan) that showed renal lesions.

Three patients had undergone radical nephrectomy and five had partial renal resection. All the eight cases had well circumscribed mass, that measured from 1.8 to 5.0 cm in maximum diameter. In cases where renal vein and adrenal gland was identified were normal and free of tumor. All the patients had T1 disease with WHO nuclear grade 1 on histology.

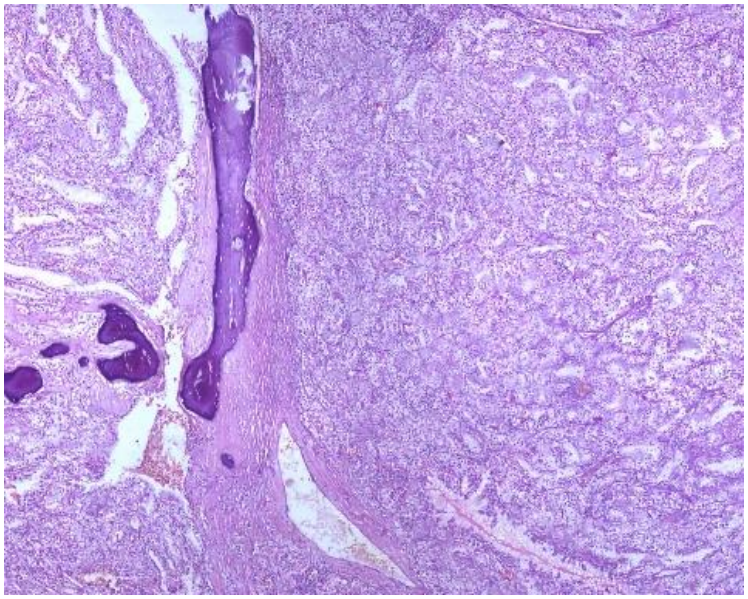

Fig. 1: photomicrograph showing osseous metaplasia in clear cell RCC. (10X H&E)

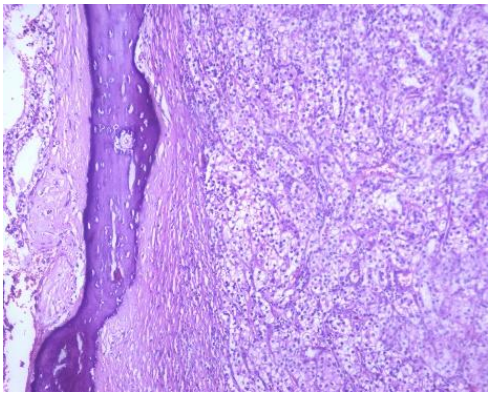

Fig. 2: photomicrograph showing mature bone with osteocytes adjacent to clear cell RCC.

DISCUSSION:

Osseous metaplasia opposed to calcification is a rare finding. It has been demonstrated in several other tumors, including primary and metastatic colorectal carcinomas (6). The pathogenesis of ossification in tumors is not clear. Several hypotheses have been put forward, including the production of bone by tumor cells secondary to ischemia, necrosis or inflammation in the tumor or surrounding tissue, reparative responses in the tumor or surrounding tissues or the ossification of pre-existing mucin or calcification foci (7), proposed explanations involve a response to tissue ischemia and the expression of Bone Morphogenetic Protein 2 (BMP-2), an inducer of osteoblastic differentiation of pluripotential cells, in ossification of RCC . Osseous metaplasia results secondary to this tissue damage. The prognostic significance of osseous metaplasia in RCC is debatable. Some reports show ossification to be a favourable prognostic factor with tumors having a low nuclear grade, low stage and absence of metastatic disease at presentation (8). However, some reports suggest that ossification can also be associated with high grade tumors and poor prognosis. (9). All Our case had a favourable prognosis due to low nuclear grade, early stage and absence of metastasis at presentation. The clinical significance of heterotopic bone features is uncertain. More studies following patient long-term health are needed to determine the relevance of heterotopic bone formation in the setting of RCC (10).

CONCLUSION:

Renal cell carcinoma with osseous metaplasia is a is a rare finding. It has a favourable prognosis with limitation of tumor spread. Overall, the limited number of cases precludes definitive conclusions about the molecular drivers of this process, and it remains a subject of ongoing investigation.

Conflict of interest: On behalf of all authors, the corresponding author states that there is no conflict of interest.

Funding agency: nil

BIBLIOGRAPHY:

1. Mehmet Caglar Cakici , Gözde Kır , Mustafa Kaan Akalın , Asıf Yıldırım. Clear cell renal cell carcinoma with osseous metaplasia: Two extremely rare cases and review of the literature. Arch Esp Urol.2020 Sep;73(7):651-654.
2. Huixing Pan , Deyao Wu , Huaizhang Wang , Yan Pan , Ting Zhang, Jian Zhou. Clear Cell Renal Cell Carcinoma With Extensive Osseous Metaplasia: Report of a Rare Case. Urology 2017 Jul:105:e3-e5. doi: 10.1016/j.urology.2017.02.048. Epub 2017 Mar 22.
3. Albrecht P. Und pathologischenanatomie der malignenhypernephrome. Arch F Klin Chir 1905;77:1072.
4. Oertling E, Peters C, Wood R, Silberstein J, Sholl AB, Falk NK. Clear cell renal cell carcinoma with heterotopic bone formation: a case report and literature review. Case Reports in Clinical Pathology (2018). https://doi.org/10.5430/crcp.v5n2p16.
5. Agarwal S, Bohara S, Jha R, Khurana N, Agarwal PN. Clear cell renal cell carcinoma with osseous metaplasia:Rare case report. J Can Res Ther 2015;11:1039. doi:10.4103/0973-1482.146109.
6. Cribbs RK, Ishaq M, Arnold M, O'Brien J, Lamb J, Frankel WL. Renal Cell Carcinoma with massive osseous metaplasia and bone marrow elements. Ann Diagn Pathol. 1999; 3:294-299.
7. Harish S. Permi. Renal cell carcinoma with osseous metaplasia occurring in a contracted kidney - a rare case report. NUJHS Vol. 3, No.4, December 2013, ISSN 2249-7110.
8. Hartman RJ, Helfand BT, Dalton DP. Clear cell renal cell carcinoma with osseous metaplasia: a case report. Can J Uro 2011; 18:5564-5567.
9. Bielsa. O, J. Loreta, O. Arango, S. Serrano, A. Gilbert-Mas. Bone metaplasia in a case of bilateral renal cell carcinoma. Urol Int 2001; 66:55–56.
10. Estelle Oertling, Cacey Peters, Robert Wood, Jonathan Silberstein, Andrew B. Sholl, Nadja K.Falk. Clear cell renal cell carcinoma with heterotopic bone formation: A case report and literature review. Case Reports in Clinical Pathology 2018; Vol. 5, No. 2: 16-18. DOI:10.5430/crcp.v5n2p16 .