Renal Cell Carcinoma Clear Cell Variant With Chromophobe Differentiation -A Rare Case Presentation

Abstract:

Renal Cell Carcinoma (RCC) is a diverse growth of various histological cell forms, as well as genetic, biological, and behavioral variations, accounting for around 2%-4% of all genitourinary cancers worldwide and having the highest mortality rate. RCC is a rare symptom that occurs from the lower pole of the left kidney. Histopathological testing is critical for diagnosis, staging, and treatment evaluation. As a consequence, proper surgical and pathological correlation is critical for the diagnosis of such an unusually presented RCC. As a result, various RCC variants should be considered for proper diagnosis. We are here presenting a case of woman aged44-yearold, complaining for two months about a lump in her abdomen. Pain in the left lumbar area was noticed, which was progressive and accompanied by hematuria. The post-nephrectomy specimen was sent for histopathological analysis, and RCC was found (Clear Cell variant with chromophobe differentiation). RCC (Clear cell variant with Chromophobe differentiation) is an unusual manifestation that arises from the left kidney's lower pole. In terms of diagnosis, staging, and treatment assessment, histopathological testing is crucial. As a result, for the diagnosis of such an unusually presented RCC, proper surgical and pathological correlation is important. It's critical to acknowledge the presence of this clinical entity, which, though uncommon, may offer yet another reason to pursue surgical or immunological treatment for metastatic renal cancer. The finding will inspire & motivate researchers to pursue immunologic and other disease-related research.

Keywords: CECT, Histopathology, RCC

Introduction:

RCC leads to around 2%-4% of the newly diagnosed adult cancers⁽¹⁾. RCC is the 7thutmostmalignancy in the Western domain, with an ever-increasing frequency^(2,3) and accounting for one-three percent of all malignant visceral neoplasms. RCC is the most deadly malignant urological tumor, with around 40% of patients dying as a result of disease progression. Currently, most RCCs are discovered by chance during imaging examinations, whether for urological or non-urological causes. Men make up the majority of RCC patients, accounting for two-thirds of all cases ⁽⁴⁾.

The typical signs were recognized as pain, abdominal mass, and/or hematuria. Fever, night sweats, weight loss, anemia, and hypercalcemia were all typical systemic symptoms in patients, and any of these symptoms may potentially be part of the clinical syndrome. Also with modern treatment, these characteristics appear to predict a worse outcome. An rise in the occurrence of RCC is because of extensive use of advanced imaging methods for other complaints that result in the discovery of a renal mass, which is commonly referred to as a small renal mass⁽⁵⁾. Due to its rising frequency, RCC has the highest death rate of all genitourinary malignancies. This tumor is heterogeneous, with various histological cell types, as well as

genetic, biochemical, and behavioral differences. We present a case of an uncommon RCC clear cell with chromophobe variant in this report.

Case Presentation:

A 44 year old female presented with the chief complaints of a lump in abdomen for two months. Clinical findings revealed pain in the left flank for 15 days. The pain in the left lumbar region was progressive in nature with hematuria.

CT scan with contrast content is called contrast-enhanced computed tomography (CECT). Contrast material is used during the CT scan, as the name suggests. CECT abdomen was suggestive of a markedly heterogeneous mass in the lower pole of left kidney with areas of necrosis, cystic changes and hemorrhage with adjacent calcifications.

RCC (Clear cell type of Chromophobe differentiation) is a rare symptom that occurs from the lower pole of the left kidney. Histopathological testing is critical for diagnosis, staging, and treatment evaluation. As a consequence, proper surgical and pathological correlation is critical for the diagnosis of such an unusually presented RCC. As a result, various RCC variants should be considered for proper diagnosis.

When staining is positive, immunohistochemistry reports (IHC) are often useful diagnostic tools. However, both positive and negative staining of main immunomarkers are comparatively significant when using IHC to subtype renal cell carcinoma (RCC). The fixative used was formalin, and the research was done on Block Number(s):B/20/8941. It was discovered that without membrane attenuation, the results are negative. CK-7 and Vimentin were used to stain it. When stained for CK-7, the tumor displayed a score of "3+," indicating that it is CK-7 positive. When stained for Vimentin, it revealed a score of "0," indicating that the tumor is Vimentin negative.

The patient underwent nephrectomy without complications and the removed mass was then sent for histological examination (HPE). Histopathological analysis of the postnephrectomy specimen was performed. A globular, brown nephrectomy specimen measuring

20 x 13.5 x 9 cm was found on gross inspection. Heterogeneous areas of necrosis and hemorrhage can be seen in the cut portion.

Fig 1.



Fig 2.



Fig 3.

Two cell populations were noticed, one predominantly with large cells and centrally placed round nuclei with vesicular nucleoli arranged into tubules, clear granular cytoplasm admixed with small sized cells with round nuclei and scanty granular cytoplasm in sheet. There are some golden yellow areas that have been found. Neoplastic cells, well differentiated with nuclear atypia, bizarre nuclei, giant cells, and pale eosinophilic cells with a perinuclear halo organized in solid sheets with intervening blood vessels where it was diagnosed as RCC were seen microscopically (Clear Cell variant with chromophobe differentiation).

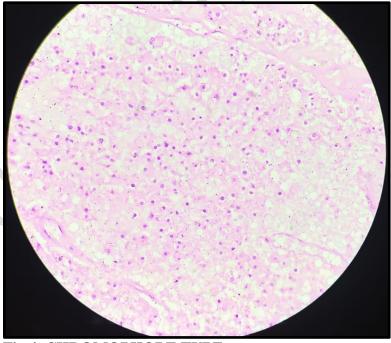


Fig 4. CHROMOPHOBE TYPE

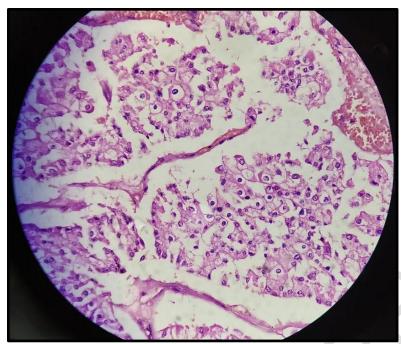


Fig 5. CHROMOPHOBE TYPE

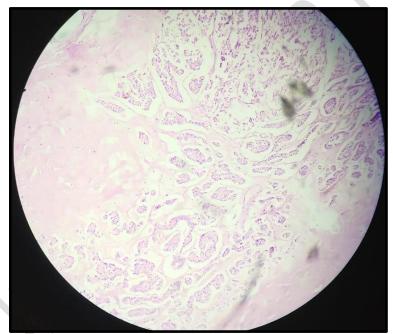


Fig 6. CLEAR CELL TYPE

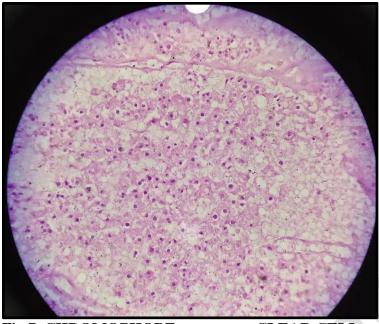


Fig 7. CHROMOPHOBE CLEAR CELL

CLEAR CELL (RIGHT) WITH CHROMOPHOBE DIFFERENTIATION (LEFT)

Discussion:

RCC makes up two percent all the tumours and its prevalence is slowly increasing. It normally appears in late adulthood and males are more likely than females to develop it. (6)

The subjects might patient may experience problems viz. haematuria, pain, or an abdominal mass, as well as systemic signs such as anemia & fever⁽⁷⁾. Patients with RCC can acquire metastatic disease in twenty-thirty percent of cases, and twenty-forty percent of patients who have a nephrectomy for clinically localized illness can develop metastasis.⁽⁸⁾ If the tumors cannot be completely removed, the prognosis is typically poor. In the first three years, relapses occur 85 percent of the time.⁽⁹⁾Numerous studies have been mentioned in the past that describe metastatic renal cancer spontaneously regressing.^(7,10)

Bumpus described the first case of metastatic renal cell cancer spontaneously regressing in 1928.⁽¹⁰⁾ Most of these cases are linked to surgical exclusion of the primary tumor, however relapse can also happen after radiotherapy or embolization of the primary tumor⁽¹¹⁾.

In 1985, the chromophobe variant of RCC was mentioned for the first time ⁽¹²⁾. Unlike conventional RCCs, which have a male preponderance, these are most typically discovered in the sixth decade of life and affect both men and women equally⁽¹³⁾. Almost 90% of ChRCCs are discovered in the early stages of the disease, i.e. stage 1 or 2. Renal vein invasion is also infrequent, occurring in only approximately five percent of cases. In chromophobeRCC, the rate of metastatic illness is lower, around 6-7 percent ⁽¹⁴⁾. In a review of 28 patients, the liver (39%) and lungs (36%) were shown to be the most common metastatic sites for ChRCC, while the lungs (more than 50%) and bones were found to be the most common metastatic sites for RCC (33 percent) ⁽¹⁵⁾. Similar cases were reported by Bhalsod et. al.⁽¹⁶⁾ and Niveditha et. al.⁽¹⁷⁾.

Because of the unusual nature of the occurrence and the wide range of clinical situations under which spontaneous disease regression occurs, there is no way to gain insight into the pathophysiologic process or to identify possible candidates for regression.

Conclusion:

Despite the presence of metastatic disease, chRCC has a better prognosis than pRCC and a prognosis similar to ccRCC, with a median survival of around 29 months compared to 5.5 months in pRCC. (15) The current evidence for the numerous available medications in advanced RCC is summarized here:

- 1 inhibitors of mTOR
- 2 inhibitors of the c-Kit pathway
- 3 inhibitors of tyrosine kinase
- 4 Alpha-interferon.
- 5 Immune checkpoint inhibitors.
- 6 Interleukin-2 (IL-2, Proleukin)

It's critical to acknowledge the presence of this clinical entity, which, though uncommon, may offer yet another reason to pursue surgical or immunological treatment for metastatic renal cancer. The finding will inspire & motivate researchers to pursue immunologic and other disease-related research. Chromophobe carcinoma is a type of RCC that is rather uncommon. We're presenting this instance because it's a rare occurrence. Clinically and histopathologically, the ChRCC is a separate entity. On microscopy, it's typically difficult to tell the difference between oncocytomas and clear cell RCCs. Histopathologists must recognize and identify ChRCCs at an earlier stage, since they have a better prognosis and have longer survival rates than conventional RCCs.

References:

- 1. Linehan WM, Spellman PT, Ricketts CJ, et al. Comprehensive molecular characterization of papillary renal-cell carcinoma. N Engl J Med 2016;374:135–45.
- 2. Jemal A, Siegel R, Ward E, et al. Cancer statistics, 2008. CA Cancer J Clin. 2008;58:71–96.
- 3. Ljunberg B, Campbell SC, Cho HY, et al. The epidemiology of renal cell carcinoma. Eur Urol. 2011;60:615–2.
- 4. Muglia VF, Prando A. Renal cell carcinoma: histological classification and correlation with imaging findings. RadiologiaBrasileira. 2015;48(3):166-74.
- 5. Dutcher JP. Update on the biology and management of renal cell carcinoma. J Investig Med. 2019;67(1):1-0.
- 6. Motzer RJ, Bander NH, Nanus DM: Renal-cell carcinoma. N Engl J Med 1996, 335:865-875
- 7. Hamid Y, Poller DN: Spontaneous regression of renal cell carcinoma: a pitfall in diagnosis of renal lesions. Journal of Clinical Pathology 1998, 51(4):334-337.
- 8. Lam JS, Brenda A, Belldegrun AS: Evolving principles of surgical management and prognostic factors for outcome in renal cell carcinoma. J ClinOncol 2006, 24(35):5565-5575.

- 9. Coppin C, Porzsolt F, Awa A, Kumpf J, Goldman A, Wilt T: Immunotherapy for advanced renal cell cancer. Cochrane database of systematic reviews 2004:Art. No: CD001425.
- 10. Bumpus HC: The apparent disappearance of pulmonary metastasis in a case of hypernephroma following nephrectomy. J Urol 1928, 20:185-191.
- 11. Lokich J: Spontaneous regression of metastatic renal cancer: case report and literature review. Am J ClinOncol 1997, 20(4):416-418.
- 12. Chromophobe renal cell cancer review of the literature and potential methods of treating metastatic disease. J ExpClin Cancer Res. 2009;28(1):134.
- 13. Alpers CE. The Kidney. In: Kumar V, Abbas A, Fausto N, Aster JC, eds. Robbins and Cotran Pathologic basis of disease. 8th ed. Saunders Elsevier. 2010. pp 963-967.
- 14. Cheville JC, Lohse CM, Zincke H, Weaver H, Blute AL, Michael L. Comparisons of outcome and prognostic features among histologic subtypes of renal cell carcinoma. Am J SurgPathol. 2003;27:612-624.
- 15. Motzer RJ, Bacik J, Mariani T, Russo P, Mazumdar M, Reuter V. Treatment outcome and survival associated with metastatic renal cell carcinoma of non-clear-cell histology. J. Clin. Oncol. 2002; 20: 2376–81.
- 16. Bhalsod HD, Khan IA. Chromophobe variant of renal cell carcinoma A rare case report. MEDICAL SCIENCE. 2021 Apr;25(110):812–5.
- 17. Niveditha, S., Abhijit Dhale, and Meenakshi Yeola. "Renal Cell Carcinoma with Tumour Thrombus Adherent to Inferior Vena Caval Wall: A Case Report." MEDICAL SCIENCE 24, no. 106 (December 2020): 4014–18.