

Chromophobe Renal Cell Carcinoma and Xanthogranulomatous Pyelonephritis in the Same Kidney? A Case Report of a Rare Coexistence

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Authors' contributions

This work was carried out in collaboration among all authors. Author IP designed the study, managed the literature searches, and wrote the first draft of the manuscript. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Introduction: ChRCC is an uncommon type of renal carcinoma classified into typical and the less met eosinophilic variant. The latter is likely to be mistaken for other renal eosinophilic tumors, needing an extended immunohistochemical investigation, in order to exclude other oncocytic renal tumors. XGP is an unusual benign condition which may mimic renal cell carcinoma grossly and microscopically, being a rare chronic inflammatory disorder forming masses in the renal parenchyma. In this report we present a rare case of coexisting ChRCC and XGP in the same kidney.

Case Presentation: A 51-year-old woman presented at the emergency unit with history of upper urinary tract infections, complaining about urinary frequency, and loin pain. An abdominal CT scan revealed lesion near the renal pelvis of the left kidney and the patient underwent left nephrectomy on a regular basis. The specimen we received included a brown and partially yellow tumor. The microscopical examination of the brown areas revealed sheets of small tumor cells with eosinophilic cytoplasm and wrinkled irregular nuclei. Microscopy of the yellow-colored areas

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revealed replacement of the renal parenchyma by an inflammatory infiltrate composed mainly foamy or pigmented –laden macrophages and rare giant cells, extending into the tumor-free renal parenchyma and the pelvic fat. These findings led us to the diagnosis of ChRCC with coexisting XGP.

Conclusions: Since both of these entities affecting the kidney are uncommon and they rarely coexist in the same kidney, the correct clinical and histological assessment is important for the selection of proper treatment strategy

Keywords: Chromophobe renal cell carcinoma; xanthogranulomatous pyelonephritis; immunohistochemistry.

ABBREVIATIONS

CA-IX : Carbonic anhydrase IX
CcRCC : Clear Cell Renal Cell Carcinoma
CD : Cluster Differentiation
ChRCC : Chromophobe Renal Cell Carcinoma
CK : Cytokeratin
CT : Computed Tomography
EVCRC : Eosinophilic Variant of Chromophobe Renal Cell Carcinoma
PTEN : Phosphatase and Tensin homolog
RCC : Renal Cell Carcinoma
XGP : Xanthogranulomatous Pyelonephritis

1. INTRODUCTION

ChRCC consists of approximately 5% of all renal cell carcinomas [1]. The majority of cases are sporadic, with hereditary neoplasms being extremely rare. There is a wide range of age occurrence, but the peak occurrence seems to be the sixth decade [1]. Chromophobe renal cell carcinomas are classified into typical and eosinophilic variants depending on the predominant cell type. Three types of cells have been described in ChRCCs. The typical ChRCCs are composed of cells with thick well-defined borders, wrinkled or raisinoid nuclei and abundant pale granular cytoplasm which shows diffuse reticular cytoplasmic staining with Hale's colloidal iron. Eosinophilic variant is less frequent and is composed almost completely of Type I cells. The Type I cell is smaller and has granular, eosinophilic cytoplasm. The Type II cell resembles the Type I cell but is larger and has a perinuclear translucent zone [1]. The EVCRC is not as common as the typical variant but it has the same prognosis [2]. It is likely to be mistaken for other renal eosinophilic tumors, such as oncocytoma [3] because of the predominance of Type I cells.

XGP on its own is a rare benign condition, without age predilection, and it usually mimics renal cell carcinoma grossly and microscopically [4,5], being a rare chronic inflammatory disorder,

which forms masses occupying the renal parenchyma [6]. Usually it is associated with pelvicalyceal obstruction and ulceration and it rarely coexists with renal carcinomas such as squamous cell carcinoma [7], CcRCC [8], Wilm's Tumor [9] or ChRCC [10]. The major component of XGP is foamy and pigment-laden macrophages in combination with fibroblast population and occasional multinucleated giant cells and other types of inflammatory cells. It becomes interesting when an eosinophilic renal neoplasm such as in our case is associated with XGP and there are very few cases reported worldwide.

2. CASE PRESENTATION

51-year-old woman presented at the emergency unit with history of upper urinary tract infections in the last year, complaining about urinary frequency, gross hematuria, mildly elevated creatinine, and loin pain. Clinical examination and ultrasound revealed anisoechoic/hypoechoic mass which showed abnormal flow on color Doppler imaging. The patient was sent for an abdominal CT scan which revealed a 5,5cm, inhomogeneously enhancing lesion near the renal pelvis of the left kidney. A surgery was scheduled on a regular basis and a left radical nephrectomy was performed. We received a left radical nephrectomy specimen measuring 12,1x7,1x3,5cm and weighing 487gr including the perirenal fat tissue. The nephrectomy specimens were fixed in 10% buffered formalin and appropriately grossed as per the standard protocol for tissue processing and paraffin embedding. When grossly examined, it showed a 5,5x5x4,2 cm tumor at the renal pelvis with a mainly homogenous, solid light brown and peripherally, nearby the calyces, yellow cut surface. The neoplasm seemed to "push" into the pyelocaliceal system as well as infiltrate into the pelvic fat tissue. Microscopic evaluation of the brown areas revealed tumor cells with a solid sheet pattern and rarely nested pattern separated by a vascular incomplete septum.

Observation in higher magnification revealed mostly small tumor cells with fine oxyphilic granularity and focally larger cells with paler cytoplasm. The nucleus was irregular and wrinkled with "raisinoid" morphology, and focally a perinuclear halo was observed (Fig. 1). The immunohistochemical assay of these cells revealed diffuse positivity for CK7 (Fig. 2) and CD117 (Fig. 3), focal expression of CD10 and no expression for CA-IXRCC, p504s and Vimentin. Additionally, microscopy of the yellow-colored areas revealed replacement of the renal parenchyma by an inflammatory infiltrate composed mainly of foamy or pigmented –laden macrophages and giant cells (Fig. 4), positive for CD68 (Fig. 5) and CD163 between which lymphocytes, plasma cells, occasional neutrophils, cholesterol clefts and fibrosis were observed. This infiltrate was extending into both the pelvic fat tissue and into the renal parenchyma that was not affected by the tumor. The complex microscopic findings in combination with the results of immunohistochemistry assay led us to the diagnosis of a typical T2aX chromophobe renal cell carcinoma, with coexisting xanthogranulomatous pyelonephritis. Patient is free of disease for more than one year.

3. DISCUSSION

ChRCC is a relatively rare form of RCC counting for only the 5% of all cases [11] and it has in general a favorable prognosis, with 5-year survival reaching 78-100%. There are two different forms of ChRCC, the classic one and the eosinophil variant which is rare. Their main difference is the size of the neoplastic cells as well as the colour of the cytoplasm. The classic variant is represented by larger and paler cells, whereas the eosinophilic variant is represented by smaller but eosinophilic cells. As data show, ChRCC originates from distal regions of the kidney (small tubules) whereas clear cell renal cell carcinoma arises in the proximal tissue of the kidney, thus its behavior is different. An autosomal dominant disorder called Birt-Hogg-Dube syndrome seems to have higher incidence of ChRCC especially with the hybrid oncocyctic/chromophobe tumor [12]. Mutations in the folliculin gene were proved to be the reason for this syndrome. However, little is yet known about the non-hereditary ChRCC [13]. Molecular mechanisms have been accused of the sporadic development of this neoplasm, including p53 and PTEN, in 27-32% and 9%, respectively [12,14]. Mutation of mitochondrial DNA has also found to

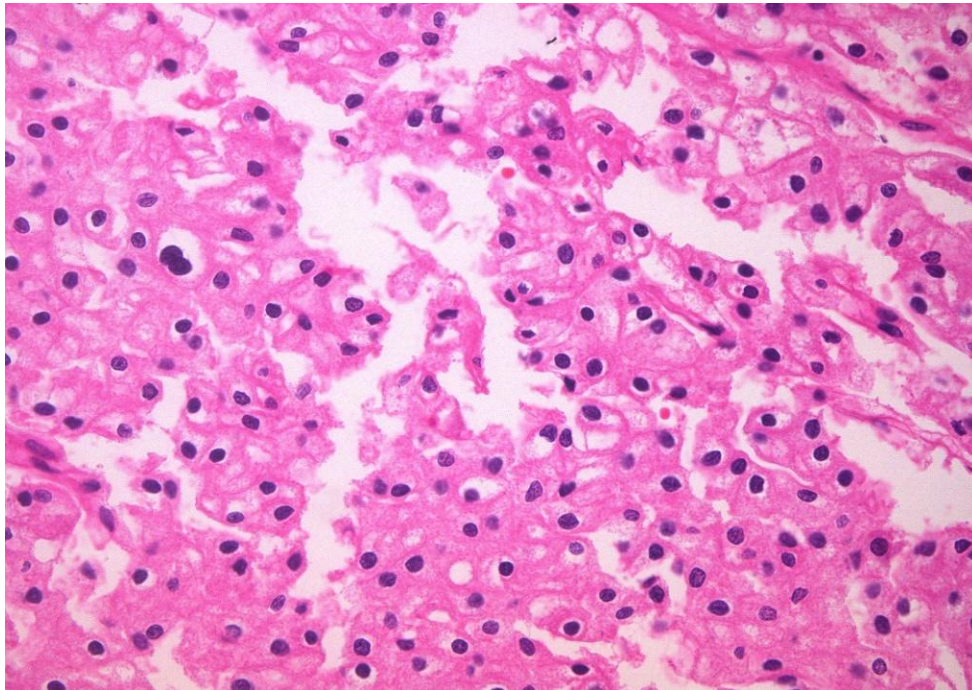


Fig. 1. ChRCC: Small tumor cells with fine oxyphilic granularity and focally larger cells with paler cytoplasm and irregular, wrinkled nuclei with a perinuclear halo. Hematoxylin-Eosin Stain x40

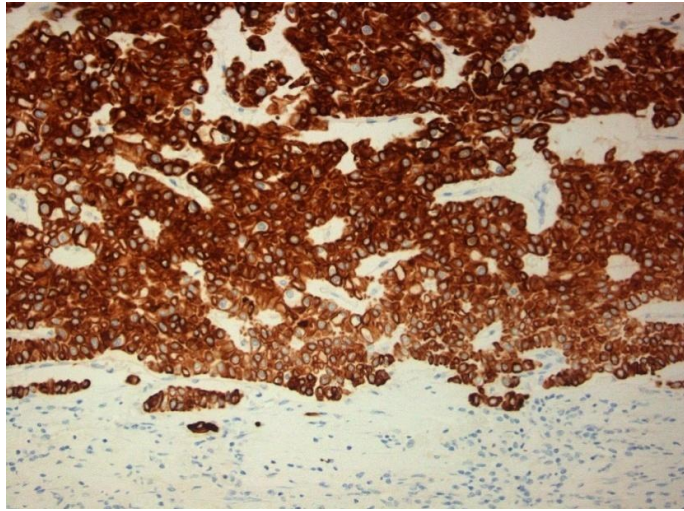


Fig. 2. ChRCC - Immunohistochemistry: Diffuse positivity for CK7

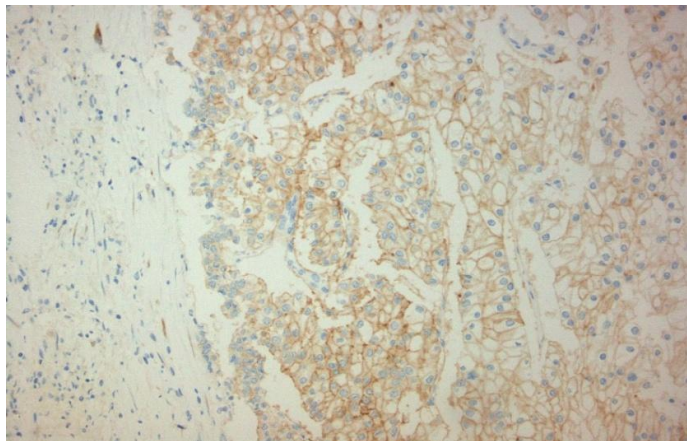


Fig. 3. ChRCC - Immunohistochemistry: Diffuse positivity for CD117

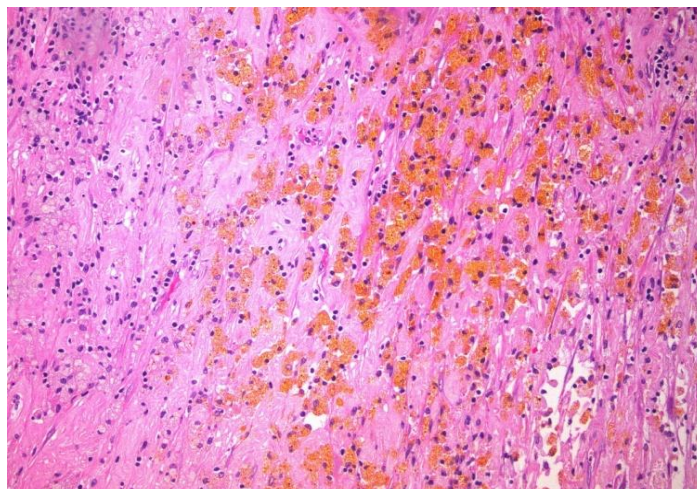


Fig. 4. XGP: Foamy and pigmented-laden macrophages. Hematoxylin – Eosin stain x20

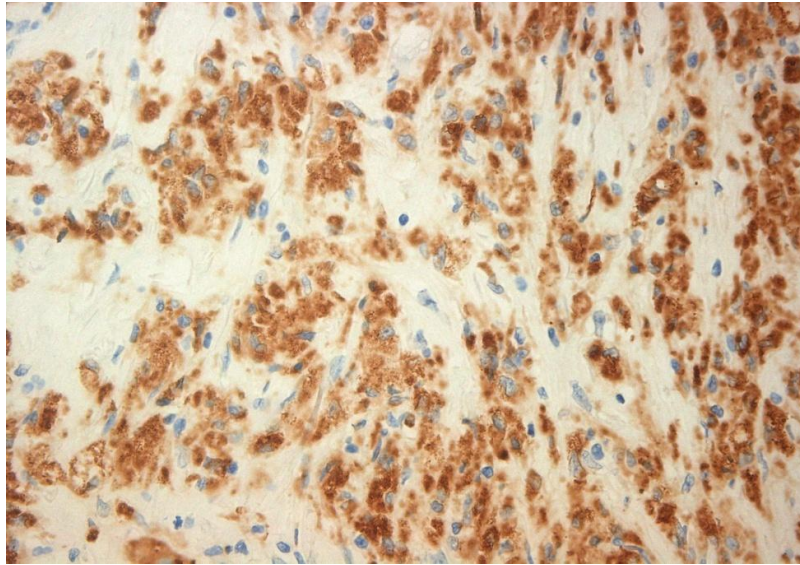


Fig. 5. XGP: Immunohistochemistry. Foamy and pigmented-laden macrophages positive for CD68

be a reason. However, the eosinophilic variant, has less possibilities of somatic mutations [12,15]. In our case, due to the cell morphology, we had to exclude both oncocytoma and clear cell renal carcinoma. A panel of basic immunohistochemical markers was ordered, including CK7, CD10, Vimentin, RCC, CA-IX and racemase (p504s). The results of this immunohistochemical assay confirmed the diagnosis of typical ChRCC, excluding oncocytoma, which is generally negative (or focally in the scar positive) for CK7 and Clear Cell Renal Cell Carcinoma, which is negative or focally positive for CK7, diffusely positive for Vimentin, positive for CA-IX and CD10 (positive cytoplasmic – membrane stain for both antibodies), and negative for CD117 [16].

However, what made really challenging our diagnosis was the coexistence of plenty of sheets of foamy or pigment-laden macrophages and giant cells nearby the neoplastic cells in the macroscopically described “yellow areas”, which were positive for CK68 and CK163 immunohistochemical markers and they were accompanied by spindle-shaped fibroblasts, as well as lymphocytes, and other types of inflammatory cells, replacing the otherwise free-of-tumor renal parenchyma and extending into the pelvic fatty tissue. Based on these findings, XGP was considered and added to the diagnosis of ChRCC. XGP is a benign entity that is defined as the inflammatory sequel of chronic renal infections, usually due to bacteria such as

Escherichia coli and *Proteus mirabilis* or obstructive situations such as nephrolithiasis, ureteropelvic junction syndrome, ureteropelvic duplication or more rarely, neoplasms. There are three stages of XGP, stage I is the nephric stage, stage II is the perinephric stage and stage III is the paranephric stage. The latter two are exceedingly rare. Furthermore, XGP develops in three patterns. Firstly, the diffuse pattern, which is the most common, arises in a completely obstructed kidney. Thus, the kidney is not functioning, and nephrectomy is the only choice of cure. The second pattern is the segmental one, which develops mostly in children and due to its polar development is easily misdiagnosed as a neoplasm. Finally, focal form develops in the cortex, it is not related with the pelvis thus no obstructive symptoms are developed. Both segmental and focal form can be treated with partial nephrectomy [17]. In our case, it was clear that stage II XGP had developed because of obstruction of the pelvicalyceal system by the above-described neoplasm, in a diffuse histological pattern.

4. CONCLUSION

ChRCC and XGP are rare entities affecting the kidney and there is little information on cases where these two are combined. They may present similar clinical and histological features or imitate other malignant conditions. For this reason, a meticulous clinical and histological investigation is needed, which will lead us to the

correct diagnosis, avoiding misdiagnosis and consequently wrong treatment.

CONSENT

A written consent of the patient was taken.

ETHICAL APPROVAL

It is not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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