



Case Report:

Chromophobe Renal Cell Carcinoma.

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Abstract: Renal cell carcinoma is the most common neoplasm of the kidney comprised of different histological variants. Chromophobe renal cell carcinoma (ChRCC) is a rare subtype of renal cell carcinoma (RCC) mainly diagnosed in the sixth decade of life. It is important to identify this entity because it has significantly better prognosis than the clear cell (conventional) and papillary renal cell carcinomas. The chromophobe renal cell carcinoma should be differentiated from oncocytoma and clear cell carcinoma. We report a case of a 70 year-old male who presented with a six month history of hematuria, left sided flank pain and a palpable non-tender lump in the left lumbar region. On radiology, the possibility of a left renal neoplasm was raised. A left radical nephrectomy was done and histopathological diagnosis of Type 2 (mixed) chromophobe renal cell carcinoma was given. We present this case owing to its relative rarity of incidence, difficulties encountered and differential diagnoses to be considered during diagnosis as the prognosis and management protocols differ with different variants.

Key Words: Chromophobe renal cell carcinoma; Type 2 mixed variant

Introduction:

Renal malignancy is the 13th most common cancer worldwide.¹ Approximately 90% of renal cancers are renal cell carcinomas (RCC).² Chromophobe renal cell carcinoma (ChRCC) is one of its rare subtypes, with an overall incidence of 5% and an equal preponderance in both the sexes.³ Mean age at diagnosis was reported to be 53 years.⁴ The clear cell RCC and the benign oncocytoma are its closest mimics on microscopy. We present this case of a

chromophobe RCC, diagnosed on routine light microscopy, owing to its relative rarity of incidence, difficulties encountered and differential diagnoses to be considered on histopathology - as the prognosis and management protocols differ with different variants.

Case Report

A 70 years old diabetic, hypertensive and obese male farmer, who was also a chronic alcoholic and beedi smoker, presented to the Surgery out-patient department of Krishna Institute of Medical Sciences, Karad, with complaints of left-sided flank pain and passing red-coloured urine over the past six months. The patient had no significant past, family, dietary history.

On examination, he was pale, tachypnoeic and had a blood pressure reading of 168/98 mm Hg. Abdominal palpation revealed a small, firm to hard, non-tender lump in the left lumbar region that did not move with respiration.

Contrast-enhanced Computed Tomography revealed a well-defined, heterogeneously-enhancing, round to oval lesion, measuring approximately 3.7 x 3.5 x 3.5 cm at the postero-medial aspect of the left kidney. The lesion had smooth margins and a distinct interface with the adjacent renal parenchyma and was seen compressing the renal pelvis. There was no evidence of any infiltration into the adjacent peri-renal structures. (Fig.1.1, Fig.1.2)

Based on these findings a provisional diagnosis of renal cell carcinoma, with a differential diagnosis of oncocytoma was made.



Fig. 1.1: Pre-contrast CT image of the well-defined, heterogeneously-enhancing round to oval lesion at the postero-medial aspect of the left kidney.



Fig. 1.2: Post-contrast CT image of the lesion showing smooth margins and a distinct interface with the adjacent renal parenchyma.

Intravenous pyelography showed a large, irregular-filling defect in the left renal pelvis causing an irregular impression on the calyces with lateral displacement of calyceal system without visualization of the renal pelvis, which was suggestive of a neoplasm of the renal pelvis.

A pelvic ultrasonogram revealed a 9.8 x 4.5 cm sized left kidney with an iso-echoic, predominantly solid, intra-renal mass along the mid-pole measuring 4.3 x 3.6 x 3.9 cm with few areas of cystic degeneration and mild vascularity without local infiltration or intra-lesional calcification. The left renal vein showed normal blood flow without thrombosis. The right kidney was essentially normal. No other pelvic abnormalities were noted.

Routine laboratory investigations revealed a microcytic, hypochromic anaemia with a mild neutrophilic leukocytosis and raised fasting and post-prandial blood sugar levels. Urine microscopy revealed numerous pus cells, RBCs and red cell casts. Urine benzidine test was positive. The rest of the haematological and biochemical investigations, including serum creatinine, protein and electrolyte levels, were within normal limits.

A left radical nephrectomy was done and the specimen sent for histopathological examination.

On gross examination, the left kidney measured 11 x 6.5 x 3.5 cm with a nodular bulge measuring 3.4 x 2.8 cm on the posterior aspect of the hilum. The rest of the kidney showed broad, irregular scars. On cut-section, a well-circumscribed, grey-tan, solid tumour measuring 3.4 x 2.8 x 1.6 cm situated beneath the capsule in the middle portion of the kidney was noted. The pelvi-calyceal system showed irregular dilatation

with three brown-black calculi. The attached ureter, artery and vein appeared uninvolved.



Fig. 2a and 2b: Gross specimen showing the tumour arising in the middle pole near the hilum



Microscopy of multiple Haematoxylin & Eosin-stained sections revealed renal tissue with a tumour composed of round to polygonal cells arranged in nests, alveolar and small areas of papillary pattern. The cells have well-defined cell-

membranes, faintly eosinophilic granular cytoplasm with perinuclear clear halos with round hyper chromatic nuclei with slightly irregular nuclear contours. Areas of necrosis are noted, the rest of the kidney shows features of chronic pyelonephritis. The sections from the ureter, renal vein, renal artery and perinephric fat show no evidence of tumour.

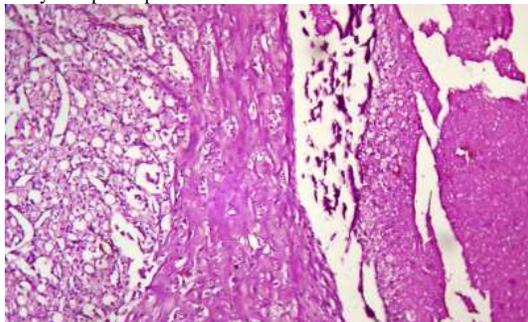


Fig. 3a: Photomicrograph showing tumour composed of round to polygonal cells arranged in nests and alveolar pattern. (100x, H&E).

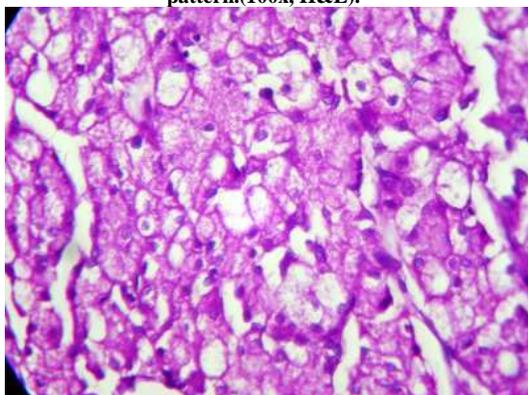


Fig. 3b: Photomicrograph showing cells with well-defined cell membranes, faintly eosinophilic granular cytoplasm with perinuclear clear halos and round hyperchromatic nuclei with slightly irregular nuclear contours. (400x, H&E).

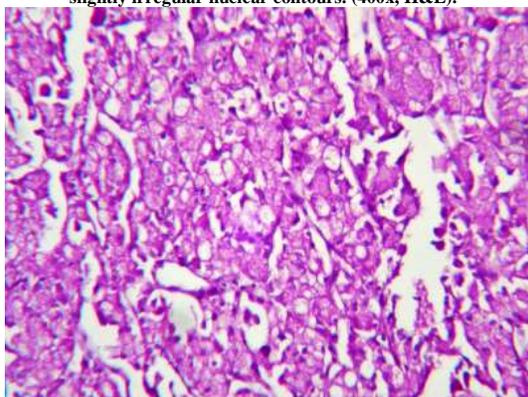


Fig. 3c: Photomicrograph showing tumour with areas of necrosis. (100x, H&E).

Discussion:

Renal malignancy is among the most frequently occurring cancers in the Western world.¹ The incidence of renal malignancy varies geographically: incidence rates are highest in Europe, North America and Australia; and low in India, Japan, Africa, and China, with approximately 2,71,000 new cases diagnosed in 2008 alone.¹

Renal cell carcinoma is the most common neoplasm of the kidney.^{2,3} It is a heterogeneous disease, comprised of

different histological variants with a distinct clinical course, genetics and response to treatment. The 2004 World Health Organization (WHO) classification of RCC recognized several of its subtypes. The commonest include: clear cell RCC (70%), papillary RCC (10-15%), chromophobe RCC (4-6%), collecting duct carcinoma (about 1%) and unclassified RCC (4-5%).⁵

The chromophobe variant of the renal cell carcinoma was first described in 1985.⁶

These are diagnosed most frequently in the 6th decade of life and have an equal incidence in both sexes,⁷ as against typical RCCs which show a male preponderance.⁸ Almost 90% of ChrCCs are diagnosed earlier, i.e., in stage 1 or 2 of the disease. Renal vein invasion is also more uncommon - seen only in about 5% of cases. Incidence of metastatic disease in chromophobe renal cell carcinoma is lower - about 6-7%.⁹

In a summary of 28 cases, the most common metastatic sites of the ChrCC were found to be the liver (39%) and the lungs (36%);¹⁰ while those of the RCC are the lungs (more than 50%) and bones (33%).⁸

Five and ten year disease-free survival rates for chromophobe RCC were 83.9% and 77.9% respectively. The median time from nephrectomy to metastasis detection, and from metastasis detection to death were twice as long for ChrCC than for other subtypes of RCC (i.e. papillary, clear cell RCC).⁷

Macroscopically, it is classically described as a solitary, circumscribed, un-encapsulated mass with a homogeneous light brown cut surface as against the bright yellow-gray-white cut surface of the conventional RCC. The median tumour size is 6.0 cm, which is larger than the other RCC subtypes.¹⁰

Microscopically, ChrCCs are classified into typical, eosinophilic and mixed variants depending on the predominant cell type.¹¹ The three types of cells described are:

- Type I (eosinophilic variant) cells are small with granular, eosinophilic cytoplasm.
- Type II (mixed variant) cells resemble the first type but are larger with a peri-nuclear, translucent zone.
- Type III (classical variant) cells have thick, well-defined borders, wrinkled or 'raisinoid' nuclei and abundant, pale, granular cytoplasm.

In this case, the tumour was composed of, round to polygonal cells with well-defined cell-membranes arranged in nests, alveolar and small areas of papillary pattern. Individual cells had faintly eosinophilic granular cytoplasm with perinuclear clear halos and round, hyperchromatic nuclei with slightly irregular nuclear contours. So, a diagnosis of Mixed (Type II) chromophobe renal cell carcinoma was made.

Routine Haematoxylin & Eosin staining is generally enough to subtype renal cell carcinomas, but differentiation between an oncocytoma, a ChrCC and a clear-cell RCC can pose occasional diagnostic dilemmas when the tumour cells show eosinophilic cytoplasm.

ChrCCs composed predominantly of Type I cells can be mistaken for oncocytomas, owing to the small cell size, eosinophilic granular cytoplasm and typical nested or alveolar arrangement of tumour cells. Though, embryologically both these tumours arise from the intercalated cells of the collecting duct system, their prognosis differs.

The oncocytoma is a benign lesion and due to similarities in imaging and cytology findings with ChrCC, proper pathological diagnosis of oncocytoma is primarily histopathological. The microscopic features that aid in the differential diagnosis include - sheeting arrangement of the tumour cells, wrinkled or 'raisinoid' nuclei and well-defined

cell borders in the ChRCC.¹⁰ Also, special staining with Hale's colloidal Iron will show a diffuse reticular cytoplasmic staining in the ChRCC, as against oncocytomas that exhibit a focal positive stain confined to the luminal borders. Ancillary techniques like electron microscopy, immunohistochemical positivity for Cytokeratin-7 (CK-7), CD-117, epithelial membrane antigen and parvalbumin can be helpful in the diagnosis of ChRCC.¹⁰

In clear cell RCC the growth pattern is different from the ChRCC - varying from solid to trabecular (cordlike) or tubular. Individual tumor cells in this classical RCC type are round to polygonal with abundant clear or granular cytoplasm, which stains positive for glycogen and lipids.⁸

ChRCCs are often associated with a favourable prognosis, earlier stage at detection and longer survival rates as compared with the conventional RCCs,¹² hence recognition and diagnosis of this variant by the histopathologist is important.

Conclusion:

Chromophobe carcinoma is a relatively rare variant of the renal cell carcinoma. We present this case on account of its relatively rare incidence. The ChRCC is a distinct entity both clinically and on histopathology. It is often difficult to distinguish on microscopy from oncocytomas and clear cell RCCs. However, as ChRCCs often show a better prognosis, an earlier stage at detection and longer survival rates as compared with conventional RCCs, recognition and diagnosis of this variant by the histopathologist is of prime importance.

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