***Case report***

# Chromophobe renal cell carcinoma (ChRCC) with osteosarcomatous differentiation and osseous pulmonary metastasis- a case report.


## Abstract

Chromophobe renal cell carcinoma, a subtype of Renal Cell Carcinoma (RCC) is associated with a better prognosis than clear cell RCC and comprises about 3-5 % of all RCCs. It is believed to originate from the intercalated cells of the distal nephron (Steven C. Campbell MD, 2016). Sarcomatoid differentiation can occur with any RCC, in which high-grade spindle cells co-exist with epithelial areas of the tumour. It suggests transformation to higher-grade malignancy and an ominous outcome. The sarcomatoid component is homologous (Akin to parent RCC cells) in the majority of cases. We herein report a case of ChRCC with osteosarcomatous (heterologous) differentiation in an elderly gentleman, who developed pulmonary metastasis with an osseous component.



**Keywords:** Chromophobe renal cell carcinoma, Sarcomatoid differentiation, osteosarcomatous (heterologous) differentiation, pulmonary metastasis


## Introduction:

Chromophobe renal cell carcinoma (ChRCC) first described by Thoenes et al (Thoenes W, 1985) in 1985 is the third most common form of RCC accounting for 3-5% of RCC. It has a favorable outcome than conventional clear cell RCC with a 5 and 10 year survival rate of 93% and 88.9% respectively (Volpe, 2012). However, sarcomatoid features in ChRCC render a poor prognosis with a five-year disease-specific and progression-free survival of 35% and 27% respectively (Amin MB, 2002). 1.3% of patients presented with distant

metastases at diagnosis. The incidence of sarcomatoid features in ChRCC is about 1-5% (Shuch B, 2012), however, ChRCC with both heterologous sarcomatoid differentiation and metastatic bone formation is extremely rare. A rare case of ChRCC with osteosarcomatous component and metachronous metastatic calcified lung deposit is reported here.

**Case report**

77 years old male diabetic patient, presented with right-sided abdominal pain radiating to the groin for 1 week. He did not have any history of LUTS, hematuria, UTI, or renal calculi in the past. He had undergone surgery for duodenal ulcer perforation in 2006 and incisional hernia repair in 2008.

An ultrasound scan of the abdomen and pelvis revealed a large complex cystic lesion in the right kidney with calcification. A triphasic contrast-enhanced computed tomography (CECT) of the abdomen and pelvis revealed a hypodense mass lesion measuring 12.5x10.6x8.2 cm, arising from the peripheral aspect of the right kidney with irregular thick calcification more along the infero-medial aspect of the lesion. The lesion was extending into the region of the upper third calyx, anteriorly and superiorly abutting the liver. However, a thin fat plane was preserved between the mass and the liver. Posteriorly, medially and inferiorly, the perinephric fat around the lesion was normal. A small non-enhancing thrombus was seen in a tributary of the right renal vein. The left kidney was normal with a few small simple cysts.

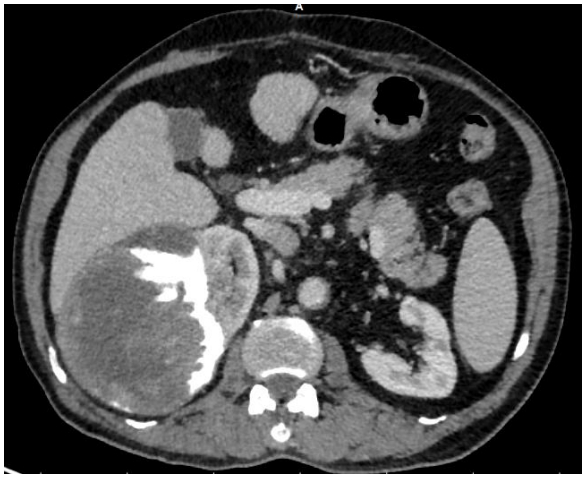

*Figure 1*: Computerized tomography abdomen shows right renal mass with irregular thick calcification

The patient underwent a Right laparoscopic radical nephrectomy with curative intent. A large hard cystic mass adherent to the liver undersurface with multiple adhesions was found. The cut section showed a large 12x9x9cm grey-white tumour occupying the middle and upper pole of the kidney. The tumor had cystic and solid areas with calcification along with areas of necrosis and hemorrhage. There were enlarged hilar lymph nodes. Microscopy revealed polygonal cells arranged in nests and lobular patterns with capillaries and fibrovascular septa in the stroma. Cells had prominent cell membranes, irregular wrinkled hyperchromatic nuclei, and abundant pale cytoplasm described as "plant cell" appearance. Perinuclear halos were seen around the cells with scattered bizarre multinucleated cells. Areas of atypical mitosis, necrosis, and calcification were also seen. There were sarcomatoid areas composed of pleomorphic spindle cells with irregular vesicular nuclei with coarse chromatin and prominent nucleoli. Osteoid formation and calcification were also seen in these areas. All features were suggestive of ChRCC with osteosarcomatous sarcomatoid differentiation. The tumour was seen involving the renal sinus, renal capsule, and extending into peri-nephric fat. The

Furhmans nuclear grade was 4 and as per TNM staging it was pT3a N0 Mx. All margins were free of tumor.

He was on regular follow-up initially at 1 month and six months thereafter. He developed hemoptysis at 2 years follow-up. A CT chest revealed multiple lobulated well-defined lesions of size about 15 to 60 mm in both lungs with areas of calcification. He was managed with palliative care because of extensive metastasis and died after 2 months.

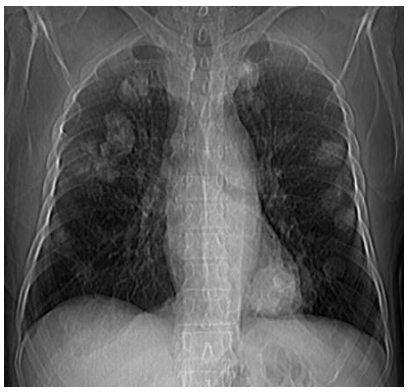

*Figure 2* Chest radiograph showing multiple pulmonary lesions

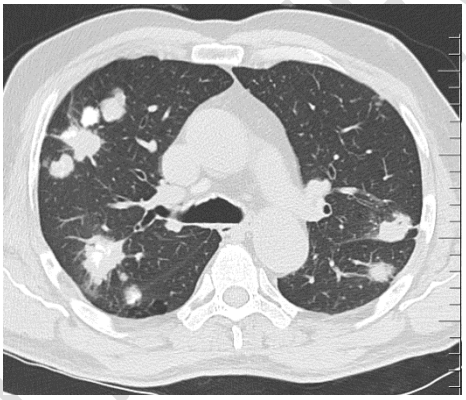

*Figure 3*: CT chest shows multiple calcified lung metastases



## Discussion

Chromophobe renal cell carcinoma (ChRCC) is the third most common type of RCC having the best prognosis among all the RCCs. Cancer-related death occurred in 8.6 % of all ChRCC (Tanaka Y, 2013). The sarcomatoid development may be due to the genetic profile, making cells prone to hyperpolarization (Akhtar M, 1997 Oct). ChRCC with sarcomatoid differentiation shows multiple gains of chromosomes 1, 2, 6, 10, and 17 (Brunelli M, 2007). Two hypotheses for ChRCC with sarcomatoid differentiation are either de-differentiation of chromophobe cells or synchronous development of two tumours. The former is more commonly accepted in which case the sarcomatoid cells show the original genomic pattern

of parent cells. This is called homologous differentiation which presents like histiocytoma or fibrosarcoma-like pattern. However, in rare cases, the sarcomatoid component showed heterologous differentiation and featured osteosarcomatous, chondrosarcomatous, and rhabdomyosarcomatous elements (Gabriela Quiroga-Garza, 2009). In our patient, there was osteosarcomatous differentiation.

The sarcomatoid dedifferentiation in itself is a poor prognostic factor and patients with it may present with metastasis at the presentation itself. Sarcomatoid components more than 50 % and lymphovascular invasion further decreases survival (Ged, 2019). The metastases can occur in the lung, liver lymph nodes, and bone. There is a drastic reduction in 5-year disease and progression-free survival of 35% and 27 % respectively (Amin MB, 2002). Our patient also had metastasis at 2 years to the lungs and succumbed to the same. Various treatment strategies including targeted therapy using antiangiogenic and Mammalian Targets of Rapamycin (mTOR) inhibitors have been used and found to have similar time to failure and overall survival rates (Colomba Emeline, 2017). The unique feature in our case is the osseous metastasis to the lungs that has not yet been reported in any series

Renal cell carcinoma most commonly has areas of necrosis, haemorrhage hyalinization, and calcification. In a Mayo Clinic review by Daniel et al. of 2709 renal masses, calcification was seen in 10% of cases (William W. Daniel, 1972). The calcification is only rarely ossified. There are various hypotheses for this ossification. It may be due to a metaplastic change, production of bone by tumour cells, ossification in previously existing mucin or calcium deposits, or a reparative response of the surrounding tissue. There are also conflicting reports on the prognostic significance of osseous metaplasia. There are some reports of the tumours being early-stage without invasion which is contradicted by others of high-grade tumours with poor prognosis.

Conclusion:

Chromophobe RCC usually has a favourable outcome, but sarcomatoid differentiation is an important independent prognostic factor that affects the disease outcome adversely.

Usual sarcomatoid differentiation is homologous but rare cases can present with heterologous elements as in our case. The clinical significance is not clear.

Time to treatment failure, time to metastatic recurrence, and overall survival drastically decrease in RCCs with sarcomatoid features. Close surveillance protocols may be warranted in these cases rather than the traditional follow-up.

Resistance to standard targeted therapies is another area of concern that needs further studies.

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