

Case report

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## Primary *de novo* malignant giant cell tumor of kidney: a case report

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### Abstract

**Background:** Osteoclast-like giant cell tumors are usually observed in osseous tissue or as tumors of tendon sheath, characterized by the presence of multinucleated giant cells and mononuclear stromal cells. It has been reported in various extrasosseous sites including breast, skin, soft tissue, salivary glands, lung, pancreas, female genital tract, thyroid, larynx and heart. However, extrasosseous occurrence of such giant cell tumors in the kidney is extremely rare and is usually found in combination with a conventional malignancy. De-novo primary malignant giant cell tumors of the kidney are unusual lesions and to our knowledge this is the second such case.

**Case Presentation:** We report a rare case of extrasosseous primary denovo malignant giant cell tumor of the renal parenchyma in a 39-year-old Caucasian female to determine the histogenesis of this neoplasm with a detailed literature review.

**Conclusion:** Primary *denovo* malignant giant cell tumor of the kidney is extremely rare. The cellular origin of this tumor is favored to be a pluripotential mesenchymal stromal cell of the mononuclear/phagocytic cellular lineage. Awareness of this neoplasm is important in the pathological interpretation of unusual findings at either fine needle aspiration or frozen section of solid renal masses.

### Background

Osteoclast-like giant cell tumors are primarily observed in osseous tissue or as tumors of tendon sheath. As the name implies, this tumor is characterized by the presence of multinucleated giant cells and mononuclear stromal cells. In spite of mitotic activity in the tumor, diagnosis of malignancy is reserved for those cases with bizarre mitoses and cellular atypia or an association with malignant stromal sarcoma [1]. Although metastasis of the tumor is not commonly observed, tumor thrombi occur in up to 5% of the tumors [2]. Occurrences of tumors with osteoclast-like giant cells, have been reported in various extrasosseous sites including breast, skin, soft tissue, salivary glands, lung, pancreas, female genital tract, thyroid, larynx and heart [3-12].

Extrasosseous occurrence of osteoclast-like giant cell tumors in the kidney is extremely rare. Such tumors are usually found in combination with a conventional malignancy. De-novo primary malignant giant cell tumors of the kidney are unusual lesions and to our knowledge this is the second such case. A review of all the cases of giant cell lesions of the kidney published in the English literature is represented in chronological order in Table 1.

### Case presentation

In March 2003, a 39-year-old Caucasian female was admitted to the Royal University hospital, Saskatoon, with a large right renal mass. Further investigations showed the presence of a tumor in the right kidney extending into the renal vein and up the vena cava. She

**Table 1: Review of published cases of giant cell lesions of the kidney and renal pelvis**

Age	Sex	Location	Immunoreactivity	Associated Malignancy	Outcome	Author & Reference	Year
56	M	Renal Parenchyma	Vimentin+, CD68+, Cytokeratin-ve, CAM 5.2-ve, AE1/AE3-ve	Malignant fibrous histiocytoma (MFH)	Disease free at 1 year	Chen C.H et al. [22]	2003
55	F	Renal Parenchyma	CD68+	Associated sarcomatoid spindle cells with osteoid production (osteosarcoma)	Disease free at 6 months	Lee, C.H et al. [19]	2003
30	M	Renal Parenchyma	Keratin & EMA -ve, Focally vimentin+	Clear cell type RCC, sarcomatoid	Disease free at 14 months	Koga, F. et al [20]	2000
81	M	Renal Parenchyma	CD68++ Scattered cytokeratin+, S100+	No	Died 2 months later	Heller, K.N et al. [2]	1998
55	F	Renal Parenchyma	CD68+, CAM2.5+, AE1/3+, EMA+, Vimentin+ (Keratin positive)	No associated sarcomatoid component	Disease free at 9 months	Chetty R, Cvijan D [14]	1997
69	M	Renal pelvis	S100+, CD68+, EMA+; Vimentin+	Papillary TCC	Liver and lung metastasis in 5 months	Molinie, V. [17]	1997
75	F	Renal Parenchyma	CD68+	Clear cell type RCC and sarcomatoid	N/A	el-Naggar, A.K et al. [15]	1993
64	M	Renal pelvis	N/A	In-situ TCC	N/A	Borg-Grech, A. et al. [13]	1987
56	M	Renal pelvis	N/A	Papillary TCC	Disease free at one month	Kenney, R.M et al. [16]	1984
60	M	Renal pelvis	N/A	No	Disease free at 1 year	Kimura, K et al. [21]	1983
77	F	Renal pelvis	N/A	SCC of the renal pelvis	N/A	Hou, L.T & Willis, R.A [18]	1963
79	F	Renal Parenchyma	N/A	Tubular and papillary adenocarcinoma	N/A	Hou, L.T & Willis, R.A [18]	1963

TCC = Transitional cell carcinoma SCC = Squamous cell carcinoma M = Male F = Female

underwent a radical right nephro-ureterectomy and partial excision of the vena cava wall was performed as a result of tumor adhesions to the vein. The immediate postoperative course was uneventful and the patient was discharged.

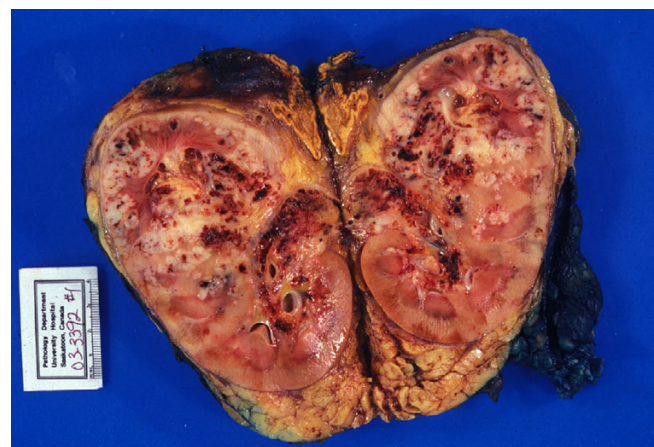
Pathological findings of the resected tissues are as follows:

**Macroscopic**

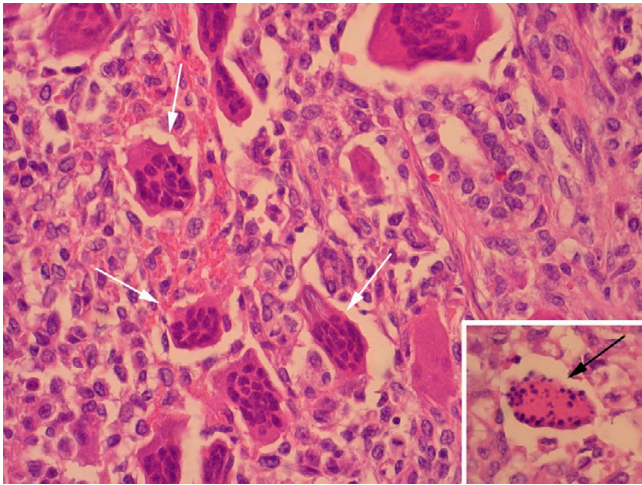
The gross specimen consisted of a right nephro-ureterectomy, adrenalectomy and fragments of the vena caval tumor thrombus. There was a pale tan tumor mass that measured 7.5 × 7 × 6 cm within the upper pole of the kidney. There was mild dilatation of the pelvicalyceal system towards the upper pole with extension of the tumor onto the mucosal surface of the pelvis. Full-faced slices of the tumor showed the tumor to extend close to the inked margins of the perinephric fat. (Figure 1)

**Microscopic**

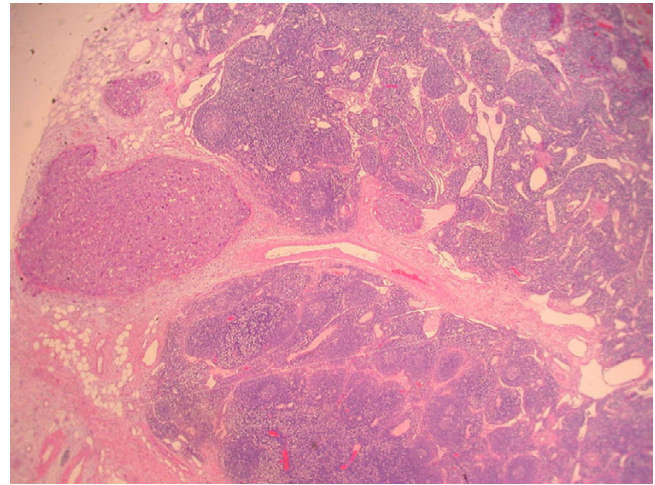
Light microscopic examination with routine hematoxylin and eosin stained slides showed the presence of ovoid plump shaped mononuclear cells interspersed with multinucleated giant cells in a vascularized stroma. Both the



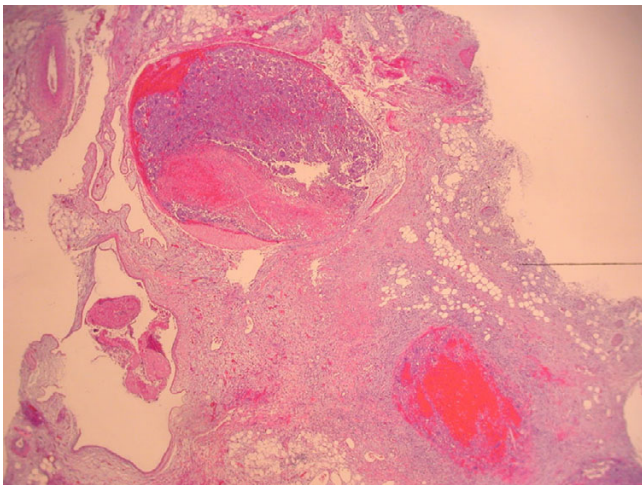
**Figure 1**  
Gross photograph of the sliced kidney demonstrates the large renal mass occupying the upper pole of the kidney.



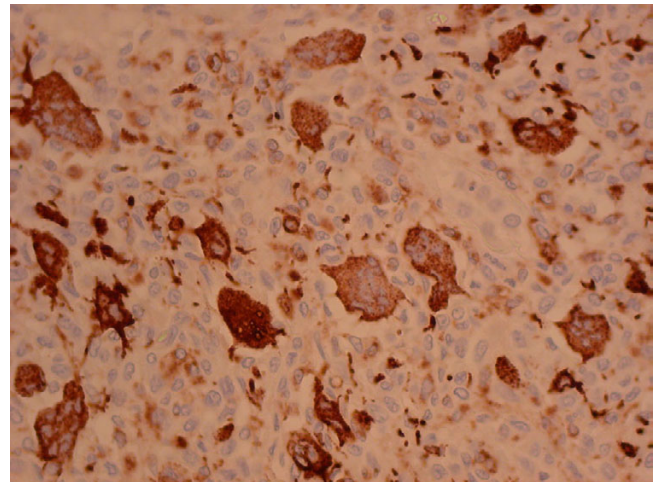
**Figure 2**  
Haematoxylin and eosin stained slides shows the stromal and multinucleated giant cell components of this neoplasm. The inset figure shows an apoptotic giant cell.



**Figure 4**  
Hilar lymph node metastasis.



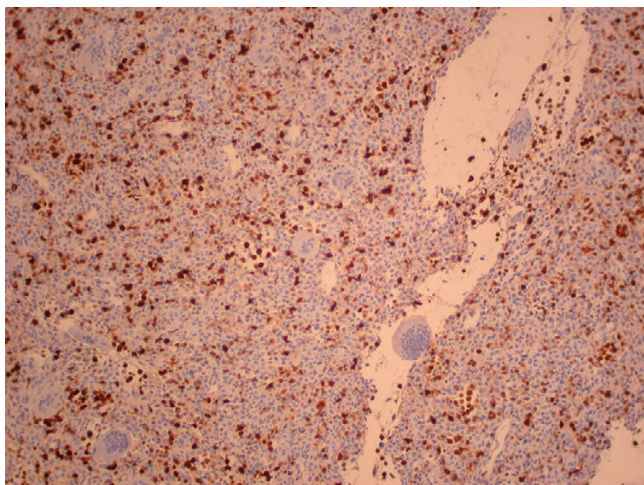
**Figure 3**  
Angiolympathic invasion with nodules of tumor in the perinephic fat.



**Figure 5**  
Staining with CD68 antibodies was strongly positive in the multinucleated giant cells.

stromal and the multinucleated giant cells appeared morphologically to be highly reminiscent of giant cell tumor lesions of bone (Figure 2). The stromal cells consisted of mononuclear round to spindle shaped cells with evidence of mitotic activity and mild cellular atypia. The giant cells had multiple nuclei, often numbering 25 to 40, many of which were ovoid with occasional nucleoli. Mitosis and pleomorphism in the giant cells was not easily observed

though apoptotic giant cells were easily observed (Figure 2-inset). Detailed examination with multiple sections revealed no evidence of any associated papillary or sarcomatoid or typical renal cell carcinoma. The tumor infiltrated widely through the hilar region into the pelvis of the kidney and extended as nodules into the adjacent cortex abutting onto the renal capsule and was also present in the adjacent perirenal fat (Figure 3) However, the tumor



**Figure 6**  
Antibodies to Mac387 highlighted the majority of the stromal mononuclear cell component.

was limited externally by the Gerota's fascia. Multiple sections of the hilar region showed the presence of tumor metastasis within the hilar lymph nodes (Figure 4) Invasion of the tumor was also observed in the renal vein, vena cava, perirenal fat, lymphatic and perineural space. Invasion to the vena cava presented as a tumor thrombus. Large areas of necrosis and hemorrhage were also seen within the neoplastic lesion. Neither osteoid nor cartilaginous differentiation were demonstrated. Sections of the non-neoplastic areas of the kidney showed mild interstitial lymphocytic infiltrate as a peritumoral response.

#### Immunohistochemical

Various immuno-histochemical markers were performed with appropriate positive and negative controls. Negative controls were achieved by omission of the primary antibody. The lesional cells showed no expression with low and high molecular weight keratin, pan-cytokeratin there was no expression of CK7, CK20, CK17, P53, BCL2, CD45 and HMB45 either. Anti body staining for S-100 was faintly expressed in some of the lesional cells. However, staining with CD68 antibodies was strongly positive in the multinucleated giant cells (Figure 5). Majority of the stromal mononuclear cell component was highlighted with antibodies to MAC387 (Figure 6). Vimentin also highlighted the same and occasional giant cells. Staining with Ki67 antibodies was over expressed in the lesional cells in keeping with the high proliferative and apoptotic nature of the lesion.

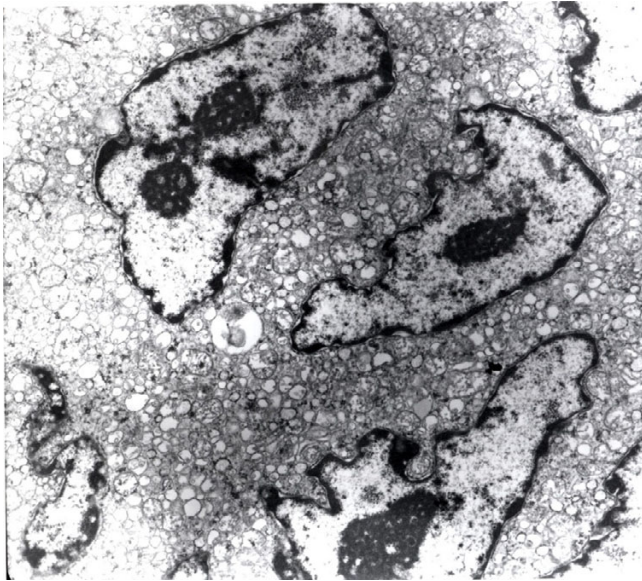
#### Ultrastructural

The electron microscopic study was performed on tissue samples obtained from the formalin fixed specimen. Both multinucleated giant cells and the stromal cells were examined in detail. Examination of the giant cells showed the cytoplasm to be filled with numerous vesicles and vacuoles many of which were consistent with primary or secondary lysosomes (Figure 7). Many of the secondary lysosomes typically exhibited a heterogeneous content with some prominent lipid accumulation. Scattered mitochondria and rough endoplasmic reticulum were also identified within these cells. They also contained multiple nuclei of various contours and irregular shapes with occasional one or two prominent nucleoli. Small foot-like projections and cell processes were observed on the surface of these multinucleated giant cells. These projections/processes did not qualify as true microvilli as they lacked the filamentous core rootlet and did not possess any evidence of secretory granules at the base of these pseudorootlets (Figure 8). Examination of the stromal cells showed abundant rough endoplasmic reticulum with dilated cisternae and mitochondria. Simple cell matrix junctions were observed but no true desmosomes were identified (Figure 9). There was no evidence of an external lamina, focal densities, microfilaments, tonofibrils or tonofilaments. Some cells showed the presence of intracytoplasmic accumulation of unusual filaments many of which were in a well-defined curving and somewhat rolled appearance in keeping with vimentin type of intermediate filaments (Figure 10). The extracellular matrix and stroma consisted mainly of filamentous collagen fibres with its distinctive cross-striated pattern.

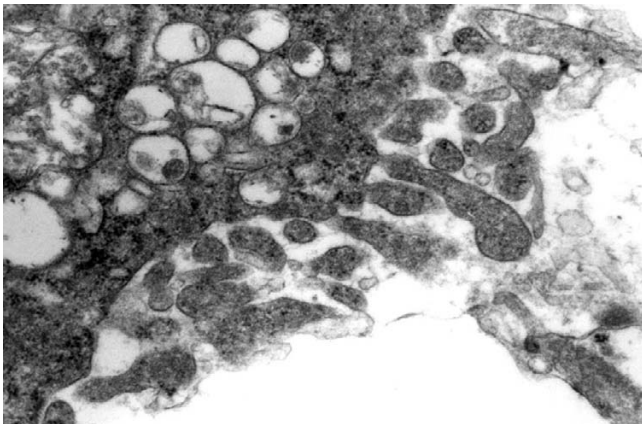
#### Discussion

Neoplasms associated with osteoclast-like giant cells have been reported in various extraosseous epithelial sites [3-12]. Frequently, these neoplasms have been associated with a conventional carcinomatous element. In the kidney this is a rare tumor and majority of the cases reported seem to occur in association with papillary, transitional, clear cell type of renal cell carcinoma or sarcomatoid carcinoma or osteosarcomatous transformation [13-20]. Kimura et al reported the occurrence of a multinucleated giant cell tumor of the renal pelvis that was considered to be primary, de-novo and benign [21]. Heller et al. [2] were the first to report malignant osteoclast-like giant cell tumor of the kidney without an association with a carcinoma or sarcoma. This case report is the second in this series of *de-novo* primary malignant giant cell tumor of the kidney not associated with any other conventional renal neoplasm.

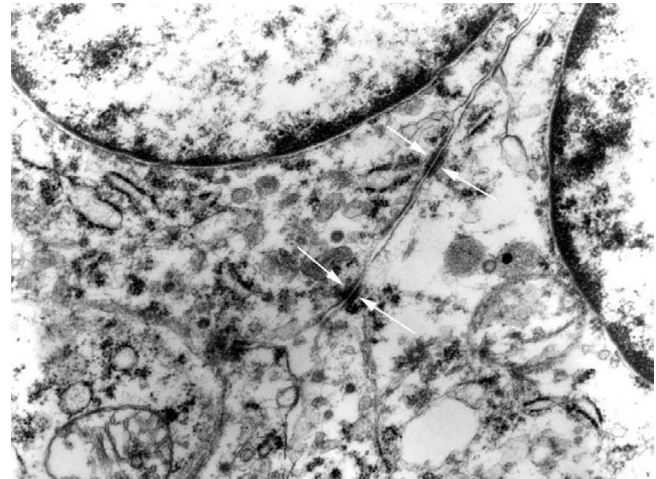
The diagnosis of primary malignancy in a giant cell tumor of bone is reserved for those lesions that display bizarre mitoses and cytological atypia or secondary malignancy



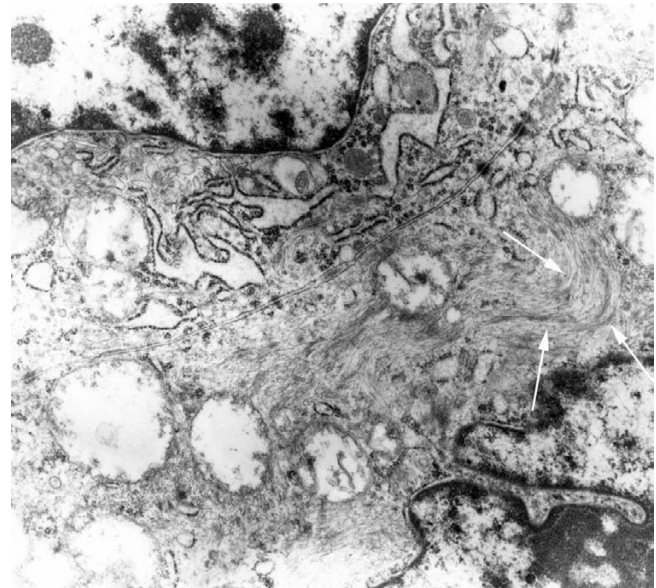
**Figure 7**  
Malignant multi-nucleated cell studded with primary and secondary lysosomes. (magnification  $\times 12,000$ )



**Figure 8**  
Pseudomicrovilli at the cell surface. (magnification  $\times 24,000$ )



**Figure 9**  
Simple cell junctions (magnification  $\times 38,400$ )



**Figure 10**  
Intracytoplasmic collection of whorled filaments of vimentin (magnification  $\times 30,000$ )

of a sarcomatous growth in previously documented benign giant cell tumor of bone [1]. Our case was diagnosed as malignant as it exhibited features such as widespread areas of necrosis and hemorrhage; perineural, vascular and angiolymphatic invasion; vena caval tumor thrombus and the presence of tumor metastasis within adjacent hilar lymph nodes.

The cell of origin of this tumor is believed to be from the mesenchymal cell of mononuclear phagocyte cell line [2,19,21], although others [13,14,17,20] suggested an epithelial origin. Some authors also felt that these giant cells were non-neoplastic and represented a stromal response to the conventional carcinomatous element [15,16,18]. The multinucleated giant cells of the present

case showed strongly positive immunoreactivity with CD68, confirming its monohistiocytic origin. CD68 is widely used to identify cells of monohistiocytic origin. The CD68 antigen is a 110 kilo Dalton highly glycosylated transmembrane protein which is mainly located in the lysosomes. The antibody stains macrophages in many human tissues. In addition, the antibody reacts with plasmacytoid T-cells that are present in many reactive lymph nodes, and these are also believed to be of monocyte/macrophage origin. However Chetty et al. [14] noted that a positive reaction to CD68, a lysosomal marker, can be positive in tumors of diverse histogenesis with a granular cytoplasm and can be misleading. The strongly positive staining of the CD68 exclusively in the giant cells of the present case indicates a monocytic/histiocytic origin of these cells. The co-expression of MAC387, lysozyme, faint expression of S-100 and a strong immunohistochemical expression of vimentin of the stromal cells favors a mesenchymal/histiocytic/monocytic origin of the tumor cells. There was no supporting evidence for an epithelial origin for this lesion despite the use of an extensive immunohistochemical epithelial marker panel.

Ultra structural analysis in the present case also supported a non-epithelial origin of the tumor by the presence of rough endoplasmic reticulum with dilated cisterna and mitochondria, absence of true desmosomes, the most important organelle in the ultrastructural definition of epithelium and also no evidence of external lamina tonofibrils or tonofilaments. These findings are also supported in Kimura's case report of giant cell tumor of the kidney [21].

## Conclusions

Primary *denovo* malignant giant cell tumor of the kidney is extremely rare. The cellular origin of this tumor is favored to be a pluripotential mesenchymal stromal cell of the mononuclear /phagocytic cellular lineage. Awareness of this neoplasm is important in the pathological interpretation of unusual findings at either fine needle aspiration or frozen section of solid renal masses.

## Competing interests

None declared.

## Authors' contributions

RK is the surgical pathologist who diagnosed and followed up the case and BT participated actively in the production of this manuscript.

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"Written consent was obtained from the patient or their relative for publication of study"

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