# Determining the diagnosis of an oncocytic renal neoplasm: a case report

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## Abstract

This is the case of a 45 year old male patient with an oncocytic renal neoplasm that was difficult to classify. Histology from a partial nephrectomy revealed a tumour comprising oncocytic cells containing rounded nuclei with some prominent nucleoli, although no necrosis or lymphovascular invasion. CK7 immunohistochemistry was focally positive, with only weak staining for CD117. There are multiple lesions to consider in the differential diagnosis of oncocytic renal tumours with borderline features between oncocytoma and chromophobe carcinoma. The increasing use of molecular pathology is also important in the diagnosis of some entities.

**Keywords** Low-grade tumour; oncocytic tumour; renal tumour; urological pathology

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## Case report

A 45 year old male presented to the emergency department with new onset left flank pain with associated tenderness on examination. Initial investigations demonstrated blood on a urine dipstick test and mildly deranged renal function tests. An ultrasound scan of the abdomen demonstrated a right renal mass and CT scan of the abdomen confirmed a 34 mm solid mass in the midpole region of the right kidney. The patient had a past medical history of type 2 diabetes mellitus, hypertension and hypercholesterolaemia, but no other significant history. He was admitted electively and underwent a partial right nephrectomy that was uneventful.

On macroscopic examination there was a solid and partly cystic, well circumscribed tumour, measuring 35 mm in maximum diameter. It had a haemorrhagic cut surface. Histology showed a tumour composed of sheets of cells forming nests and tubules (Figures 1 and 2). The cells had pale to bright eosinophilic cytoplasm, and in some cells there was finely vacuolated cytoplasm. The cell nuclei were round to oval, and in some areas, prominent nucleoli were seen (Figure 3). No evidence of necrosis or lymphovascular invasion was seen. The tumour was confined within the capsule and excised with a margin of 0.2 mm.

Immunohistochemistry on tumour sections was positive for PAX-8 (Figure 4) and SDHB, focally positive for CK7 (Figure 5), CD10 and e-cadherin, and weakly staining for CD117. The tumour was negative for CK20, CD15, RCC marker, vimentin, Alk-1, HMB 45, and Melan-A. There was no loss of staining for fumarate dehydratase.

Tumour samples were sent for fluorescence in situ hybridization (FISH) testing which showed no evidence of TFE3-associated or TFEB-altered renal cell carcinoma.

Following these results, the final diagnosis was an oncocytic renal neoplasm of low malignant potential, reflecting that the pattern of features was difficult to classify. The patient made a full recovery and continued a low risk follow up management plan. Initial CT imaging after six months showed no evidence of tumour recurrence.

## Discussion

This case had histological features of both oncocytoma and chromophobe carcinoma, with focally positive CK7 and weak CD117 staining, meaning that other diagnoses were considered before reaching the final diagnosis. Given the combination of histological appearances, immunohistochemistry, molecular pathology and clinical context, it was felt that this was best described as an oncocytic neoplasm of low malignant potential in this case, given that it didn't exactly fit a defined entity. It is sometimes difficult to classify oncocytic tumours with borderline features, and a number of differential diagnoses should be considered with appropriate histological features, immunohistochemistry and molecular testing (Table 1).

For borderline/low grade tumours, there are several specific entities to be considered. Low grade oncocytic tumour (LOT) is an emerging entitiy with overlapping or intermediate features between an oncocytoma and chromophobe carcinoma, which does not show aggressive histological features and has a good prognosis.[1] They are usually characterised on immunohistochemistry as being CK7 positive and CD117 negative, although

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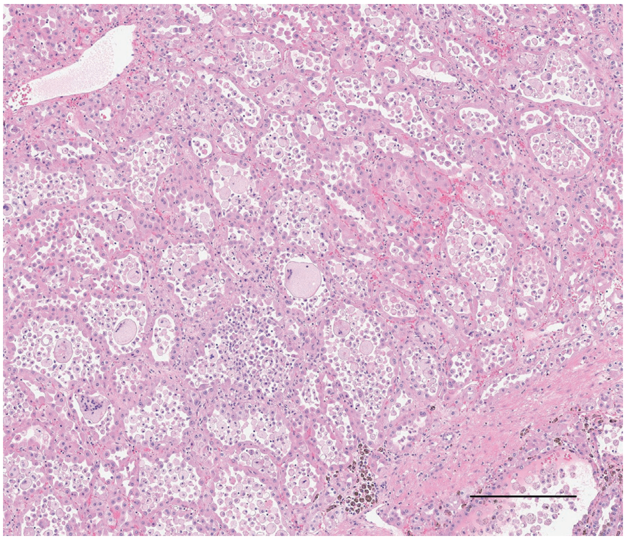

**Figure 1** Tumour with eosinophilic cells forming tubules (300 μm scale).

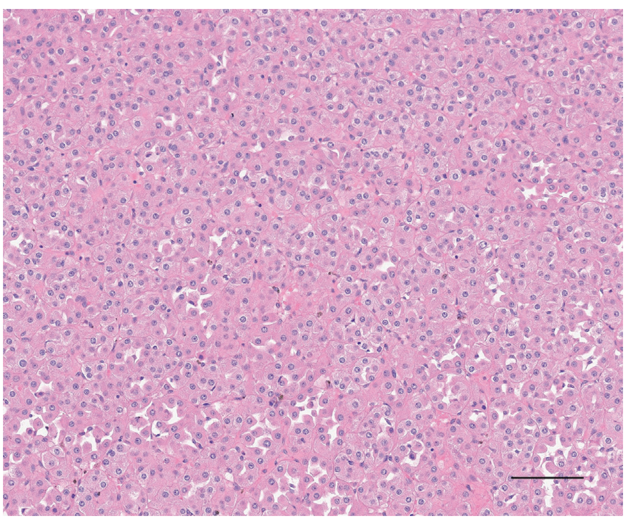

**Figure 2** Tumour with sheets of eosinophilic cells forming nests (200 μm scale).

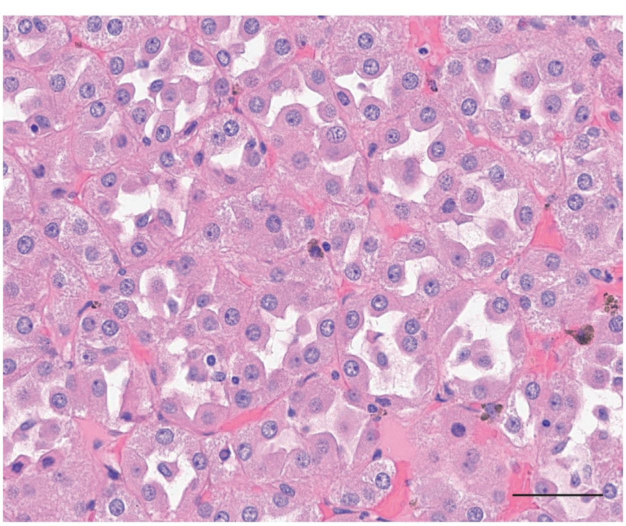

**Figure 3** Cells with finely vacuolated cytoplasm and some prominent nucleoli (50 μm scale).

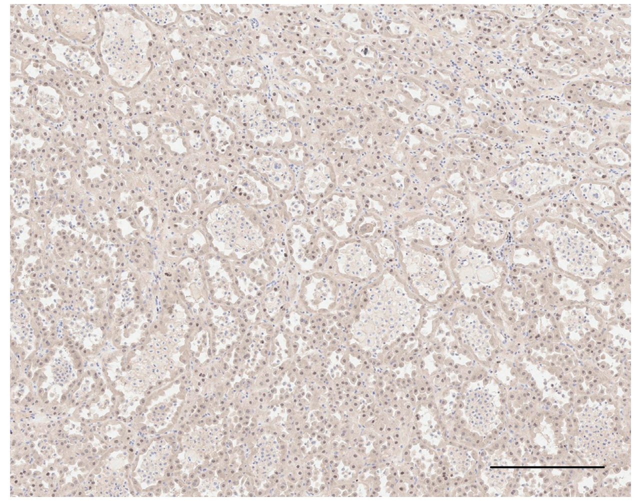

**Figure 4** PAX-8 positive tumour cells forming tubules at 10× magnification (300 μm scale).

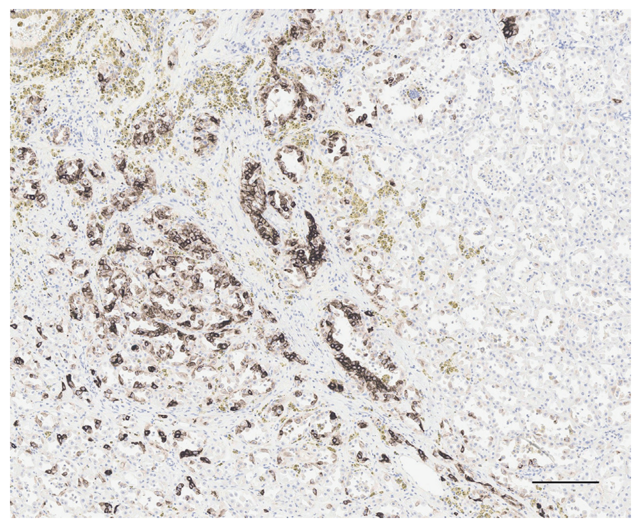

**Figure 5** Focal positivity of CK7 in tumour cells at 20× magnification (200 μm scale). This demonstrates more positive cells than usually expected in oncocytoma.

sometimes focal or weak CD117 staining is noted.[1] One study found that all patients examined were alive after a mean of 31.8 months follow up, with no disease progression.[1]

The increasing use and availability of molecular testing in diagnosing oncocytic renal tumours is important to note. MiT family translocation renal cell carcinomas may have a range of histological appearances and comprise tumours with Xp11 translocations with TPE3 gene fusions and also t(6;11) renal cell carcinomas with TFEB gene fusion.[3] Immunohistochemistry is considered sometimes unreliable in the diagnosis of these tumours, with the gold standard method being demonstration of chromosomal rearrangement on FISH.[3]

Succinate dehydrogenase (SDH) deficient renal cell carcinomas are malignant tumours with a solid, nested or tubular architecture and cells with flocculent cytoplasm.[2] Tumour cell nuclei are characterised by smooth borders with inconspicuous nuclei.[2] Loss of the SDHB gene on immunohistochemistry is

 

**Differential diagnoses to be considered in borderline/low grade oncocytic renal tumours where classification may be challenging. This includes some emerging entities[1–5]**

| Tumour | Histological appearances | Typical immunohistochemistry/molecular findings | Tumour malignant potential |
|---|---|---|---|
| Oncocytoma | Nested or tubular pattern tumour. Round nuclei, small nucleoli and eosinophilic cytoplasm. | CD117 and PAX-8 positive<br>CK7 negative | Benign |
| Chromophobe carcinoma (eosinophilic variant) | Wrinkled, rasinoid nuclei and perinuclear halos.<br>Necrosis<br>Prominent cell membranes | CD117 positive<br>CK7 positive | Malignant |
| Hybrid oncocytic/chromophobe tumour (HOCT) | Solid sheet-like pattern<br>No necrosis<br>May have renal vein or perinephric fat infiltration (may be in syndromic settings or sporadic) | CD117 and CK7 positive | Borderline/low grade |
| SDH deficient renal cell carcinoma | Flocculent cytoplasm and vacuoles.<br>Lacks perinuclear halos. | CD117, SDH and AE1/AE3 negative | Malignant |
| Oncocytic papillary renal cell carcinoma | Papillary growth pattern | AMACR, CD10 and Vimentin positive | Malignant |
| Eosinophilic variant of conventional renal cell carcinoma | Solid and cystic growth, lacks perinuclear halos | CK20 positive<br>CK7 and CD117 negative | Malignant |
| Epithelioid angiomyolipoma | Epithelioid cells lacking perinuclear halos. Can be pleomorphic. | HMB45 positive<br>PAX-8, AE1/AE3 and CK7 negative | Usually benign but can be malignant |
| MiT family translocation renal cell carcinoma | Spectrum of appearances | PAX8 positive<br>Vimentin and CK7 negative<br>TFE3 or TFEB rearrangement on FISH | Malignant |
| Low grade oncocytic tumour (LOT) | Solid sheets and nests, with trabecular areas.<br>Oedematous stromal areas with loose cell growth<br>Perinuclear halos | CK7 positive<br>CD117 negative (rarely weak +) | Borderline/low grade |
| Eosinophilic solid and cystic RCC (ESC RCC) | Solid and cystic, voluminous eosinophilic cells, cytoplasmic coarse granularity | CK20+, Vimentin+ and cathepsin K+<br>CK7− and CD117− | Malignant |
| Eosinophilic vacuolated tumour (EVT) | Solid, eosinophilic cells with frequent, large cytoplasmic vacuoles and prominent nucleoli. | Cathepsin K± and CD117±<br>CK7+ in rare cells only<br>CK20− and vimentin− | Malignant but indolent behaviour |

**Table 1**

diagnostic of SDH deficient renal cell carcinoma.[2] An analysis of retrospective renal tumour cases screened 273 oncocytomas for SDH deficiency and identified that three of these tumours were subsequently reclassified as SDH deficient RCC.[6] This highlights the importance of considering this entity in the differential of low grade oncocytic tumours.

Hybrid oncocytic/chromophobe tumours (HOCT) of the kidney represents another tumour entity with overlapping histological features of both oncocytoma and chromophobe carcinoma but when studied show molecular differences to both tumours.[7] They are associated with syndromes such as Birt-Hogg-Dubé, but may occur sporadically.[2,7] These tumours usually comprise solid sheets of cells with oncocytic cytoplasm.[2] They are usually CD117 and CK7 positive on immunohistochemistry.[2] This would be important to consider in the list of differential diagnoses.

Other tumours to consider in this setting, depending on the histological appearances and immunohistochemistry, would include oncocytic papillary renal cell carcinoma, eosinophilic variant of conventional renal cell carcinoma, eosinophilic solid and cystic RCC (ESC RCC), eosinophilic vacuolated tumour (EVT) and epithelioid angiomyolipoma.[1–5]

## Conclusion

Cases with borderline features can be challenging to classify in oncocytic renal tumours. It is important to consider the potential benign, malignant and borderline differentials and to select the appropriate immunohistochemistry and molecular tests to best identify rarer entities.

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## Practice points

- Oncocytic tumours with borderline features have a range of differential diagnoses that should be considered (Table 1)
- Growing use of molecular techniques is important in determining some renal tumour entities
- SDH deficient renal cell carcinoma should be considered in borderline oncocytic tumours and can be identified by testing for SDHB gene loss on immunohistochemistry
- Hybrid oncocytoma/chromophobe tumours (HOCT) may be associated with syndromes, such as Birt-Hogg-Dubé

## Self-assessment multiple choice questions

**1. Which of these tumours would be most likely to have a TFE3 rearrangement on FISH?**

**a. SDH deficient renal cell carcinoma**
**b. Low grade oncocytic tumour (LOT)**
**c. MiT family translocation renal cell carcinoma**
**d. Hybrid oncocytic/chromophobe tumour (HOCT)**

Correct answer: c

**2. An oncocytic tumour that is CK7 positive and CD117 negative, with borderline features of oncocytoma and chromophobe is best described as:**

**a. Oncocytoma**
**b. Low grade oncocytic tumour (LOT)**
**c. Eosinophilic variant chromophobe carcinoma**
**d. Hybrid oncocytic/chromophobe tumour (HOCT)**

Correct answer: b

**3. A hybrid oncocytic/chromophobe tumour (HOCT) can sometimes have renal vein infiltration?**

**a. True**
**b. False**

Correct answer: a

 