

## CASE REPORT

# Association of angiomyolipoma and oncocytoma of the kidney: a case report and review of the literature

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**Aim:** The association between renal carcinoma and angiomyolipoma is rare. Only 14 cases have been reported in the literature. The purpose of this paper is to present an additional case and review the literature on this association.

**Patient and methods:** A healthy 42 year old woman was found to have a left flank mass incidentally when she presented for a Papanicolaou smear. The computerised tomography scan revealed a left lower pole renal mass consistent with a renal cell carcinoma. A nephrectomy was performed and the patient recovered uneventfully. The nephrectomy specimen was processed routinely. In addition to haematoxylin and eosin staining, immunohistochemistry for CAM 5.2, vimentin, CD34, antismooth muscle actin, and HMB45 was carried out. Transmission electron microscopy was also performed.

**Results:** Macroscopically, the lower pole of the kidney contained a well circumscribed, non-encapsulated, tan coloured tumour with a large area of central haemorrhage measuring 10.5 cm. In addition, there was a 0.4 cm poorly circumscribed unencapsulated yellow nodule adjacent to the tumour. Microscopically, the larger tumour showed characteristic features of an oncocytoma. Numerous mitochondria were seen on electron microscopy. The smaller yellow nodule was an angiomyolipoma.

**Conclusions:** This paper presents an additional case of oncocytoma associated with angiomyolipoma. Of the 15 cases described in the literature, three were associated with the tuberous sclerosis complex, all from a single study. In tuberous sclerosis, angiomyolipomas are more commonly associated with renal cell carcinoma. If angiomyolipomas are found incidentally in nephrectomy specimens together with other tumours, it is important to exclude tuberous sclerosis retrospectively.

The association between renal oncocytoma and angiomyolipoma is rare. To the best of our knowledge, only 15 cases have been reported in the literature (including our present case).<sup>1–7</sup> In the case described by Schneck *et al* the oncocytoma was present in a partial left nephrectomy specimen. The right nephrectomy specimen showed a transitional cell carcinoma involving the pelvis and calyceal system, with an incidental cortical angiomyolipoma.<sup>3</sup> Jimenez *et al* reported five cases, and one of these patients had multiple oncocytomas (oncocytosis).<sup>7</sup> Oncocytomas have also been associated with cortical adenomas and renal cell carcinoma, whereas angiomyolipomas have been associated with renal cell carcinomas, a papillary adenoma, and a metanephric adenoma.<sup>2,7,8</sup>

## CASE REPORT

A 42 year old asymptomatic woman presented for a routine Papanicolaou smear and was incidentally found to have a left abdominal mass. She was unaware of the mass and denied



**Figure 1** Computed tomography scan of the abdomen showing a large left renal neoplasm.

any pain, haematuria, or loss of weight. There was no significant medical history, specifically seizures or mental retardation. On examination, the head, neck, heart, and lungs were normal. Neurological testing gave normal results. Abdominal examination demonstrated a left flank mass that was firm and moved late on respiration. Creatinine, electrolytes, and haemoglobin were normal. The chest x ray was normal. Ultrasound showed an 11 cm mass in the left lower pole of the kidney with no associated adenopathy. Computerised tomography with contrast enhancement confirmed these findings and also found the left renal vein to be clear of tumour (fig 1). The right kidney was unremarkable radiographically. A working diagnosis of renal cell carcinoma was made.

Left radical nephrectomy was performed and the patient recovered uneventfully.

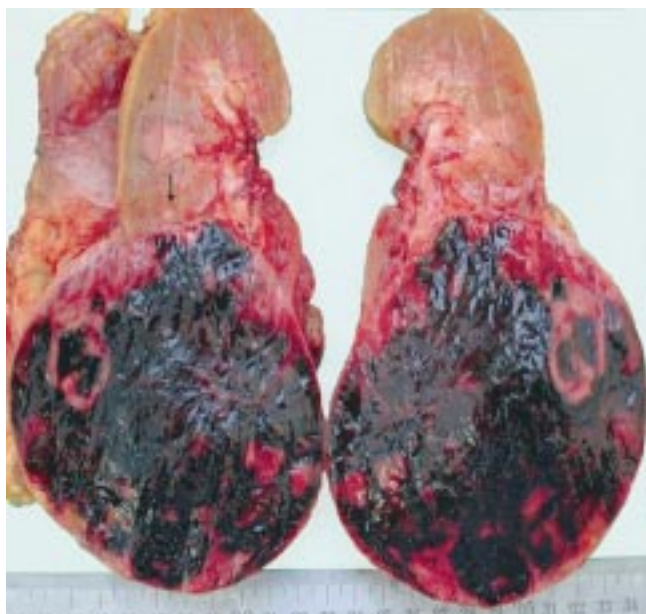
## METHODS

The nephrectomy specimen was fixed in 10% buffered formalin and processed in a routine manner. Immunohistochemistry was performed on the formalin fixed, paraffin wax embedded tissue using the streptavidin biotin complex technique after microwave retrieval. The following antibodies were used: CAM 5.2 (dilution, 1/20; monoclonal; Becton Dickinson, Oxford, UK), Vimentin (dilution, 1/300; monoclonal; Dako, Glostrup, Denmark), antismooth muscle actin (dilution, 1/500; monoclonal; Dako), anti-CD34 (dilution, 1/50; monoclonal; Dako), and HMB45 (dilution, 1/50; monoclonal; Dako). In addition, transmission electron microscopy was performed.

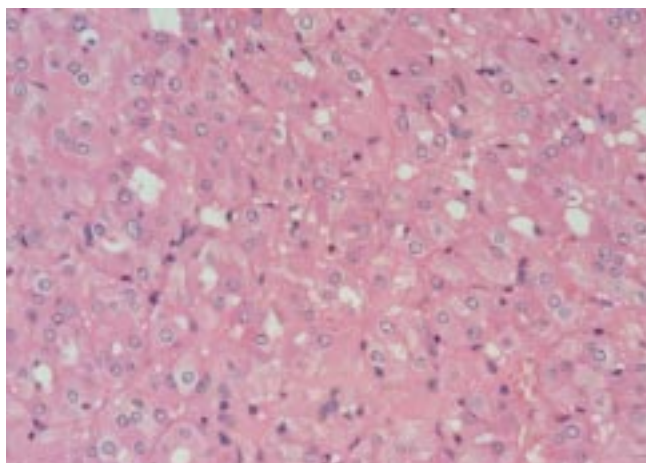
## PATHOLOGICAL FINDINGS

### Macroscopic findings

A nephrectomy specimen measuring 18 × 11 × 8 cm and weighing 726 g was received. On sectioning, in the lower pole



**Figure 2** Bisected nephrectomy specimen showing a large well circumscribed, tan coloured oncocytoma with a large area of central haemorrhage. A much smaller yellow nodule, the angiomyolipoma, is present superiorly (arrow).

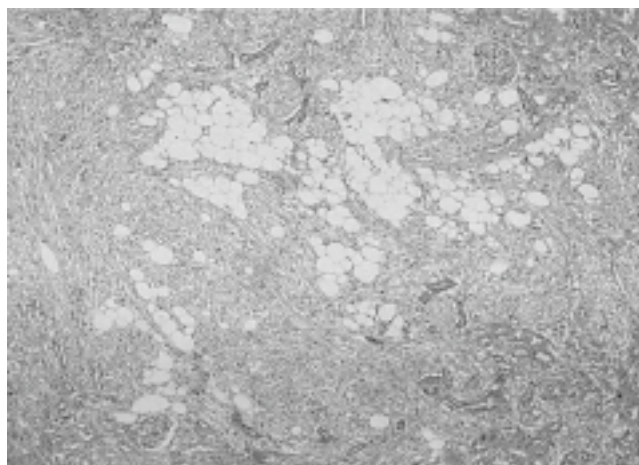


**Figure 3** Oncocytoma displaying compact tubules with polygonal cells showing eosinophilic cytoplasm and uniform nuclei (haematoxylin and eosin stain).

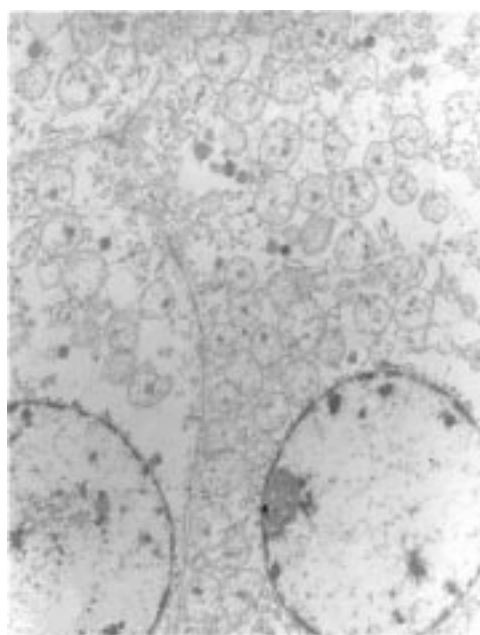
of the kidney, there was a well circumscribed, non-encapsulated, tan coloured tumour, with a large central area of haemorrhage, measuring 10.5 cm in diameter. There was no evidence of necrosis, perirenal fat involvement, or involvement of the renal vein. In addition, there was a 0.4 cm poorly circumscribed unencapsulated yellow nodule adjacent to the tumour (fig 2).

#### Microscopic findings

Sections of the kidney showed a well circumscribed tumour composed of cells with abundant granular eosinophilic cytoplasm growing in a tubular manner (fig 3). The nuclei were small, round, and regular with a centrally placed nucleolus. Focal nuclear pleomorphism was noted, although there were no mitotic figures present. There was no evidence of a papillary architecture, areas of clear cell carcinoma, or sarcomatoid or spindle cell areas. There were areas of stromal hyalinisation, myxoid change, and haemorrhage, but there was no evidence of necrosis. The tumour cells were positive with CAM 5.2 and negative for vimentin.



**Figure 4** Angiomyolipoma showing an admixture of mature adipose tissue, smooth muscle, and vessels (haematoxylin and eosin stain).



**Figure 5** Electron microscopy: oncocytoma showing abundant mitochondria within the cytoplasm of the cells (original magnification,  $\times 5000$ ).

The adjacent renal parenchyma showed a non-encapsulated, irregular tumour displaying mature adipose tissue, smooth muscle, and blood vessels (fig 4). The last two components were highlighted by the antismooth muscle actin and CD34 immunostains, respectively. The smooth muscle component showed some nuclear pleomorphism and hyperchromasia. The features were those of a renal angiomyolipoma. The HMB45 stain was negative in this case.

#### Electron microscopy

The cytoplasm of the cells in the larger tumour was filled with mitochondria (fig 5). The diagnosis of an oncocytoma was made.

#### LITERATURE REVIEW

Table 1 lists the available details of the other published cases.

#### DISCUSSION

Renal oncocytomas, first described by Zippel in 1942,<sup>9</sup> are benign, relatively uncommon neoplasms accounting for 3–5% of renal parenchymal tumours.<sup>6</sup> Most of these tumours are

**Table 1** Age, sex, and association with tuberous sclerosis of the 15 patients with angiomyolipoma in association with oncocytoma

Ref	Number	Age	Sex	Tuberous sclerosis
1	1	70	F	No
2	2	NK	F	NK
2	3	NK	F	NK
2	4	NK	F	NK
3	5	69	F	NK
4	6	62	M	No
4	7	42	F	No
5	8	65	F	NK
6	9	69	F	No
7	10	54	F	No
7	11	NK	NK	No
7	12–14	NK	NK	Yes
Our case	15	42	F	No

NK, not known.

single and unilateral, although bilateral and multifocal cases have been described.<sup>10–11</sup> The characteristic histological features of oncocytomas are the dense eosinophilic cytoplasm, which may be exclusively or predominantly granular, generally uniform nuclei, and abundant mitochondria.<sup>10–11</sup> The cell of origin is the intercalated cell of the cortical portion of the collecting tubule.<sup>12–13</sup> Surgical excision/nephrectomy remains the treatment of choice because there is no definite preoperative method of identifying these tumours.<sup>14–15</sup>

Renal angiomyolipomas are uncommon neoplasms accounting for less than 1% of surgically removed tumours.<sup>6</sup> However, they are the most common mesenchymal tumour of the kidney and are characterised by the presence of a variable mixture of mature adipose tissue, blood vessels, and smooth muscle.<sup>16</sup> The perivascular epithelioid cell is thought to be the cell of origin of angiomyolipomas.<sup>17</sup> Although renal angiomyolipomas, like other tumours derived from the perivascular epithelioid cell, are characteristically positive for HMB-45, a small proportion of these tumours do not stain with this antibody.<sup>18–19</sup> Renal angiomyolipomas are commonly associated with tuberous sclerosis, which is an autosomal dominant disorder characterised by seizures, mental retardation, skin lesions, and hamartomatous lesions in many organs. Rarely, angiomyolipomas can be associated with von Hippel-Lindau disease, von Recklinghausen syndrome, and autosomal dominant polycystic kidney disease.<sup>20–21</sup> However, most angiomyolipomas occur sporadically.<sup>20</sup> In tuberous sclerosis, angiomyolipomas are found predominantly in women in the third and fourth decades of life and they tend to be asymptomatic, small, multifocal, and bilateral. In sporadic cases, they are seen in 40 to 70 year old women and are usually larger, symptomatic, single, and unilateral.<sup>22</sup>

In a series of 36 cases of concurrent angiomyolipoma and renal cell neoplasia reported by Jimenez *et al*, the median size of angiomyolipomas was 0.5 cm in the sporadic cases and 3 cm in those patients with tuberous sclerosis. In both clinical settings, angiomyolipomas were more commonly the incidental finding. The mean ages of the patients with sporadic and tuberous sclerosis tumours were 59 and 53 years, respectively.<sup>7</sup> These findings are in contrast to previously published reports in which the patients with tuberous sclerosis were significantly younger at presentation.<sup>8</sup>

“Renal angiomyolipomas are commonly associated with tuberous sclerosis, which is an autosomal dominant disorder characterised by seizures, mental retardation, skin lesions, and hamartomatous lesions in many organs”

Although, the presence of fat in angiomyolipomas may aid in the radiological diagnosis, these tumours can still mimic a

### Take home messages

- This is only the 15th case of oncocytoma associated with angiomyolipoma to be reported
- Although our case did not occur in the setting of the tuberous sclerosis complex three of the previously reported cases have done so
- In tuberous sclerosis, angiomyolipomas are more commonly associated with renal cell carcinoma
- If angiomyolipomas are found incidentally in nephrectomy specimens removed because of the presence of other tumours it is important to exclude tuberous sclerosis retrospectively

renal cell carcinoma, particularly if the fat content is low or if the fat is obscured by blood.<sup>1</sup> Interestingly, Martignoni *et al* described two cases of oncocytoma-like angiomyolipomas in a 56 year old woman and a 35 year old man measuring 2.5 cm and 5 cm, respectively. These tumours were composed of sheets of deeply eosinophilic cells with no fascicles of smooth muscle, tortuous blood vessels, or fat cells. The tumour cells were positive for HMB-45 and negative for epithelial markers. In addition, the first patient had an incidental subcapsular 5 mm renal angiomyolipoma. No signs of tuberous sclerosis were found in either patient. These authors suggested that in some of the reported cases of simultaneous oncocytoma and angiomyolipoma, the oncocytoma may in fact be an oncocytoma-like angiomyolipoma.<sup>23</sup> This may also be the case in a few reported cases of oncocytoma not associated with angiomyolipoma arising in patients with tuberous sclerosis.<sup>24–25</sup>

In cases where the relevant information was available, the age of the patients with concurrent angiomyolipoma and oncocytoma ranged from 42 to 70 years. Most cases occurred in women with only one case occurring in a man. Our patient was a 42 year old woman, which fits in with this profile. As mentioned previously, angiomyolipomas with or without associated tuberous sclerosis tend to occur in woman; however, oncocytomas are more common in men, with a male to female ratio of 2–3 : 1.<sup>1–7–14</sup> Therefore, the observation that coexistent angiomyolipomas and oncocytomas are found more frequently in women is consistent with the higher incidence of angiomyolipomas in women. In three of the 15 cases, there was a documented association with tuberous sclerosis.<sup>7</sup>

Of note, 15 of the 42 reported cases of angiomyolipoma in association with renal cell carcinoma occurred in patients known to have tuberous sclerosis.<sup>7–8–26–28</sup>

The size of both tumours varied greatly and in some patients the presence of two tumours was not detected preoperatively.<sup>1–3</sup> In patients where the preoperative radiography was described, the presence of renal cell carcinoma could not be excluded.

In our case, the angiomyolipoma was only 0.4 cm. In the series reported by Jimenez *et al* the median size of the sporadic angiomyolipomas was 0.5 cm and in the tuberous sclerosis category the size ranged from 0.2 cm to 9 cm.<sup>7</sup> These figures highlight the fact that these tumours may be very small and thorough examination of the nephrectomy specimen is required for their detection.

In conclusion, we present an additional case of an oncocytoma associated with an angiomyolipoma. Our case did not occur in the setting of tuberous sclerosis. Of the 15 cases that have been described, there are three documented cases associated with the tuberous sclerosis complex, all from a single study. In tuberous sclerosis, angiomyolipomas are more commonly associated with renal cell carcinoma. If angiomyolipomas are found as an incidental finding in nephrectomy specimens along with other tumours, it is important to exclude tuberous sclerosis retrospectively.



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