CASE REPORT

Pulmonary metastasis from renal epithelioid angiomyolipoma in the setting of breast cancer

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SUMMARY

A 68-year-old woman presented with visible haematuria. Ultrasonography and triphasic CT revealed a 2.6 cm mass in the lower pole of the left kidney. A biopsy suggested low-grade renal cell carcinoma. Radical nephrectomy was performed and revealed an epithelioid angiomyolipoma. At year 3, the patient developed ductal carcinoma of the right breast and underwent a wide local excision and sentinel lymph node biopsy followed by chemotherapy and radiotherapy. 4 months later, she was noted to have a 1.6 cm nodule in the middle lobe of her right lung. The primary differential diagnosis was a breast cancer metastasis. Biopsy revealed a metastatic renal epithelioid angiomyolipoma. The patient elected to have stereotactic radiotherapy over surgical excision. Renal angiomyolipomata are generally regarded as benign tumours. In the present report, we describe the first case of pulmonary metastasis from renal epithelioid angiomyolipoma in the setting of breast cancer.

BACKGROUND

Angiomyolipomata (AMLs) are generally regarded as benign tumours composed of fat, muscle and blood vessels. The diagnosis relies on identifying fat in the tumour on imaging. Indications for intervention include bleeding, pain, suspicion of malignancy or prophylactic intervention in women of childbearing age.¹ Two histological variants exist; classic and epithelioid. The more aggressive epithelioid subtype is significantly less common, accounting for 4.6% of AMLs.² It is considered to be a potentially malignant tumour. Patients found to have an AML following nephrectomy for suspected renal cell carcinoma are often discharged or undergo surveillance imaging on an annual basis.

Figure 1 Triple phase CT (coronal) demonstrating left renal mass.

Figure 2 Triple phase CT (axial) demonstrating left renal mass.

This study presents a case of pulmonary metastasis from renal epithelioid AML after 3 years of follow-up in the setting of a secondary malignancy which commonly metastasises to lungs.

CASE PRESENTATION

A 68-year-old woman presented with a 6-week history of painless, visible haematuria. She was a non-smoker. She had no medical history of note and was taking no regular medications. There was no family history of tuberous sclerosis. Examination was unremarkable. Routine bloods, including haemoglobin, and renal function were within normal limits. Urine culture and sensitivity yielded no growth. No cause for haematuria was identified on cystoscopy.

Figure 3 Renal biopsy; cells demonstrating coarse chromatin, with occasional conspicuous nucleoli. Minimal cytological atypia is present.

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Figure 4 Renal biopsy; cells were positive for vimentin and negative for CK7, S100 and CD 117.

Ultrasonography revealed a 2.6 cm mass in the lower pole of the left kidney. This lesion demonstrated low attenuation on triple phase CT imaging (figure 1, figure 2).

A renal biopsy was performed and comprised a core of renal parenchyma partially replaced by a lesion. The biopsy was composed of sheets of epithelioid cells, with prominent, granular, eosinophilic cytoplasm. The lesional cells had coarse chromatin, with occasional conspicuous nucleoli. Minimal cytological atypia was present (figure 3). The lesional cells were positive for vimentin and negative for CK7, S100 and CD117 (figure 4). The morphological and immunohistochemical features were of an epithelioid neoplasm, favouring low-grade renal cell carcinoma.

A radical nephrectomy was performed and showed the presence of a relatively well-circumscribed 6.5 cm yellow and tan lesion (figure 5). The tumour did not extend into perinephric fat or into the renal sinus fat. Histology showed a proliferation of epithelioid cells arranged in sheets (figure 6) and evidence of dystrophic vessels (figure 7). The tumour cells were round

Figure 5 Radical left nephrectomy specimen demonstrating a well-circumscribed 6.5 cm yellow and tan lesion.

Figure 6 Left kidney; histology showing a proliferation of epithelioid cells arranged in sheets.

to polygonal with abundant granular, eosinophilic cytoplasm. The cells had enlarged vesicular nuclei and conspicuous nucleoli (figure 8). Mitotic count was 1 per 10 high-power field (HPF). Microscopic venous invasion and focal necrosis were present. Immunohistochemistry showed focal positivity for Melan A and calponin. The lesional cells were negative for HMB-45 and cytokeratins (AE1/3, Ker903) (figure 9). Smooth muscle actin immunohistochemical staining was negative in tumour cells and positive in dystrophic vessels (figure 10). PAX-8 and TFE3/TFEB translocation studies were all negative. The features were those of epithelioid AML, confined to the kidney. Six regional lymph nodes were negative for malignancy.

At year 3 postnephrectomy, she developed invasive ductal carcinoma of the right breast. CT thorax at the time of diagnosis was negative for metastatic disease. The tumour was oestrogen receptor positive, progesterone receptor positive and HER2 negative. The Ki67 labelling index was <15%. The patient underwent wide local excision and sentinel lymph node biopsy followed by chemotherapy and radiotherapy. Four months later, she was noted to have a 1.6 cm nodule in the middle lobe of her right lung on CT imaging (figure 11).

Figure 7 Left kidney; histology showing dystrophic vessels.

Figure 8 Left kidney; tumour cells were round to polygonal with abundant granular, eosinophilic cytoplasm. The cells had enlarged vesicular nuclei and conspicuous nucleoli.

INVESTIGATIONS

This patient had a recent history of two distinct tumours with the potential to metastasise to the lung. Following discussion at a multidisciplinary team meeting, the decision to proceed to a lung biopsy was taken to determine the patient's suitability for certain management options, including chemotherapy, radiotherapy, targeted therapy and metastasectomy. Biopsy of the right middle lobe of the lung showed fragments of alveolated lung parenchyma infiltrated by an epithelioid tumour with histological features similar to the previously resected renal epithelioid AML (figure 12). A small biopsy fragment encompassed 4 high power fields and no mitoses were seen but this was likely not representative. Immunohistochemistry showed that the tumour cells were positive for Melan-A and negative for HMB-45, AE1/3 and TTF-1 (figure 13). The features were consistent with metastatic epithelioid AML.

DIFFERENTIAL DIAGNOSIS

The case was discussed at a multidisciplinary team meeting prior to a biopsy. At that time the differential diagnosis included an

Figure 9 Left kidney; Microscopic venous invasion and focal necrosis were present. Immunohistochemistry showed focal positivity for Melan A and calponin. The lesional cells were negative for HMB-45 and cytokeratins (AE1/3, Ker903).

Figure 10 Smooth muscle actin staining negative in tumour cells.

inflammatory mass, metastasis related to ductal carcinoma of the breast or, less likely, a metastasis related to epithelioid AML.

TREATMENT

The patient elected not to undergo surgical excision of the metastasis and treatment with a mechanistic target of rapamycin inhibitor. Instead the patient was treated with stereotactic radiotherapy.

OUTCOME AND FOLLOW-UP

Management with radiotherapy is ongoing at the time of the case report.

DISCUSSION

AMLs characteristically arise as solitary lesions in middle-aged females. They may be sporadic or occur in association with tuberous sclerosis complex. Two histological variants exist; classic and epithelioid. The liver and lung are the most commonly reported sites of metastasis.³ The incidence of metastatic disease from epithelioid AMLs is 5%.²

Classic AMLs are typically identifiable radiologically by the presence of fat in the tumour, however the epithelioid subtype are often fat-poor on imaging and can mimic renal cell carcinoma.⁴ Liu *et al*⁴ reported that epithelioid AMLs display hyperdensity on unenhanced CT with or without fat component and demonstrate rapid wash-in to slow wash-out dynamic enhancement

Figure 11 CT thorax demonstrating 1.6 cm nodule in the middle lobe of the right lung.

Figure 12 Lung biopsy demonstrating fragments of alveolated lung parenchyma infiltrated by an epithelioid tumour with histological features similar to the previously resected renal epithelioid angiomyolipoma.

pattern. They recommended consideration of epithelioid AML in the differential diagnosis of a fatty renal mass containing large amounts of soft tissue.⁴ Brimo *et al*⁵ suggested that the presence of certain histological findings could predict malignant progression in these tumours. The features they described were atypia in $\geq 70\%$ of the epithelioid cell population, mitotic count greater than 2/10 HPF, presence of atypical mitotic figures and necrosis.⁵ We present a case of an AML demonstrating microscopic venous invasion and focal necrosis, however the mitotic count was 1 per 10 HPF and it did not demonstrate atypia in $\geq 70\%$ of the epithelioid cell population.

He *et al* described a series of 437 renal AMLs.² An epithelioid component was found in 20 cases (4.6%) and one (5%) of these patients developed metastatic disease after a mean follow-up of 82.5 months.² Cusano *et al*⁶ described an interesting case of a 68-year-old female with simultaneous presentation of renal epithelioid AML and ductal carcinoma of the

breast. They described nodal and liver metastases from the AML at the time of presentation.⁶ In contrast, we present the case of a 68-year-old woman who developed ductal carcinoma of the breast 3 years post resection of an AML and subsequently developed pulmonary metastasis related to the AML. In both cases, the breast cancer was oestrogen receptor positive. The female preponderance in AMLs is associated with the high prevalence of oestrogen receptor immunoreactivity.⁷ Cho *et al*⁷ reported a 4.4% incidence of ductal carcinoma of the breast in their AML series. There are two reported cases of oestrogen receptor-positive ductal breast carcinoma metastasising to renal AMLs.^{8,9}

Our case presentation is particularly unique as we describe the first case of pulmonary metastasis from renal epithelioid AML in the setting of breast cancer.

Learning points

- ▶ While angiomyolipomata (AMLs) are generally regarded as benign tumours, the epithelioid subtype is a potentially malignant tumour. Epithelioid AMLs are often fat-poor on imaging and can be mistaken for renal cell carcinoma.
- ▶ Epithelioid AML must be considered in the differential diagnosis of epithelioid renal tumours that are PAX-8 negative.
- ▶ Oestrogen receptor is significantly associated with epithelioid AMLs.

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Competing interests None declared.

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Figure 13 Lung biopsy; immunohistochemistry showed that the tumour cells were positive for Melan-A and negative for HMB-45, AE1/3 and TTF-1.

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