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CASE REPORT

Loss of intratumoral macroscopic fat in renal angiomyolipoma following chemoradiation therapy for pancreatic cancer

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ABSTRACT

Angiomyolipoma (AML) is the most common benign mesenchymal tumour of the kidney. Classically, AML can readily be diagnosed by identifying the negatively attenuating intratumoral macroscopic fat component on non-enhanced CT scans. However, intratumoral macroscopic fat may not be visible on CT scans, mimicking renal cell carcinoma. We report a case of renal AML with CT scan evidence of macroscopic intratumoral fat that was not readily visible on subsequent CT or MRI, presumably owing to a generalized rapid loss of adipose tissue due to cachexia in a patient with pancreatic adenocarcinoma. Radiologists should be aware that AML may lose its intratumoral fat on follow-up imaging and may simulate renal cell carcinoma.

CASE REPORT

A 64-year-old female with newly diagnosed Stage 1B pancreatic adenocarcinoma was treated by neoadjuvant gemcitabine chemotherapy and radiation, followed by a Whipple procedure at an outside institution 1 month after the completion of neoadjuvant therapy, resulting in a substantial weight loss of 40 pounds (18 kg). The patient was admitted to our institution with dizziness and hypotension.

A contrast-enhanced CT scan of the abdomen was performed with a 16-slice multidetector CT scanner (Somatom Sensation 16, Siemens Medical Solutions, Forchheim, Germany) using a routine single-phase abdomen and pelvis protocol in the portal venous phase after administration of 125 ml of iohexol 350 mg ml⁻¹ (Omnipaque 350, GE Healthcare, Milwaukee, WI) at a rate of 3 ml s⁻¹ with 5 mm slice thickness and 120 kV. The contrast-enhanced CT scan revealed an incidental solid enhancing mass measuring 2.5 cm in diameter in the lower pole of the left kidney, which was suspicious for renal cell carcinoma (RCC; [Figure 1](#)). On comparison with pre-treatment imaging performed 9 months earlier, the mass corresponded to a 3.0 cm lesion ([Figure 2](#)) that demonstrated regions of negative attenuation (−39 Hounsfield units), characteristic of intratumoral fat and consistent with angiomyolipoma (AML). The subcutaneous fat thickness seen on the post-chemotherapy CT scan was 1.0 cm, compared with

2.5 cm on the pre-treatment CT scan, and consistent with the substantial reported weight loss. Several CT and MR examinations of the abdomen were subsequently performed for various reasons unrelated to the AML, demonstrating continued decrease in the size of the mass, reaching a size of 2.0 cm. The intratumoral fat component remained imperceptible on imaging, including an MR of the abdomen performed more than 2 years after the initial CT ([Figure 3](#)) and an unenhanced CT that had shown minimal hyperattenuation of the mass compared with the surrounding parenchyma ([Figure 4](#)).

DISCUSSION

Although it constitutes only 1–2% of all tumours seen in the kidney, renal AML is the most common benign renal neoplasm, comprising variable amounts of abnormal blood vessels, smooth muscle and adipose tissue.¹ While AML most commonly occurs sporadically, up to 20% can occur in association with the tuberous sclerosis complex.² AML is typically diagnosed incidentally in patients undergoing imaging work-up for other diseases.³ Demonstration of negatively attenuating intratumoral fat on unenhanced CT scans usually provides pathognomonic evidence of AML and virtually excludes the diagnosis of RCC,⁴ although fat-containing RCCs have been rarely described when the RCC engulfs normal adjacent renal sinus or perinephric fat, when osseous metaplasia results in marrow content

Figure 1. Contrast-enhanced CT scan of the abdomen and pelvis following treatment for pancreatic adenocarcinoma showing an enhancing lesion at the lower pole of the left kidney measuring 2.5 cm (large arrow). Evidence of macroscopic fat suggesting angiomyolipoma is not readily identified, likely owing to significant loss of fat (small arrowhead).



without ossification or when cholesterol necrosis mimics the presence of true adipose tissue.⁵ Other rare renal tumours may also contain fat and mimic the appearance of AMLs, such as Wilms tumours, liposarcomas, oncocytomas and solitary fibrous

tumours.^{4,6} However, in rare cases, the tumour may be composed mostly of smooth muscle and blood vessels, with only a minimal amount of mature adipose tissue that is not detected on CT scans. These minimal fat renal AMLs contain only 3–10% mature adipose tissue^{2,7} and pose a diagnostic dilemma for even experienced radiologists.⁸ Minimal fat renal AML and RCC, mostly clear cell and papillary RCCs, but also the more rare chromophobe and sarcomatoid RCCs, can have similar imaging appearances on CT scans, particularly when small in size (< 4 cm).⁹ Since small renal AMLs measuring < 4 cm have traditionally been managed conservatively based on their lack of malignancy and decreased propensity for haemorrhage, and masses > 4 cm may undergo selective embolization rather than partial or radical nephrectomy, distinguishing renal AML from RCC is critical in clinical management.¹⁰

Several different imaging parameters and techniques have been investigated to distinguish minimal fat renal AML from RCC using CT and MR, but none have proven conclusive thus far.¹¹ On unenhanced CT scans, minimal fat AMLs have typically been described as homogeneous and hyperattenuating when compared with surrounding renal parenchyma,^{12,13} with tumour-to-cortex attenuation ratio significantly higher for minimal fat AML compared with clear cell and papillary RCCs, but not significantly different from the ratio in other types of RCC.⁷ This lack of specificity precluded this finding from being used as a reliable differentiating factor between benign and malignant tumours. Homogeneity of tumour enhancement and a prolonged enhancement pattern are the most valuable CT findings for differentiating minimal fat AML from RCC,¹² but are also not reliable enough. CT attenuation histogram analysis using pixel distribution analysis and counts of negative attenuation pixels has shown mixed results.^{14–16} CT texture analysis has shown promise in differentiating minimal fat AML from RCC¹⁷ but has not been studied

Figure 2. (a) Unenhanced and (b) contrast-enhanced CT scans of the abdomen and pelvis before treatment for pancreatic adenocarcinoma shows an incidental 3.0 cm lesion at the lower pole of the left kidney with areas of fat attenuation (large white arrows), consistent with angiomyolipoma. The contrast-enhanced CT scan shows the pancreatic head mass from adenocarcinoma (black arrowhead). A noteworthy feature is the abundance of subcutaneous fat compared with imaging done after treatment (small white arrowheads).

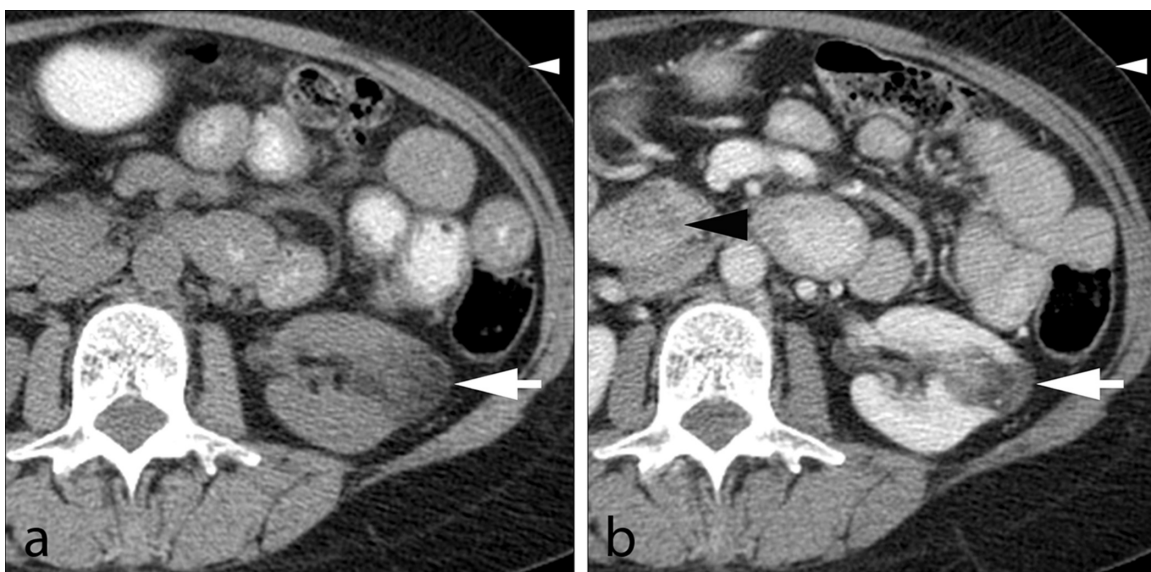
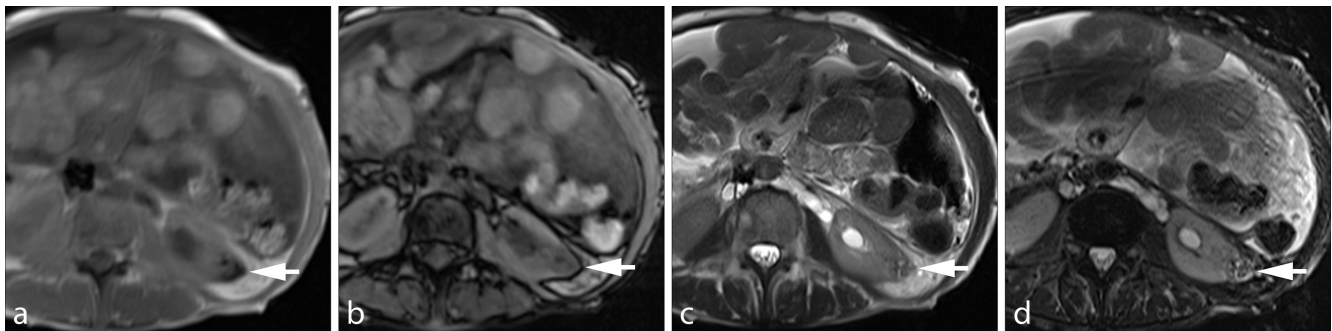


Figure 3. An MR examination more than 2 years after the initial CT scan shows the angiomyolipoma (arrows) with lack of microscopic intratumoral fat on the in-phase (a) and opposed-phase images (b). A small focus of low signal intensity seen on both images may relate to haemosiderin. In addition, T_2 weighted images without (c) and with fat suppression (d) demonstrate the lack of macroscopic intratumoral fat.



sufficiently. Zhang et al¹⁸ used CT parameters such as unenhanced attenuation characteristic, intratumoral vessels, and attenuation values of unenhanced and early excretory phase scans to differentiate minimal fat AML from papillary RCC. While other reports have shown that CT and MR can aid in distinguishing clear cell RCC from minimal fat AML,^{14,19} Hindman et al¹¹ have shown that differentiation between minimal fat AML and clear cell RCC often is not possible on the basis of MR alone, and others have shown that the MR appearance of minimal fat AML and papillary RCC overlap.⁷

We present a case of renal AML in which CT evidence of intratumoral macroscopic fat disappeared on subsequent imaging, presumably owing to rapid interval loss of large amounts of

adipose tissue due to cancer cachexia. A serious side effect of malignancy occurring in nearly half of cancer patients, cachexia is a multifactorial syndrome characterized by depletion of > 10% body weight, loss of adipose tissue and skeletal muscle mass, and alterations in metabolic homeostasis.²⁰ While the mechanisms for muscle degradation in cancer cachexia have been well studied,²¹ the mechanisms behind adipose tissue loss are only recently being elucidated. Activation of the acute phase response cascade²² and enhanced expression and function of adipocyte hormone-sensitive lipase²³ have recently been proposed as the primary mediators of fat loss in cancer cachexia. Combined with an elevated resting energy expenditure and lower oral food intake,²⁴ pancreatic cancer cachexia produces a dramatic reduction in body fat with a nearly twofold increase in lipolytic activity mediated by hormone-sensitive lipase.²³ The patient's significant weight loss and loss of measurable adipose tissue are readily identified on CT scans prior to and following neoadjuvant chemoradiation therapy (Figures 1 and 2).

This case also illustrates the importance of comparison with previous imaging studies before planning for intervention in a solid renal mass. Although the morphology of solid renal masses may vary over time with changes in enhancement pattern or development of regions of necrosis, loss of macroscopic fat in a solid renal tumour has not been reported to our knowledge. Review of prior imaging studies in patients with solid renal masses concerning for RCC, especially when patients have a known malignancy or report marked weight loss, may help detect prior presence of intratumoral macroscopic fat to avoid misdiagnosing AML as RCC.

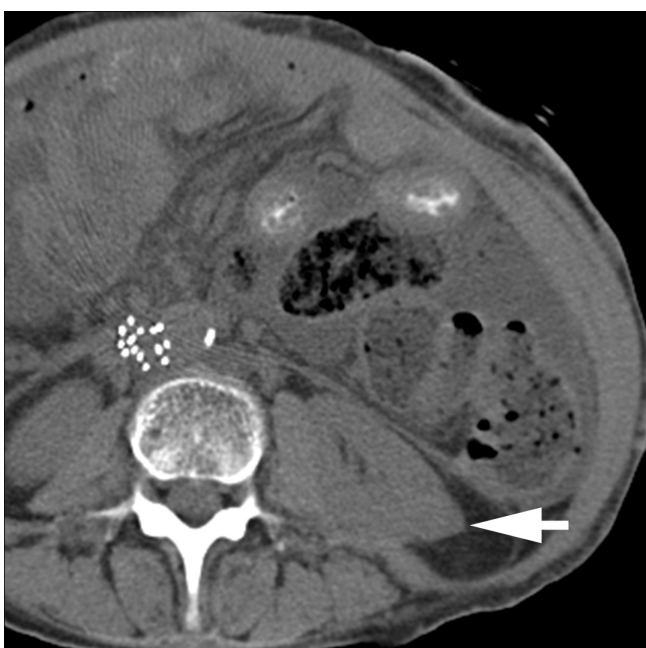
LEARNING POINTS

1. Renal masses that lack fat may nonetheless be AMLs.
2. The loss of macroscopic fat in a solid renal tumour may be caused by rapid weight loss related to cancer or chemoradiation therapy.
3. It is important to review old scans, if available, to assess for the presence of intratumoral macroscopic fat to avoid misdiagnosis of AML as RCC.

CONSENT

This paper has been sufficiently anonymized to protect patient identify. Despite multiple attempts, informed consent could not be obtained.

Figure 4. An unenhanced CT scan performed almost 2 years after the initial CT scan shows that the mass has homogeneous attenuation (arrow), with minimal hyperattenuation of the lesion (35 Hounsfield units) compared with the surrounding renal parenchyma (32 Hounsfield units), with attenuation ratio of 1.09.



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