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Is the follow-up of small renal angiomyolipomas a necessary precaution?

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AIM: To investigate the natural history and rationalize follow-up of renal angiomyolipomas (AMLs).

MATERIALS AND METHODS: A prospectively gathered radiology database was scrutinized to identify patients with renal AMLs over a 3 year period (January 2006 to December 2008). Radiological investigations were examined to identify those AMLs exhibiting change during surveillance.

RESULTS: A total of 135 patients were identified. Mean age at first detection was 49.6 years and patients were followed up for a median 21.8 months (6–85.3 months). Small AMLs (≤20 mm) were less likely to grow than their larger counterparts [odds ratio 13.3, confidence interval (95% CI) 1.4–123.9, $p = 0.02$] and exhibited a slower growth rate (0.7 versus 9.2 mm/year). Patients with AMLs that increased in size were significantly younger (median age 43 versus 52 years, $p < 0.001$). Multiple AMLs or those associated with genetic conditions grew at a significantly greater rate (3 versus 0.1 mm/year, $p < 0.001$). AMLs with a large extra-renal component are less reliably measured on ultrasound (median error 7 versus 1 mm, $p < 0.001$).

CONCLUSION: This is the first study with the primary purpose to investigate growth of small AMLs (≤20 mm). Small, solitary AMLs (≤20 mm) do not require follow-up due to their low probability of growth. Patients with multiple AMLs and younger patients require closer monitoring due to their comparatively greater AML growth rate. Ultrasound-detected AMLs with an extra-renal component may require computed tomography (CT) to confirm their size.

Introduction

Renal angiomyolipoma (AML) is the most common benign renal neoplasm with an incidence of 0.1–0.3%.[1] Most often they are incidental findings on abdominal ultrasound or computed tomography (CT).[2] Their diagnosis has become more frequent with advances in ultrasound imaging, enabling the detection of smaller and more subtle AMLs.[3]

Renal AMLs >4 cm have a significant risk of bleeding. When haemorrhage occurs it can be sudden and catastrophic, with one-third of patients presenting in hypovolaemic shock.[3,4] Despite this, little is known about the natural history of renal AMLs.[5] It can only be assumed larger, potentially symptomatic AMLs developed from smaller lesions. Therefore, the rationale behind follow-up of small AMLs is to monitor their growth and identify those at risk of becoming symptomatic. However, as the natural history of small AML is poorly understood, it is currently not known whether their risk of growth is significant enough to warrant surveillance.

Despite a wealth of recommendations outlining treatment of larger AMLs,[4–6] no current guidelines exist with

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regard to follow-up of small lesions, which are potentially clinically insignificant. This ambiguity can lead to unnecessary monitoring of AMLs with a negligible threat of complication, a cost to radiology and urology departments in terms of both time and resources. A recent review article[5] made recommendations regarding follow-up of small AMLs based on a paper from 1986,[6] when imaging equipment was not at the current standard. This highlights the need for a modern investigation into the natural history of small AMLs on which to base guidelines for their follow-up.

However, factors other than size seem predictive of complications. Some studies have suggested not all AMLs progress in a common fashion. AMLs found in patients with multiple AMLs seem to progress more rapidly.[7,8] This also holds true for those associated with genetic conditions such as tuberous sclerosis.[8]

The focus of this paper is AMLs for which a diagnosis has assuredly been made. It does not refer to lesions that raise any suspicion of renal cell carcinoma as these need careful consideration and potentially further investigation before making a distinction.[9]

The present study aims to address three main issues: first, to explore whether a correlation exists between AML size and probability of growth. Do all small AMLs have the potential to become large, symptomatic lesions? The second aim is to identify whether AMLs exhibiting a higher rate of growth can be identified by any common characteristics. Can we target AMLs at higher risk of growth with appropriate follow-up? The third aim is to investigate the reliability of ultrasound when assessing AML size in comparison with CT. Is ultrasound an appropriate technique for follow-up for all AMLs?

Materials and methods

A prospectively gathered radiology database (IMPAX software) was scrutinized, searching for the term "AML" in imaging reports over 3 years between January 2006 to December 2008. Patients were excluded if an alternative diagnosis was made at any stage, if the patient was lost to follow-up, or the AML did not meet the criteria for a "classic AML" based on fat content outlined by Lane et al.[10] Records of all imaging investigations were reviewed and parameters of AMLs were recorded. These parameters included number of AML, size, location within the kidney, description, and radiodensity measurement. Any studies lacking a formal report or mention of size were re-measured by a consultant radiologist. Patient demographics were collected, along with co-morbidities, complications, and treatment of the AML. Only measurements made using a common technique were used to calculate growth, to eliminate disparity in measurement between CT and ultrasound.

To achieve the three main aims, analysis was conducted by three different techniques. First, AMLs were divided into small ($\leq$20 mm), intermediate (20$<\times<$40 mm), and large ($\geq$40 mm) cohorts. AML growth was then compared between these categories, looking specifically at growth rate and the proportion of enlarging AMLs against static AMLs in each group.

To satisfy the second aim of identifying those AMLs at greater risk of growth, patients were divided into two groups; those that grew and those that did not. Patient and AML parameters were compared between the groups to identify characteristics that may help predict which AMLs are at most risk of growth.

To compare ultrasound and CT, the margin of error (mm) for each ultrasound measurement was calculated against a CT reference standard measurement. Comparison was only made if both techniques had been performed $<$12 months apart.

AMLs were classified in relation to the edge of the renal cortex. Grade 1 was an AML well within the cortex. Grade 2 was an AML with a boundary in contact with the edge of the kidney, and grade 3 was an AML with a large component (more than a third its total size) outside of the kidney (Fig 1).

Statistical method

For all statistical tests, data were analysed using IMB SPSS version 19 software. Mann–Whitney *U*-test was employed for comparison of all data, and *p*-values $<$0.05 were considered statistically significant. A simple odds ratio was used to calculate risk of AML growth between groups, $p < 0.05$ being considered significant.

Results

One hundred and thirty-five patients were identified as having AMLs over a 3 year period (January 2006 to December

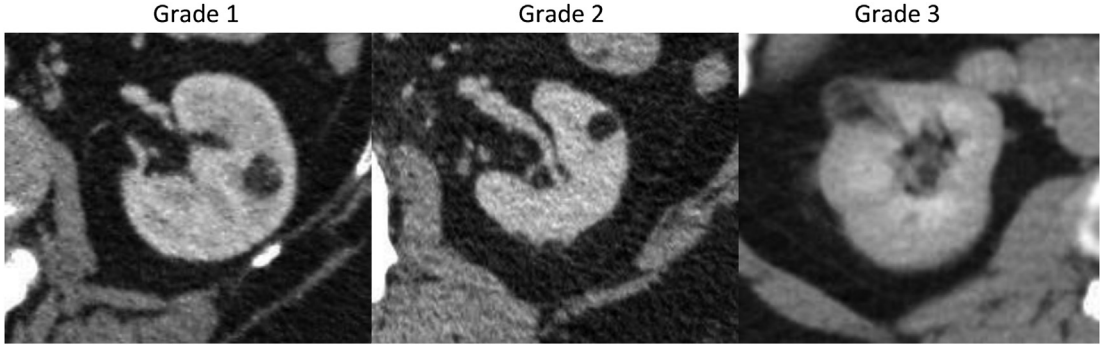

Figure 1 Demonstration of AML grading system.