Perls' positive, and GMS negative staining pattern.^{1–4} Analysis by energy dispersive radiographic microanalysis of two cases^{1,2} showed the pseudofungi contained phosphorus, sulphur, potassium, calcium, and iron, with ultrastructural examination showing that septation was a result of fracturing of the calcified structures. Interestingly, one of these cases also involved nodes associated with resection of a large haemorrhagic gastrointestinal stromal tumour²; other cases have been associated with malignant melanoma^{1,4} and large cell lung carcinoma.³ It is theorised that haemorrhage associated with such tumours may lead to haemosiderin deposition in the draining nodes, with eventual degradation leading to iron deposition on collagen or reticulin fibres.^{2,4} This is supported by the presence of background Perls' positive haemosiderin laden macrophages observed in our case.

Awareness of fungal mimics is important to avoid misdiagnosis of a fungal infection. In addition to histological examination, a panel of special stains should be employed to assist to differentiate fungal organisms from pseudofungi. Our case highlights the strong resemblance of pseudofungi to true fungi, and the utility of special stains for accurate diagnosis.

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Intranuclear inclusions are a distinguishing morphological feature of renal cell carcinoma with leiomyomatous stroma

Sir,

Renal cell carcinoma with leiomyomatous stroma (RCCLMS) is an uncommon neoplasm classified as a provisional entity in the 2016 World Health Organization classification of kidney tumours. The relationship of RCCLMS to clear cell renal cell carcinoma and clear cell papillary renal cell carcinoma remains unclear, although increasing evidence supports it as a distinct entity with a unique molecular profile.¹ In particular, RCCLMS does not appear to harbour alterations in chromosome 3p or the *VHL* gene as seen in conventional RCC.² A recent study showed recurrent mutations of *TSC1/TSC2*, *MTOR*, and/or *TCEB1* genes in all 14

tested cases of RCCLMS,³ supporting the hypothesis that these tumours represent the sporadic counterpart of histologically similar tumours presenting in patients with tuberous sclerosis. Further elucidation of the morphological features of RCCLMS could assist pathologists to identify this rare tumour.

We retrospectively compiled four cases of RCCLMS; three were reported at our institution and one was an external consultation (Table 1). None of the patients had tuberous sclerosis or end stage kidney disease. The tumours were small and confined to the kidney (pT1a), with no recurrence or metastasis documented in the limited follow-up period (<2 years). The morphology and immunohistochemical findings were similar to previously reported cases.¹ The tumours were circumscribed by an irregular pseudocapsule and showed nodules of clear cells with inconspicuous nucleoli arranged in nests, tubules and occasional papillary structures (Fig. 1). Immunohistochemistry revealed a consistent pattern with positive staining for CK7 and CD10 in the epithelium and smooth muscle actin positivity in the leiomyomatous stroma (Fig. 1). In addition, all four cases showed optically clear to pale eosinophilic inclusions within the nuclei of the lesional clear cells (Fig. 2). The inclusions could be appreciated at 200× magnification and occupied most of the nucleus. Ultrastructural analysis by electron microscopy showed invaginations of the nuclear membrane containing cytoplasmic organelles (Fig. 2) within tumour cells, consistent with intranuclear cytoplasmic inclusions. Tumour cells with intranuclear inclusions varied in proportion across and within the tumours but were present at least focally in all sections examined. Interestingly, one of the patients (Case 1) had three discrete synchronous tumours each resected separately from the same kidney. The RCCLMS, papillary RCC and clear cell papillary RCC each had distinct morphological and immunohistochemical profiles, consistent with previous reports.¹ Intranuclear inclusions were present within the RCCLMS only.

A search of the literature did not reveal any prior documentation of intranuclear inclusions in RCCLMS, however such inclusions could be appreciated in multiple micrographs of published case reports of RCCLMS (Fig. 2).^{4–6} Intranuclear inclusions have been reported in RCC, with a higher frequency in papillary and chromophobe carcinoma.⁷ However, these inclusions were described as eosinophilic in colour and were associated with tumours of grade 3/4. In contrast, the inclusions in our series were colourless and present in tumours with inconspicuous nucleoli consistent with WHO/ISUP grade 1/2.

Table 1 Clinicopathological features of four renal cell carcinoma with leiomyomatous stroma cases

Case	Sex	Age	Size (cm)	No. tumours	Colour	Stage
1	M	50	1.4	3 ^a	Tan and grey	pT1a
2	F	53	2.6	1	Tan to yellow and grey	pT1a
3	M	67	2.6	1	Tan and grey	pT1a
4	F	62	3.5	1	Tan to yellow	pT1a

^a The three tumours were renal cell carcinoma with leiomyomatous stroma, papillary renal cell carcinoma and clear cell papillary renal cell carcinoma, each resected separately.

Fig. 1 (A) Case 2 is a typically well circumscribed renal tumour with an irregular pseudocapsule. (B,C) Histology reveals a clear cell renal cell carcinoma associated with prominent smooth muscle fibres extending into perirenal fat (B). (D) The tumour stained positive for CK7 with (E) membranous staining seen for CD10. (F) Smooth muscle actin is strongly positive within the leiomyomatous stroma.

Intranuclear inclusions are a previously unreported histological characteristic of RCCLMS, present in all tumours in this series and appreciable in published images of previous

case reports. Formal analysis in a larger series is required to determine the prevalence of intranuclear inclusions in RCCLMS and their relationship to molecular findings. The

Fig. 2 Cases 1–4 (A–D, respectively) all show scattered optically clear to pale pink intranuclear inclusions, appreciable at 400 $\times$ magnification. (E) Similar inclusions can be appreciated in a previously reported case.⁴ (F–H) Electron microscopy performed on formalin fixed, paraffin embedded tissue from Case 2 shows the nuclear inclusions to be invaginations of the nuclear membrane containing cytoplasmic organelles (scale bar = 1 μ m).

limited available data suggest that RCCLMS has indolent biological behaviour and this readily assessable morphological feature may prove useful in distinguishing RCCLMS from other clear cell renal neoplasms.

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The dangers of herbal weight loss supplements: a case report of drug-induced liver injury secondary to *Garcinia cambogia* ingestion

Sir,

Drug-induced liver injury (DILI) should be suspected in patients presenting with unexplained liver disease. Recent data from the US Drug Induced Liver Injury Network reports 16% of acute liver failure cases are causally related to dietary supplements.¹ Up to 50% of the Australian adult population take

dietary supplements.² *Garcinia cambogia* (hydroxycitric acid) is a herbal extract from the fruit rind of the *Garcinia cambogia* tree found in South East Asia, India and Africa. It is a commercially available, over the counter weight loss supplement claiming to suppress fatty acid synthesis and appetite, although several small randomised trials report nil efficacy for these purposes.³ *Garcinia cambogia* has been implicated in causing acute liver injury in several recent case reports.

We present a case of a 54-year-old woman presenting to her local hospital with acute liver failure requiring transplantation after consuming *G. cambogia* for two months. Her initial complaints included malaise, jaundice and dark urine. She reported consuming four to six standard alcoholic drinks per day on a background of binge drinking since age 20. Liver function tests showed ALT 714 U/L (10–35 U/L), AST 644 U/L (10–U/L), ALP 103 U/L (30–110 U/L), bilirubin 666 µmol/L (0–9 µmol/L) and INR >12.0. Routine viral serology and autoantibodies were negative. The progressive nature of the patient's acute liver failure with consistently high serum bilirubin >300 µmol/L and a prothrombin time >100 s deemed urgent liver transplantation necessary to ensure survival. Post-liver transplantation the patient progressed well with improving graft function and normal liver function tests.

Macroscopically the explanted liver showed extensive necrosis with small residual islands of hepatic parenchyma seen. Microscopically, the liver showed submassive necrosis (Fig 1). The islands of surviving hepatocytes showed non-specific changes including extensive ballooning and cholestasis with adjacent extensive ductular reaction (Fig. 2). Portal tract regions showed a moderately heavy inflammatory cell infiltrate predominantly composed of lymphocytes. No diagnostic evidence of underlying chronic liver disease was identified; in particular, features of alcoholic liver disease including steatosis, Mallory–Denk bodies and perivenular fibrosis were not identified.

The findings were regarded as consistent with DILI secondary to *G. cambogia* in view of the close temporal correlation with the supplement ingestion and absence of other possible causes on clinical history and serology. The histopathological features seen were consistent with the biopsy findings in previous published case reports of *G. cambogia* liver toxicity.^{4–7}

A literature review using PubMed was performed to identify similar cases using search terms 'liver failure', 'hepatitis', 'DILI', 'herbal supplement', 'weight loss supplement' and 'G.

Fig. 1 Low power view showing extensive necrosis present.