

Spontaneous regression of renal cell carcinoma: a pitfall in diagnosis of renal lesions

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Abstract

Two cases of renal cell carcinoma, both of which underwent extensive spontaneous regression, are reported. The first occurred in a 56 year old man, forming a well circumscribed renal cortical nodule which contained only very occasional foci of viable renal cell carcinoma with areas of hyalinisation and calcification, and with metaplastic ossification. The second lesion was removed from an 82 year old man, comprising a cystic cavity containing necrotic debris with only occasional viable foci of classical renal cell carcinoma. Spontaneous regression of renal cell carcinoma is a rare but recognised entity. These two cases emphasise the important differential diagnoses: metastatic secondary carcinomas, xanthogranulomatous pyelonephritis, and infective granulomatous conditions of the kidney. The importance of adequate tissue sampling of all renal nodules cannot be overemphasised in the processing for examination of lesions within the kidney.

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Renal cell carcinoma generally presents in late adult life and is more common in males than females. Although associated with von Hippel Lindau disease,¹ adult polycystic kidney disease,² and multicystic nephroma,³ most renal cell carcinomas occur spontaneously. The patient may present with urological symptoms

such as haematuria or flank pain, or with an abdominal mass, or alternatively with systemic manifestations or a paraneoplastic syndrome such as anaemia, fever, symptoms of metastatic disease, and other rarer phenomena. The surgical pathology of most renal cell carcinomas is that of a moderately defined, often haemorrhagic, tumour affecting the renal cortex, commonly extending into the medulla, and with expansion of the renal capsule and extension into surrounding fat. In some instances the tumour may be multifocal. Haemorrhage, necrosis, calcification, and cystic change are common, giving a variegated appearance; nevertheless necrosis to the extent that little, if any, evidence of viable tumour remains is most unusual in surgical resection specimens unless renal vasculature has been embolised, a procedure which has fallen out of fashion. We present two cases of renal cell carcinoma showing extensive necrosis which were only diagnosed after thorough sampling of the surgical specimen, and in the first case only confirmed by immunohistochemical examination. We emphasise the importance of thorough sampling of the resected specimen, with the use of immunohistochemistry as an adjunct.

Case 1

A 56 year old man presented with left flank pain, passing calculi. A large calculus occupying the lower half of the left kidney with a right sided renal tumour was identified on computerised tomography (CT) of the upper abdomen. A right radical nephrectomy was performed. The resected surgical specimen comprised a kidney measuring 11.5×6.2×5.0 cm with a well circumscribed cortical nodule measuring 4.1×4.1×3.2 cm present within the renal cortex and extending through the renal capsule into surrounding perinephric fat at the upper pole of the kidney. There was no evidence of tumour within the renal medulla or calyces, and the kidney elsewhere appeared unremarkable. The total kidney with associated perinephric coverings weighed 273 g. Microscopically the tumour was an extensively involuted/hyalinised lesion (fig 1) with extensive metaplastic ossification and also foci of dystrophic calcification. However, within the foci of hyalinisation were occasional foci of cells with clear cytoplasm and ovoid or slightly rounded nuclei (fig 2), which showed positive immunostaining with low molecular weight cytokeratin (Cam 5.2)(fig 3) and epithelial membrane antigen (EMA). The appearances were undoubtedly those of an extensive involuted renal cell carcinoma. Local excision

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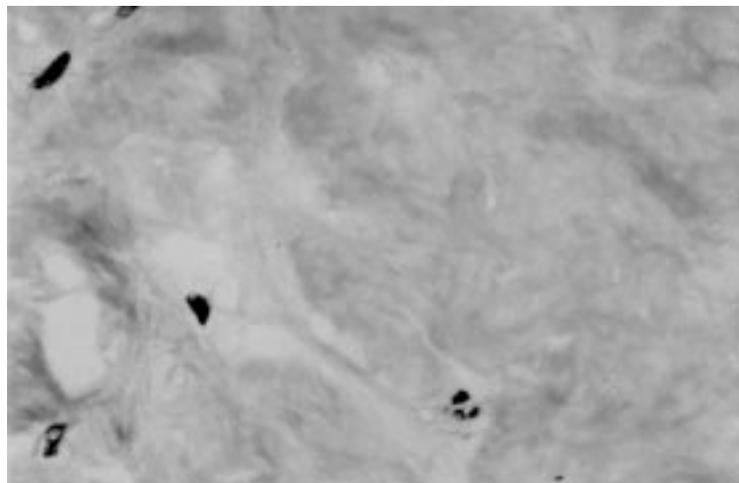


Figure 1 The majority of the tumour blocks in case 1 showed hyaline material only, without evidence of amyloid.

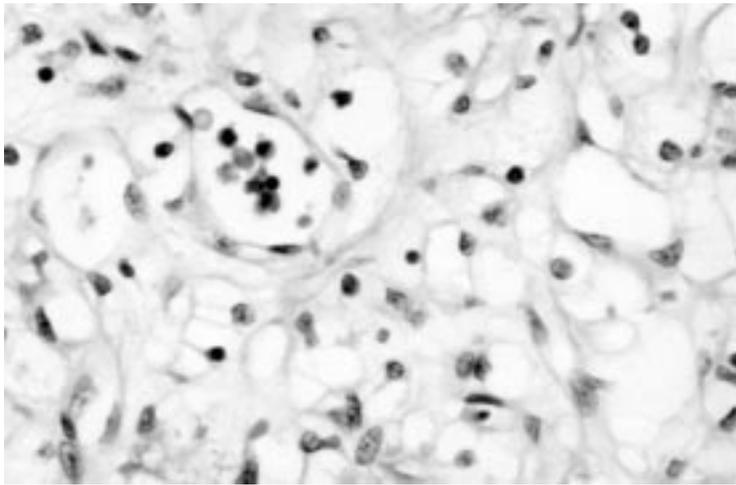


Figure 2 Occasional foci of viable malignant cells with clear cytoplasm identified within area of hyaline change.

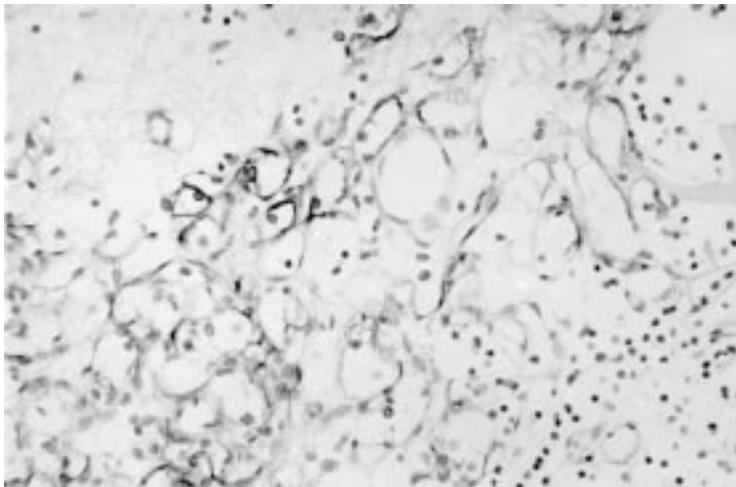


Figure 3 The epithelial rather than vascular endothelial nature of these cells is confirmed by positive immunostaining with low molecular weight cytokeratin Cam5.2 (shown above) and EMA (not shown).

of the tumour appeared complete at the perinephric excision margins. There was no evidence of involvement of the renal vessels by tumour.

Case 2

The second case was an 82 year man who presented with colicky left sided abdominal pain with minor weight loss for one month. Abdominal ultrasound scan showed a large renal tumour, confirmed on intravenous urogram. The patient had a left nephrectomy with splenectomy. The nephrectomy specimen showing a cystic cavity containing necrotic debris and brown fluid occupying virtually the whole of the specimen, measuring 18.0×15.0×13.0 cm. Around the periphery of the cystic area was a compressed rim of normal renal cortical tissue of 4.0 cm thickness but no normal kidney was identified otherwise. Occasional foci of viable renal cell carcinoma were seen in the renal capsular area, and the blocks of macroscopically uninvolved renal cortex appeared unremarkable. The ureteric and renal vascular resection margins were free of carcinoma, and local excision of tumour appeared

complete at the fascial excision planes. Again multiple blocks were required to identify that this was indeed a renal cell carcinoma

Discussion

Spontaneous involution of renal cell carcinoma is described,⁴ although most published reports refer to regression of metastatic lesions following resection of a primary renal cell carcinoma,^{5,6} particularly after cytokine treatment⁷ rather than regression of primary renal cell carcinomas. The identification of viable tumour in extensively necrotic lesions may cause diagnostic difficulty and it is accepted that multicystic lesions containing small populations of clear cells may require extensive sampling to confirm the presence of a very small population of malignant cells, indicating renal cell carcinoma.⁸ Immunohistochemistry is often very useful in this situation, as it can positively confirm the epithelial nature of cells which are morphologically suspicious. Renal cell carcinomas typically express keratins, epithelial mucin antibody (EMA), carcinoembryonic antigen (CEA), and vimentin, often with coexpression of keratin and vimentin.⁹ Expression of other antigens, for example villin, α 1-antitrypsin, α -chymotrypsin, S100 protein, Lewis blood group antigens, angiotensin converting enzyme, parathormone related protein, and prealbumin is also described, as well as other miscellaneous antigens.⁹ Monoclonal antibodies have also been generated against epitopes present in renal cell carcinoma, some poorly characterised or uncharacterised, suggesting that most renal cell carcinomas show proximal tubular differentiation.⁹ Cells suspicious of tumour within necrotic cystic renal lesions may also arise as a result of macrophage-like cells in benign inflammatory lesions of the kidney, such as xanthogranulomatous pyelonephritis.¹⁰ These cells characteristically stain with macrophage/histiocytic markers such as MAC387 and CD68, failing to stain with keratins, EMA, CEA, or vimentin. The differential diagnosis of spontaneously regressed renal cell carcinoma would also include:

- previous tumour embolisation, which may have been performed without the surgical pathologist's knowledge (although this procedure has fallen out of fashion in urological practice)
- malacoplakia, in which typical Michaelis-Guttman bodies should be readily identifiable on D-PAS or Von Kossa stains and confirmed as bacterial-like bodies on electron microscopy
- xanthogranulomatous reaction to the presence of a staghorn calculus
- tuberculosis and other infective granulomatous conditions of the kidney
- sinus histiocytosis with massive lymphadenopathy (Rosai-Dorfman disease).

Regressed renal cell carcinoma is an important differential diagnosis of solitary renal lesions. Only thorough tumour sampling of the pathological specimen, or in the case of CT guided core or fine needle aspiration (FNA)

biopsy, previous knowledge of the ultrasound, CT, or magnetic resonance imaging findings will ensure that the correct diagnosis is made, or in the case of a non-diagnostic core biopsy or FNA, that further appropriate clinical action is taken.

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