Teaching Point
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An asymptomatic patient with multiple solid renal masses: errors in diagnosis

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First step: suspecting renal carcinoma

A 63-year-old man was referred to us in December 1997 from an out-patient clinic for further work-up and treatment of a 'presumed bilateral renal carcinoma'.

At admission, the patient had no symptoms except for a vague suprapubic discomfort with occasional dysuria, both of which had started several weeks earlier. He had a history of similar symptoms 7 years earlier (1990). At that time, he had dysuria for several weeks before seeking medical consultation, which resulted in a presumed diagnosis of prostatitis. His intravenous urogram then was normal, except for a double pelvis in the left kidney, and his ultrasound examination had revealed a small prostatic adenoma. His symptoms had disappeared completely after a short course of rifampicin. No further examinations were carried out as his symptoms did not reappear until November 1997, when ultrasonography showed a prostatic adenoma and, incidentally, an area of increased echogenicity at the upper pole of the right kidney. A computed tomographic (CT) scan disclosed multiple solid areas in both kidneys, leading us to diagnose a malignancy [1–3].

The physical examination on admission revealed a healthy appearing individual with a blood pressure of 144/85 mmHg. Laboratory tests provided the following results: white blood cell count 4760/mm3, with 58.6% of neutrophils; slightly increased erythrocyte sedimentation rate (ESR; 13 mm/h, normal < 10), C-reactive protein < 3.5 mg/dl (normal < 5); normal blood urea nitrogen (BUN; 30 mg/dl), creatinine (1.0 mg/dl), urea (46 ml/min) and creatinine clearance (98 ml/min). Urinalysis was negative for protein, blood and nitrates. The microscopic examination of the urine showed hyaline casts and a few red and white blood cells. Urine cultures yielded no growths of common organisms or acid-fast bacilli. Cultures from the urethral meatus and of semen were also negative for many pathogens, including Chlamydia, Gardenella, Mycoplasma and Ureaplasma urealyticum.

Second step: choice of biopsy as diagnostic tool

Ultrasonography, CT scan and magnetic resonance imaging (MRI) yielded considerably discrepant results. Ultrasonography revealed only one isoechogenic area, in the centre of the right kidney (Figure 1, A1), whereas the CT scan showed multiple irregular solid areas bilaterally (Figure 1, A2). The MRI confirmed the bilateral presence of multiple irregular nodular areas, with well-defined inhomogeneous hyperintensity in the renal cortex visualized on non-enhanced T1-weighted images (Figure 1, A3).

A renal perfusion scan showed bilateral functioning kidneys with areas in the upper pole of each kidney which, although not fully functional, showed no signs of obstruction. Therefore, we biopsied the upper pole of the right kidney under CT visualization (Figure 1, A4).
Fig. 1. (A) 1997. (A1) Ultrasonic examination showing an isoechogenic area surrounded by a thin hypoechogenic halo in the upper pole of the right kidney (arrow). (A2) Axial contrast-enhanced abdominal CT scan demonstrates dishomogeneous, hypodense bilateral renal lesions (arrows) showing mainly peripheral contrast enhancement. (A3) T1-weighted MRI without contrast shows dishomogeneous hyperintensity of the lesions in both kidneys (arrows). (A4) A fine needle (gauge 20), CT-guided percutaneous biopsy was performed of the upper pole of the right kidney (arrow). (B) 2001. MRI images—coronal plane, T2-weighted, without contrast agent. On the right kidney, one lesion is evident at the upper pole where a biopsy had been performed 4 years earlier (arrow in B1). On the left kidney, one nodular lesion is shown at the lower pole (arrow in B2).
Third step: histological diagnosis of xanthogranulomatous pyelonephritis

The biopsy specimen of the nodular lesion at the upper pole of the right kidney did not disclose any atypical or malignant cells. The renal parenchyma appeared to have been completely replaced by chronic inflammatory tissue made up of a large amount of amorphous hyaline material along with collagen and areas of fibrosis and calcifications. On the basis of these findings, a diagnosis of an advanced form of xanthogranulomatous pyelonephritis was made, supported by the fact that foamy, lipid-laden macrophages were absent, replaced by chronic inflammatory elements.

Xanthogranulomatous pyelonephritis may be the result of chronic renal infection and obstruction [4–6]. Since the only element which might have caused recurrent infection ascending to the renal parenchyma was the noxa, in this case prostatitis, we speculated that an undiagnosed vescico-ureteral reflux could have caused an infection to ascend from subclinical prostate infections and over time led to the bilateral focal xanthogranulomatosis pyelonephritis.

Fourth step: prostatectomy to remove a trigger for infection

The patient underwent cystography, which excluded vesico-ureteral reflux. Some hours later, the patient had fever, leukocytosis and an acute urinary obstruction that led to an increase in his serum creatinine to 2 mg/dl. This episode advanced the prostatectomy, already planned, intended to obviate future obstructions that would worsen the kidney disease.

Microscopic examination of the excised prostate revealed benign hyperplasia: several small and large nodular aggregations and even glands that had dilated into cysts, as well as fibrous and muscular proliferations of the stroma.

It was speculated that previous subclinical prostatitis (along with the only clinically documented episode 7 years earlier) may have led to subacute processes inside the renal parenchyma. We thought that a form of ‘healing’ had taken place over time, forming the chronic inflammatory tissue, ‘scarred areas’, in both kidneys. The patient was discharged with the pathological diagnosis of xanthogranulomatous pyelonephritis, and was to have strict follow-up and periodic radiological examinations.

Fifth step: toward a surgical confirmation of the previous diagnosis

At the beginning of 2001, the patient had a repeat MRI, at a time when he had no clinical symptoms and had stable renal function (serum creatinine 1.2 mg/dl and creatinine clearance of 90 ml/min). The MRI confirmed the presence in the right and left kidneys of two solid masses whose dimensions and appearance were identical to those found 4 years earlier (Figure 1B).

We reasoned that, if the diagnosis of xanthogranulomatous pyelonephritis were right, the solid renal masses should have been anachronous, some lesions older and some more recent, and also that the removal of the infected prostate ‘identified’ as the original locus of the ascending pyelonephritis should have allowed a partial regression of the solid masses, of at least the most recent and florid one, the one logically most susceptible to some form of ‘healing’.

The fact that this had not taken place not only fed the seeds of the diagnostic doubts that had never been completely dispelled, but also gave rise to second thoughts: the foci had silhouettes that went beyond the contours of the kidneys and showed mild contrast enhancement and central ‘scars’.

A team decision was made to perform a surgical biopsy of the two lesions in the left kidney.

Sixth step: surgical diagnosis of oncocytoma

The patient had a surgical exploration of the left kidney via a loin incision. Two well-encapsulated ruddy masses, of 3.3 and 3 cm, were found in the lower and upper poles. They were well circumscribed, had cut surfaces of a uniform mahogany-brown colour, and had no foci of necrosis. As frozen sections suggested an initial diagnosis of a renal oncocytoma, a conservative enucleation was adopted, and both masses were carefully enucleated.

The definitive histological examination showed the masses to be composed of oncocytes—large cells with granular eosinophilic cytoplasm and abundant mitochondria (Figure 2). The final diagnosis was renal oncocytoma.

At discharge, the patient’s serum creatinine was 1.6 mg/dl and his creatinine clearance 67 ml/min. Two years later (in 2003), the patient’s repeat MRI showed substantial stability of the previous picture. At the time of this report, he is in excellent health, with no evidence of any clinical problems, a serum creatinine stable at 1.6 mg/dl, and creatinine clearance at 69 ml/min.

Discussion

The neoplasm this patient had posed a difficult diagnostic challenge. Renal oncocytoma is a solid epithelial tumour thought to arise from the proximal convoluted tubules of the kidneys. It is rare; bilateral multicentric renal oncocytomas are even more rare. This disease, often misdiagnosed as a malignant tumour, generally has a benign course [7–10].

The results of the histological examination of larger samples of renal tissue obtained from our patient by surgical excision demonstrated that his true diagnosis had eluded us for 4 years. It was only the last,
and most invasive, procedure that provided the correct diagnosis.

In conclusion, we report an uncommon case of renal oncocytoma, which highlights the difficulties of making a correct diagnosis even with the available modern diagnostic modalities. In this case, two diagnostic errors were made: a wrong initial hypothesis of malignant renal carcinoma was made followed by a wrong diagnosis of bilateral xanthogranulomatosis.

Although our patient has histologically proven multifocal left renal oncocytoma and biopsy-proven right chronic pyelonephritis (the left renal lesions are identical to the right one on MRI), our final diagnosis was bilateral multifocal renal oncocytoma, with a putative diagnosis of pyelonephritis based on tissue located in a marginal portion of a tumour (also present in the right kidney). A sampling error during the fine needle biopsy had led us to miss the principal diagnosis.

Several important points are raised by this case. (i) in the evaluation of patients with multiple renal solid masses, watchful management is not advocated, because urological imaging modalities do not provide specific diagnoses; (iii) clinical thinking is important when interpreting the results of pathological investigation and radiological findings; (iii) a benign tumour is one that is non-cancerous. While not immediately life-threatening, many tumours classified as benign may grow; finding them is to be regarded as fortuitous, something to be evaluated and treated with nephron-sparing surgery at an early stage.

**Teaching point**

The lesson of this case is that a probabilistic approach to clinical decision making can be of little help in patients with bilateral solid renal masses.

1. In patients who have evidence of multiple bilateral renal masses, renal oncocytoma should be in the differential diagnosis.

**Fig. 2.** Histological features of the renal oncocytic lesions obtained by surgical removal of the upper and lower polar masses of the left kidney. In the intraoperative frozen section, an intense eosinophilic lesion was evident both at low (A) and high magnifications (B). In (B), it is also possible to recognize cell components: a large, eosinophilic cytoplasm and central nucleus. Histological examination of the surgical specimen confirmed the pattern already observed during intraoperative frozen section examination. In addition, a certain nuclear pleomorphism was present (arrowheads) (C). At low magnification, the neoplastic eosinophilic area (outlined by arrowheads) is surrounded by sclerotic renal parenchyma, the result of previous inflammation (D).
2. The combined use of ultrasound, CT and MRI may help identify such lesions, and should today permit diagnostic certitude pre-operatively, so that conservative, rather than radical, surgery can be employed, especially in the face of an early or incidental diagnosis (often the most common situation at present).

3. This diagnosis needs histological evidence obtained through the surgical exploration of the kidney, as clinical history may be non-contributory and radiological images insufficient to provide definite diagnostic criteria.

4. Lastly, radiologically guided biopsy, though a useful technique in many situations, may be insufficient and may even lead to the wrong diagnosis in others.

Conflict of interest statement. None declared.

References


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