comments

INTRODUCTION

The incidence of RCC has increased over the last 50 years, largely due to enhanced detection of asymptomatic renal masses with the expanded use of imaging techniques such as ultrasonography and CT. Currently, more than a third of renal tumours are discovered incidentally [1]. The mainstay of diagnosis for renal tumours is cross-sectional imaging, but a group of solid and complex cystic lesions cannot be differentiated as definitely malignant or benign. In essence, many radiologists label such a renal mass as 'indeterminate' in contemporary practice, especially small lesions [2]. The dilemma for urologists then is how to manage this subgroup of patients.

Traditionally patients are offered either radical surgical procedures or active surveillance, even though it is well known that 20% of patients undergoing surgery for a suspicious renal mass will have a histopathologically benign lesion [3]. Data on the natural history of untreated enhancing small lesions are limited. A recent meta-analysis showed that although most small renal masses grow at a slow rate, radiological 'watchful waiting' is not without the potential risk of disease progression and metastasis [4]. Progression to metastatic disease was noted in three patients, representing 1.0% of the total lesions followed. Also, there was no significant correlation between lesion size at presentation and the growth rate. Furthermore, oncocytomas could not be distinguished accurately from RCC using imaging alone, and no difference was noted in tumour size at presentation or the tumour growth rate, between oncocytomas and RCCs.

Percutaneous needle biopsy has been an accepted diagnostic tool for solid intra-abdominal masses, but its role has largely remained unclear in the evaluation of solid renal tumours. Biopsy can be used to obtain a definitive tissue diagnosis to direct future

MANAGEMENT OF SMALL INDETERMINATE RENAL TUMOURS: IS THERE A CASE FOR NEEDLE BIOPSY?

Azhar A. Khan, Iqbal S. Shergill*, Sandeep S. Gujral* and Anthony G. Timoney –
Bristol Urological Institute, Southmead Hospital, Bristol, and *Urology, Harold Wood Hospital, Essex, UK

Accepted for publication 12 January 2007

therapy in patients with inoperable disease, because of locally advanced RCC and the presence of metastatic disease and comorbidities [5]. In addition, recently, minimally invasive ablative methods such as radiofrequency ablation and cryotherapy have shown great promise in the treatment of small renal masses, and it is well understood that biopsy might provide the only chance for a tissue diagnosis in such cases [6]. If biopsy is safe in such circumstances, the question to the urologist is whether indications could be expanded to include the group of lesions that cannot be classified as definitely benign or malignant on imaging.

From unpublished data, we explored the current practice on this issue in the UK amongst consultant urologists. We sent a questionnaire to all UK consultant urologists on the BAUS register in October 2005. The participants were asked initially whether they used needle biopsy in their practice and, if so, the indications for its use. If biopsy was not used, factors precluding its use were established. A repeat mailing was sent to those not responding 8 weeks after the initial mailing. Of the 525 questionnaires sent, 336 (64%) were returned, of which 325 valid answers were analysed.

We found that 139 (43%) consultant urologists never use biopsy, whereas 111 (34%) always use it for the diagnosis of indeterminate renal masses. Moreover, 75 (23%) urologists use biopsy only for a selected patient group. Figure 1 illustrates the main indications used by the participants who use percutaneous biopsy in their practice. A mass in a solitary kidney (57%), bilateral renal masses (51%), and a previous history of non-renal cancer (46%) were the main indications. Medically unfit patients with a renal mass, a multidisciplinary team decision after inconclusive radiology, and patients with possible metastatic RCC were less common indications.

Of the participants who did not use biopsy, 87% described false-negative results as the main reason, whereas 58% thought that the use of biopsy would not change the eventual management of their patients (Fig. 2). Tumour seeding, biopsy-related complications and histopathological concerns were other less common factors mentioned against the biopsy.

High false-negative results, and especially the problem of managing a negative biopsy, has always been an argument against the use of biopsy. Most urologists also suggested that a biopsy did not alter the management of their patients. Although these concerns are valid, many recent studies show that biopsy can significantly alter the management of indeterminate renal masses. Wood *et al.* [7] reported only 6% false-negative results in 79 biopsies, and Neuzillet *et al.* [8] reported a false-negative result of 5.6% in 88 biopsies. Most of these false-negative results were because of either insufficient tissue material or sampling necrotic tissue with the biopsy needle. In all such cases, it is crucial to interpret the biopsy result in conjunction with radiology. For example, all patients with a

negative biopsy but inadequate cellular tissue sample, and with suspicion of enhancement or hypervascular elements on imaging, should be offered either a repeat biopsy or surgical options [7]. Helical CT guidance can help to direct the biopsy needle accurately in real-time mode, avoiding necrotic areas [8]. Neuzillet *et al.* also emphasized the importance of obtaining a good quality core and advocated the need to repeat the biopsy if the core length was <10 mm. The clinical management was altered due to the biopsy in >40% of patients in both studies. Vasudevan *et al.* [9] showed that 33% of the 70 renal biopsies taken for incidental asymptomatic renal masses of <5 cm, considered malignant on radiological features, ultimately proved to be benign. Richter *et al.* [10] assigned a definitive diagnosis to 76% of renal mass lesions diagnosed as indeterminate by imaging methods.

It is important to differentiate between indolent and potentially aggressive small renal tumours. Results can be improved by using core biopsy in preference to fine-needle aspiration cytology, or a combination of both techniques [11]. Renal core biopsy and fine-needle aspiration can provide essential information on molecular or genomic characterization for making decisions about treatment, and should therefore be considered in the diagnostic evaluation of all small renal masses [12]. This can provide not only better architectural information, but also tissue for additional histopathological and biochemical procedures. Lactate dehydrogenase and protein assessment of the biopsy specimens can be used to differentiate neoplastic from inflammatory lesions [10]. In some cases, the distinction between chromophobe RCC, oncocytoma and even clear cell RCC (eosinophilic variant) can be problematic. Shah *et al.* [5] advised using Hale's colloidal iron and a contemporary immunohistochemical panel in all such cases, to define the morphology. Biopsy can thus reliably identify patients with high-risk histological subtypes of RCC, such as papillary RCC, and help in deciding the treatment options.

The risk of tumour seeding is greater in patients with TCC, and most recent studies of RCC reported no such complication even after a long follow-up [7–11]. The risk of bleeding and haematoma appears to be small, and will only require conservative management in most cases. Results can also be improved by taking biopsies only in highly specialized uro-radiology centres, by expert radiologists.

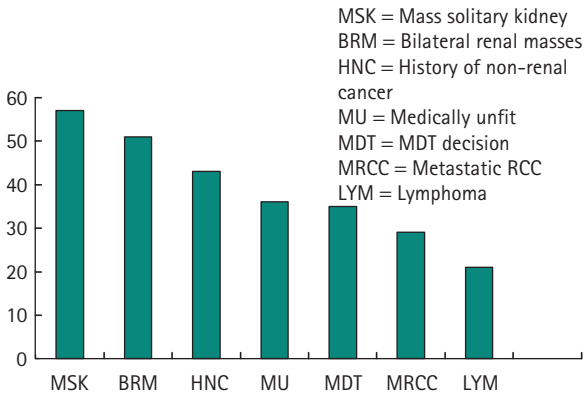

FIG. 1.
Indications for biopsy (%).

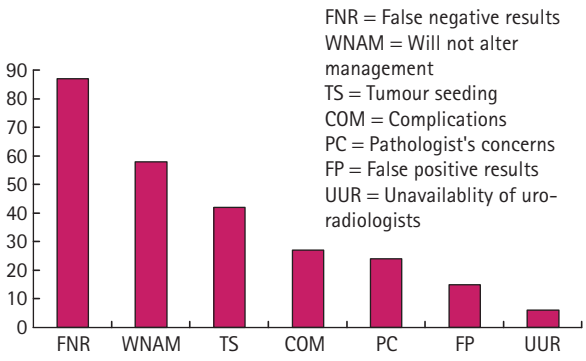

FIG. 2.
Reasons for choosing not to take a biopsy (%).

In conclusion, there is a wide and varied practice amongst UK consultant urologists in the management of indeterminate renal masses. Most urologists think that biopsy confers no benefit. Although there is a paucity of good evidence to confirm whether or not a biopsy should be taken, recent published evidence shows that biopsy results can provide critical information in a significant majority of patients with renal masses. It not only differentiates benign from malignant tissue, but can also help in deciding the management option for patients undergoing minimally invasive treatments. There might be a case to set up a multicentre randomized trial to establish whether needle biopsy should be used or not.

CONFLICT OF INTEREST

None declared.

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Correspondence: Azhar A. Khan, Urology Research Registrar, Bristol Urological Institute, Southmead Hospital, Bristol, UK.
e-mail: docazhar@gmail.com

THE PHOSPHODIESTERASE INHIBITORS AND NON-ARTERITIC ANTERIOR ISCHAEMIC OPTIC NEUROPATHY: INCREASED VIGILANCE IS NECESSARY

Amrith R. Rao, Ali Thwaini, Hashim U. Ahmed, Iqbal S. Shergill and Suks Minhas – The Institute of Urology, London, UK

Accepted for publication 6 September 2006

KEYWORDS

sildenafil, tadalafil, vardenafil, phosphodiesterase inhibitors, NAION, blindness

INTRODUCTION

The main action of the cGMP phosphodiesterase inhibitors (PDEIs) sildenafil, tadalafil and vardenafil is on the PDE5 enzyme. However, they act on the other PDE enzymes, including PDE6i, which is present in the rods and cones of the retina. Therefore, disturbances in colour vision and excessive brightness have been reported as adverse events of PDEIs; both side-effects seem to be dose-dependent although completely reversible. Due to these potentially debilitating effects, such medication is contraindicated in patients with hereditary degenerative retinal disorders such as retinitis pigmentosa.

Recently there has been an alarming increase in the reporting of sudden loss of vision due to non-arteritic anterior ischaemic optic neuropathy (NAION) occurring in men taking PDEIs. This has raised significant concern in the medical community and in the media, culminating in CBS, the USA television network, raising the issue on their evening news [1].

NAION is the most common cause of acute optic nerve disease in men age >50 years and therefore shares several common risk factors with erectile dysfunction (ED), e.g. hypertension, diabetes mellitus, atherosclerosis, smoking, myocardial infarction and hypercholesterolaemia. The common criteria for the diagnosis of NAION includes: (a) a history of sudden painless monocular/binocular loss of vision; (b) optic disc oedema noted on fundoscopic examination, that eventually resolves, leaving optic disc pallor; (c) a visual field defect corresponding to the pathology at the level of the optic nerve head; (d) lack of findings on examination suggesting another disorder that could be causing the symptoms; (e) exclusion of the more common arteritic AION by clinical history, examination and erythrocyte sedimentation rate.

Although in 40% of patients the condition does not change, the prognosis is variable amongst the remaining 60%. There is subsequent improvement in 40% of patients and 20% have deterioration [2].

The first reported case of NAION in relation to the use of sildenafil for ED was in 2000 [3]. Up to 2005, 43 men with NAION taking PDEIs were reported to the USA Food and Drug Administration (FDA, 38 sildenafil, four tadalafil, one vardenafil), with 26 having continued or permanent visual loss [4]. The significance of the difference among these three different drugs might either be a real effect or reflect the predominant and longer-term use of sildenafil in the market. In response, the FDA issued a statement advising patients who have sudden or gradually decreasing visual impairment in one or both eyes to stop taking these medicines, and call a doctor or healthcare provider immediately.

Furthermore, those patients taking or considering taking these products were strongly advised to inform their healthcare professionals if they had ever suffered severe loss of vision, reflecting a previous episode of NAION. Such patients were deemed at increased risk of developing NAION if a PDEI were prescribed. The FDA also approved the updated labelling of these drugs by their respective companies, cautioning the possibility of NAION [5].

The Drug Safety Research Unit from the UK analysed a cohort of 8893 patients from a Prescription-Event Monitoring study and found only one reported case of NAION. Although epidemiological data suggest that one case of NAION might be expected in such a large cohort, it is clear that physicians who prescribe PDEIs should specifically ask about previous sudden visual disturbance before prescribing, whilst continuing to show pharmacovigilance and report any new cases [6].

Most of the reported cases in which NAION has occurred in men taking a PDE5I also have underlying anatomical or vascular risk factors associated with the development