INTRODUCTION

Many imaging modalities have been used in the evaluation of patients with hematuria. Historically, intravenous urography (IVU) has been the primary method of imaging in these patients ***(Amis, 1999 and Mcnicholas et al., 1998)***. Currently, the examinations that are commonly used to evaluate patients with hematuria include IVU, ultrasonography (US), computed tomography (CT), magnetic resonance (MR) imaging, retrograde ureterography and pyelography, cystoscopy, and ureteroscopy ***(Grossfeld et al., 2001)***.

Hematuria can have a wide range of causes, including calculi, neoplasms, infection, trauma, drug toxicity, and coagulopathy ***(Grossfeld et al., 2001)***. Occasionally, the cause is revealed by a clinical history of prolonged exercise or recent instrumentation.

Evaluation of patients with hematuria frequently requires several imaging modalities. Assessment for urologic malignancy is probably the most important reason for evaluating these patients; therefore, examinations with a high sensitivity for the detection of neoplasms are essential. The ability to detect other possible causes of hematuria is also important.

Unenhanced CT is routinely used to evaluate for calculi and hydronephrosis ***(Smith et al., 1995)***. Renal masses are usually diagnosed by CT, US, or MR imaging. Urothelial disease has traditionally been evaluated with IVU or retrograde ureterography and pyelography. Excretory-phase CT can now be used to evaluate the ureters ***(McNicholas et al., 1998 and heneghan et al., 2001)***. Although excretory-phase CT is a relatively new technique, preliminary results demonstrate a high sensitivity (95%) in detecting upper tract uroepithelial malignancy ***(Caoili et al., 2003)***.

Although CT may also demonstrate bladder disease, flat tumors of the bladder are unlikely to be identified with CT, and cystoscopy remains the study of choice in evaluating for bladder malignancy.

With the advent of spiral CT and particularly multi–detector row CT, it is possible to perform a comprehensive evaluation of hematuria patients with a single examination ***(Chai et al., 2000; Cahili et al., 2002 and Caoili et al., 2003)***.

CT urography can be performed with a combination of unenhanced, nephrographic-phase, and excretoryphase imaging. The unenhanced images are ideal for detecting calculi. Renal masses are detected and characterized with a combination of unenhanced and nephrographic-phase

imaging. The excretory-phase images provide evaluation of the urothelium.

Three-dimensional (3D) reformation of the excretory-phase images can produce images that mimic the appearance of intravenous urograms, thus providing images in a format that is familiar to many referring physicians.

Alternatively, post-CT conventional radiography can provide similar information ***(Vrtiska et al., 2000)***.

In this Study, we review multi–detector row CT technique in patients with hematuria. We also discuss and illustrate a variety of entities that are frequently associated with hematuria, including calculi, renal masses, papillary and caliceal abnormalities, renal pelvic and ureteral disease, bladder disease, and congenital anomalies. With special stress on the comparison between CT scan and other imaging modalities in the evaluation of hematuric patients.

AIM OF THE WORK

The essay is a trial to spot the updated information and resources found in the literature as regards a Role of Multidetector computed tomography in evaluating and managing a hematuric patient.

DIFFERENTIAL DIAGNOSIS OF HAEMATURIA

Definition of haematuria:

Haematuria is presence of blood in voided urine. Blood in voided urine, or hematuria, can originate from anywhere along the urinary tract and may be the only presenting sign of significant urologic disease. Haematuria is broadly divided into macroscopic (frank and Microscopic (occult) varieties. Refinements in imaging modalities and advances in endoscopic technologies have made the outpatient evaluation of hematuria simple, safe, and cost effective. An understanding of the potential etiologies for hematuria and diagnostic regimen by the primary care physician results in appropriate referral to a urologist and ensures that optimal treatment decisions, if needed, can be made in a timely manner.

Gross hematuria typically brings the patient promptly to the physician and little debate surrounds the need for a thorough evaluation. Indeed, visible blood in the urine is the presenting symptom in up to 85% of patients with bladder cancer and 40% of patients with renal cell carcinoma ***(Belldegrun and DeKernion 1998).*** The proper evaluation of microscopic hematuria remains a matter of considerable debate, however, because of the fact that it is a common problem (representing 6% of new patients seen

by urologists) and that some patients have no identifiable etiology ***(Fracchia et al., 1995)***. The challenge has been to determine the best strategy to identify patients with significant disease while minimizing the cost and morbidity of unnecessary tests and procedures.

Etiology

Hematuria in the adult patient can have many etiologies, some life-threatening, such as bladder or renal malignancy, and others progressive but benign, such as prostatic hyperplasia. Investigators have categorized these possible entities by the anatomic source, clinical significance, and likelihood of disease based on patient age and gender ***(Abuelo, 1983)***. Potential diagnoses discovered during a typical hematuria evaluation are listed as follows:

Renal (nonglomerular)

Renal cell carcinoma

Transitional cell carcinoma

Nephrolithiasis

Renal infarction

Renal vein thrombosis

Arteriovenous malformations

Papillary necrosis

Pyelonephritis

Sickle cell disease

Medullary sponge kidney

Polycystic disease

Hydronephrosis

Ureteropelvic junction obstruction

Renal (glomerular)

IgA nephropathy

Thin glomerular basement membrane disease

Acute glomerulonephritis

Lupus nephritis

Hereditary nephritis (Alport's syndrome)

Lower urinary tract

Transitional cell carcinoma

Interstitial cystitis

Bacterial cystitis

Radiation-induced cystitis

Bladder diverticulum

Bladder papilloma

Bladder stone

Prostate cancer

Prostatitis

Benign prostatic hyperplasia

Bladder neck contracture

Epididymitis

Urethritis

Urethral stricture disease

Miscellaneous

Strenuous exercise

Excessive anticoagulation

Genitourinary tuberculosis

Genitourinary trauma

Abdominal aortic aneurysm

Lymphoma Multiple myeloma

The most common glomerular etiologies include IgA nephropathy (Berger's disease) and thin glomerular basement membrane disease, whereas common extrarenal sources are stones, infection, and malignancy ***(Tiebosch et al., 1989).***

In those studies in which the patient underwent a full evaluation, typically including urine culture, upper urinary tract imaging, cystoscopy, and urine cytology, a cause for asymptomatic microscopic hematuria can be identified in 32% to 100% patients. Indeed, in the urologist's view, hematuria in a patient over 40 years of age represents a

malignancy until proved otherwise. In referral-based studies, up to 26% of patients with microhematuria are discovered to have genitourinary malignancies, depending on the population evaluated ***(Golin, 1980)***. ***Mariani and associates (1989)*** found that 92% of cancers discovered on work-up for microhematuria were diagnosed while still localized and curable, providing further evidence to support complete evaluation of these patients.

The decision to screen a patient for asymptomatic microscopic hematuria relies on the judgment of the physician and findings of history and physical examination. Risks factors for significant underlying disease should be considered and are as follows:

Cigarette smoking

Occupational exposure (benzene, aromatic amines)

Age greater than 40 years

Previous urologic history

Urinary tract infection

Analgesic abuse

Irritative voiding

Pelvic irradiation

Cyclophosphamide

Common urologic causes of hematuria

Urinary tract calculi

Urolithiasis is associated with idiopathic hypercalciuria, secondary hypercalciuria, and hyperuricosuria ***(Dyer et al., 1998)***. Stones are most commonly composed of calcium oxalate and phosphate (34%), calcium oxalate (33%), calcium phosphate (6%), mixed struvite and apatite (15%), uric acid (8%), and cystine (3%) ***(Dunnick et al., 2001)***. Nephrocalcinosis is characterized by the formation of calculi within renal tubules and interstitium, leading to impaired renal function ***(Pressler et al., 2006)***. Nephrocalcinosis is associated with medullary sponge kidney, renal tubular acidosis, and hyperparathyroidism, and may present with haematuria ***(Joffe et al., 2003)***. Urinary tract calculi frequently present with ureteric colic caused by obstruction of the urinary collecting system. With regard to the association of urinary tract calculi with development of microscopic hematuria, a recent study by ***Edwards and colleagues (2006)*** showed a prevalence of urinary tract calculi of 7.8% in adult patients with microscopic hematuria and 8.8% in patients with macroscopic hematuria.

Malignancy

The most common malignant conditions associated with hematuria in adults are renal cell carcinoma, transitional cell carcinoma, prostate carcinoma, and less commonly, squamous cell carcinoma, which can result from chronic inflammatory conditions ***(Pantuck et al., 2001)***. RCC is the most common malignant neoplasm of the kidney, representing up to 90% of renal neoplasms and up to 3% of all neoplasms ***(European network of cancer registries, 2001)***. RCC is more common in men than women, has a peak incidence at 60 to 70 years of age, and is associated with smoking, obesity, and antihypertensive therapy ***(Bergstrom et al., 2001)***.

In recent years, the triad of flank pain, hematuria, and a palpable mass is less frequently the mode of presentation for RCC, because over 50% of lesions are identified by cross-sectional imaging, either incidentally or when performed for vague and apparently unrelated symptoms. This is not surprising, as systemic symptoms, such as anorexia and weight loss, are commonly associated with RCC ***(Thurston et al., 2005)***. Urothelial tumors account for 10% of upper urinary tract neoplasms ***(Kirkali et al., 2003)***.

Although urothelial malignancies are most likely to occur in the bladder, the ureters have been reported to be involved in 2%, and the renal pelvis (extrarenal pelvis in

preference to infundibulocalyceal regions) in 5% of cases ***(American Cancer Society, 2004)***. The multifocal and bilateral nature of TCC makes this a challenging condition for the radiologist ***(Thurston et al., 2005)***. Synchronous tumors occur in up to 2% of renal and 9% of ureteric lesions, with metachronous lesions typically occurring within the bladder in up to 50% of cases with upper ureteric tumors on presentation ***(Wong-You-Cheong et al., 1998)***. Therefore, imaging is required for primary diagnosis of TCC but is also very commonly used for detection of synchronous and metachronous lesions ***(Thurston et al., 2005)***. Bladder neoplasia is the fifth most common malignancy in Europe and the fourth most common cancer in the United States ***(Jensen et al., 1990)***.

TCC of the bladder occurs more commonly in men than women, is associated with smoking (fourfold greater than in nonsmokers), exposure to chemicals such as benzene and 2-naphtylamine, and structural abnormalities (horseshoe kidney) ***(Lee et al., 1997)***. Squamous cell carcinoma and adenocarcinoma are significantly less common in the bladder than TCC ***(Dawson et al., 1996)***. Greater than 70% of bladder cancers are superficial and 25% invade muscle at the time of diagnosis ***(Stein et al., 2005)***. Bladder cancer most frequently presents with hematuria but can be associated with more nonspecific

signs, such as urinary frequency and urgency, dysuria, and suprapubic pain ***(Thurston et al., 2005)***.

Evaluation

History and physical examination:

The work-up for heamturia should begin with a detailed medical history, including recreational, occupational and radiation exposures, and all medications. Cigarette smoking is a known risk factor for transitional cell carcinoma of the bladder, conferring a threefold to fivefold increased risk ***(Silverman et al., 1992)***. Occupational exposure to aromatic amines and amides, such as 4-aminobiphenyl, benzidine, and 2-naphthylamine, may occur in leather and rubber manufacturing, and especially worrisome is exposure from work in production factories of aniline dyes ***(Cohen et al., 2000)***.

Several classes of medications have been implicated in causing hematuria. Most notable are the chemothera-peutic agents cyclophosphamide and mitotane, which may induce hemorrhagic cystitis. Papillary necrosis and resultant hematuria have been reported from the chronic ingestion of nonsteroidal anti-inflammatory agents, particularly phenacetin, the use of which has also been implicated in malignant transformation of the urothelium ***(Gonwa eta l., 1980)***. Finally, many drugs may cause an allergic interstitial

nephritis, including the penicillins and cephalosporins ***(Roxe, 1980)***.

A special mention should be made regarding patients on oral anticoagulants, such as warfarin. Anticoagulation alone does not commonly induce hematuria de novo, and the fact that a patient is on the medication does not imply that a complete hematuria evaluation can be omitted. Patients on anticoagulation with undiagnosed urologic pathology may actually present earlier in their disease process, and may represent a population more likely to benefit from prompt investigation and treatment. Indeed, a significant urologic condition was identified in 13% to 45% of this cohort in published series ***(Van Savage and Fried et al., 1995)***.

In addition to the medical history, the physical examination often provides insight into the etiology of hematuria. Peripheral edema is associated with the nephrotic syndrome. Cardiac abnormalities, such as atrial fibrillation, predispose patients to renal artery embolism. Examination of the abdomen may reveal a flank mass, bruit, or a pulsatile aortic aneurysm. Costovertebral angle tenderness suggests nephrolithiasis, ureter-opelvic junction obstruction, or pyelonephritis. The genital and rectal examination can give evidence of prostatitis, prostate cancer, epididymitis, or meatal stenosis in men. In women, urethral

and vaginal examinations are necessary to exclude any local causes of microscopic hematuria.

Repeat urinalysis is warranted if a nonmalignant cause is clearly suggested during clinical evaluation of the patient, including menstruation, vigorous exercise, sexual activity, or viral illness. If such an etiology is suspected, repeat urinalysis can be obtained in 48 hours. Patients with persistent hematuria require a complete evaluation. Similarly, patients with hematuria and evidence of a urinary tract infection should be rechecked 6 weeks after antibiotic therapy; those with resolution of the hematuria need only consideration of factors predisposing to the infection.

A patient with microscopic hematuria and other signs including significant proteinuria, RBC casts, dysmorphic RBC, or renal insufficiency should undergo evaluation for potential underlying renal parenchymal disease. If a systemic disorder cannot be identified (eg, lupus, vasculitis), renal biopsy may be warranted to establish a diagnosis, determine prognosis, and help guide therapy. As mentioned, IgA nephropathy and thin basement membrane disease are the most common glomerular causes of isolated hematuria and typically have an excellent prognosis; however, these patients require follow-up given the potential for developing hypertension and increasing proteinuria.