LEADING ARTICLE

USE OF URINARY RED CELL MORPHOLOGY IN DETERMINING THE SOURCE OF HAEMATURIA

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INTRODUCTION

Haematuria, gross or microscopic, is a common diagnostic problem that may indicate an underlying glomerulonephritis or a urological problem. In patients with glomerular disease, the presence of proteinuria and red cell casts help to distinguish it from other urological diagnoses; however both these accompanying features may be absent in as many as 21%[1] of patients with biopsy proven glomerulonephritis. These patients with glomerular bleeding but no proteinuria may be subjected to unnecessary investigations such as cystoscopy and intravenous urography when renal function testing and a biopsy may be more appropriate.

In 1979, Birch and Fairley[2] described a method of distinguishing glomerular bleeding from other causes of haematuria by examining the appearance of red cells in the urine sediment using the phase-contrast microscope.

URINALYSIS USING THE PHASE-CONTRAST MICROSCOPE

Urinalysis using the phase-contrast microscope offers several advantages over the standard Addis method using the light microscope. All the sediments can be quantitated accurately when using the phase-contrast microscope whereas the Addis method is a semi-quantitative method; moreover the morphology of the red cells can also be studied under the phase-contrast microscope. Red cells that are "glomerular" in origin are described as "dysmorphic" as they show a wide variation in morphology differing in size, shape and haemoglobin content[2-4]. In contrast, non-glomerular cells derived from bleeding into the renal pelvis, ureter or bladder display the conventional morphology of the red blood cell and are described as "isomorphic".

Dysmorphic red cells can be observed in all forms of glomerulonephritis with significant haematuria. The cause of the red cell dysmorphia that occurs in glomerular bleeding is not known although it is likely to be the result of environmental changes that the cell is exposed to as it travels along the renal tubular lumen. In a recent study[5] using an in vitro model consisting of a polycarbonate filter with pore diameters of 3 μm through which red cells, suspended in urine or buffer of varying pH and osmolality, were pumped, the authors concluded that both passage through a narrow pore membrane and changes in pH and osmolality affect red cell morphology. This hypothesis is supported by the observation that Frusemide, the loop diuretic, can reduce the percentage of dysmorphic cells in patients with glomerulonephritis[5-7]. This occurs as a result of dilution of the urine from increased diuresis leading to a change in osmolality and a reduced frequency of glomerular shapes. This change is reversed after 6 hours[7].

Isomorphic red cells are seen in a variety of conditions including renal calculi, renal or bladder carcinoma, acute cystitis and acute papillary necrosis.

At times a mixed picture of dysmorphic and isomorphic red cells is observed and this is commonly associated with IgA nephropathy and renal calculi[1]. In IgA nephropathy, IgA deposits are present in the skin and muscle[8] of the patients and it seems possible that similar vascular lesions may occur in the urinary tract giving rise to the non-glomerular bleeding in these patients. In significant glomerular bleeding, the sensitivity of this method of distinguishing red cells of glomerular origin is 99% and the specificity is 93%[3]. This is similar to a paper in this issue by Ahmad et al[9] who demonstrated a sensitivity of 93.6% and a specificity of 97.7%.

Osmani et al[6] studied the relationship between glomerular lesions and the degree of haematuria and observed that patients excreting 80,000 dysmorphic RBC/ml were more likely to have underlying glomerular crescents or global sclerosis. There was, however, no relationship between the degree of haematuria and other parameters such as segmental sclerosis, serum creatinine, creatinine clearance or proteinuria.

CURRENT CONTROVERSIES

At present there are two areas of disagreement in the use of this method and these are: 1) the criteria regarding the level of haematuria which is pathologically significant, and 2) the percentage of dysmorphic cells that can be considered as normal. Various workers have offered different levels of haematuria that may be considered as normal and these values range from 1,000 RBC/ml to 8,000 RBC/ml[1-4,10]. In this issue, Ahmad et al examined the erythrocyte count in urine using a relatively unfamiliar method of assessing uncentrifuged urine rather than the more commonly practised method of assessing centrifuged urine. The normal value stated for this method is 13,000 RBC/ml.

Some workers have noted that isomorphic cells are not seen in healthy individuals[3] while others accept a certain percentage of isomorphic cells in normal individuals and quote a figure of greather than 80% dysmorphic cells as a indication of glomerular bleeding[11]. In an attempt to address the second problem, Pollock et al studied 27 volunteers and 59 patients (31 patients prior to renal biopsy and 28 with renal calculi or bladder tumours) and concluded that dysmorphic red blood cells are a useful clinical indicator of renal pathology (both glomerular and medullary), as opposed to lower urinary tract bleeding, only if they account for more than 75% of the number of urinary red cells. On the other hand, lower tract bleeding can only be diagnosed with certainty when there are more than 83% isomorphic cells in the urine. Because of the great differences in criteria, it is important for each individual centre that is setting up this method of studying red cell morphology to determine its own range of normality.

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NEWER METHODS OF EXAMINING URINARY CELL MORPHOLOGY

In order to improve on the technique of examining urinary red cell morphology, several workers have used a variety of alternative approaches. These include the use of the red cell analyser to qualitate variations in cell size[12], the scanning microscope to improve images of the red cell[3] (which is obviously impractical in the clinical setting) and most recently, a new method based on electronic processing of the images obtained by the traditional light microscope has been proposed[13].

CONCLUSIONS

Examination of urinary red cell morphology using the phase-contrast microscope provides a useful adjunct to the investigations of a patient with haematuria and may spare the patient from unnecessary procedures.

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