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The value of red cell morphology in differential diagnosis of hematuria

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Summary

Phase contrast microscopic examination of the urinary sediment was performed in 38 children with hematuria in order to identify glomerular or nonglomerular origin. The rate of dysmorphic erythrocytes were above 80 % in 12 (80 %) of 15 patients, definitely diagnosed to have glomerular hematuria, whereas the same rate was found to be below 20 % in 15 (75 %) of 20 patients who had nonglomerular hematuria. Urinary sediment examination of the patients with acute glomerulonephritis revealed higher rates of dysmorphic erythrocytes in the second examinations compared to first ones, which were performed one week before.

It is concluded that phase contrast microscopic examination of the urinary sediment is a simple and safe method for identifying the origin of hematuria in children.

Key words: Hematuria, red cell morphology

Introduction

Hematuria, may be a sign of glomerulonephritis; or it may originate from other parts of the urinary tract. It is important to know origin of hematuria while selecting the methods to be performed in differential diagnosis. Kidney biopsy is the only method for definite diagnosis of glomeru+lar hematuria, if non-invasive means fail to do so. On the other hand in case of nonglomerular hematuria, it is reasonable to begin laboratory investigations by radiologic and/or endoscopic methods.

It has been suggested that erythrocyte morphology might play an important role in localization of hematuria, since 1970 [2,3,4,5,6,9]. Recently, this method has been used more frequently due to its simplicity and safety.

We assumed that urinary sediment examination of the hematuric children could play an important role in differential diagnosis. In order to investigate the reliability of the method, we decided to perform a prospective trial including 38 patients.

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Patients and Methods

38 hematuric children were included in the study, which were followed and treated in Pediaric Department of Cerrahpaşa Medical Faculty. The number of male and female patients were equal and mean age was 7.7±3.8. Hematurias thought to be related glomerular and non-glomerular origin were examined twice (with an interval of one week) and once, respectively. Total number of the urinary sediment examinations were 56 (Figure 1).

Unspun and mixed urine samples, containing more than 5 erythrocytes per mm3 were defined as hematuric [8]. Ten milliliters of these samples were centrifuged at 1500 rpm, for 10 minutes, and the sediment (0.5 ml) was mixed in order to get a suspension. This sediment was examined by an independent physician who was unaware of the patient, clinical and laboratory findings, using

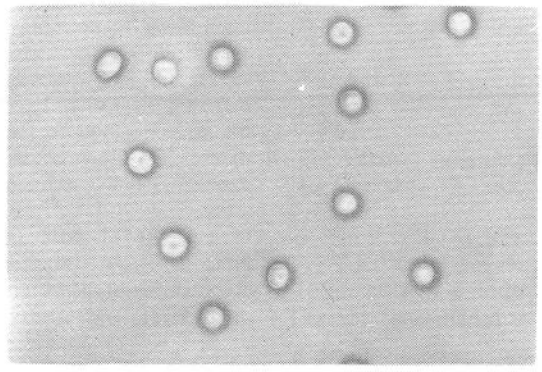

Fig. 1 Morphic erythrocytes in urinary sediment (Phase contrast microscopy, x 400)

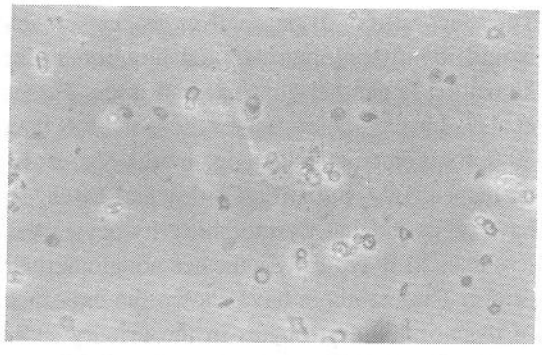

Fig. 2 Dysmorphic erythrocytes in urinary sediment (Phase contrast microscopy, x 400)

Olympus CH 2 phase contrast microscopy (X400). Minimum 200 erythrocytes were examined in each sample. Red cells with smooth surfaces which were uniform in size were defined as "morphic", whereas nonhomogen erythrocytes showing variation in size with distorted shapes noted as "dysmorphic" (Figure 2) [2,4,5,6,9]. Some cells with regular spikes and similar to peripheral blood cells in their echinocyte form were regarded as morphic [5]. The rate of morphic and dysmorphic cells for each sample was determined. Also, erythrocytes showing excessive variation in size were thought to represent glomerular hematuria [10]. Osmolarity, pH and protein measurements were done for each sample and presence of casts were noted.

Exact origin of hematuria was determined by hematologic, urinary, bacteriologic, radiologic, ultrasonographic, scintigraphic, endoscopic and histopathologic examinations. Then these results were compared with urinary sediment findings and the reliability of the procedure was assessed.

Results

A definite diagnosis was achieved in 35 of the 38 patients which were included in the study. The etiopathogenetic factors resulting in hematuria are listed in Table I.

Table I. The etiopathogenetic factors resulting in hematuria.

Glomerular hematuria	
Acute post-infectious glomerulonephritis	10
Henoch-Schönlein nephritis	1
Chronic glomerulonephritis	4
	15
Nonglomerular hematuria	
Postoperative hematuria	11
Urolithiasis	3
Abdominal trauma	2
Cystitis	2
Renal tuberculosis	2
	20

The rate of dysmorphic erythrocytes in these 35 patients are shown in (Figure 3). Rates related to glomerular hematuria, belong to the second examination of the sediments. Rates of dysmorphic erythrocytes were more than 80 % in 12 of 15 (80 %) cases with glomerular hematuria. In the other 3 cases the rates were found to be 63 %, 59 % and 40 %, respectively. The rate of dysmorphic erythrocytes in 15 of 20 (75 %) nonglomerular hematurias are lower than 20 %. Dysmorphic erythrocyte rates were 40 %, 46 %, 50 %, 62 % and 74 %, respectively, in the other 4 cases. Definitely undiagnosed 3 patients' urinary sediment examinations yielded different rates with a range of 11 % and 89 %. Further investigations for these patients are being carried out.

In acute glomerulonephritic cases the rate of dysmorphic erythrocytes differed in two examinations, performed with one week interval. The rates were higher in the second examination, excluding one case (Figure 4). It was noted that patients with acute glomerulonephritis were admitted to the hospital in the 2 to 9 days after the first symptom of the disease.

In the urinary sediments, containing dysmorphic

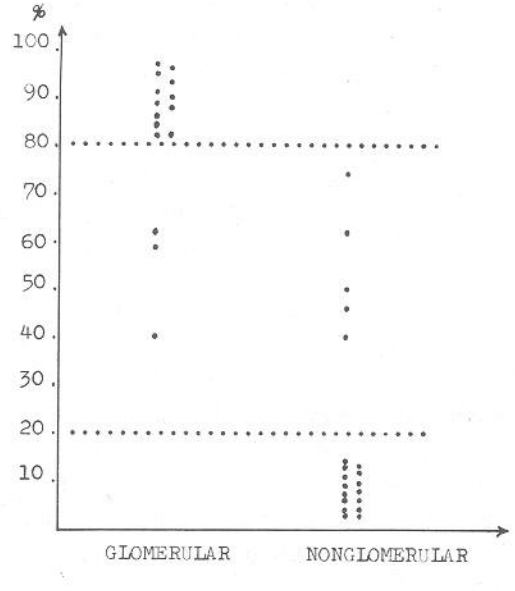

Fig. 3

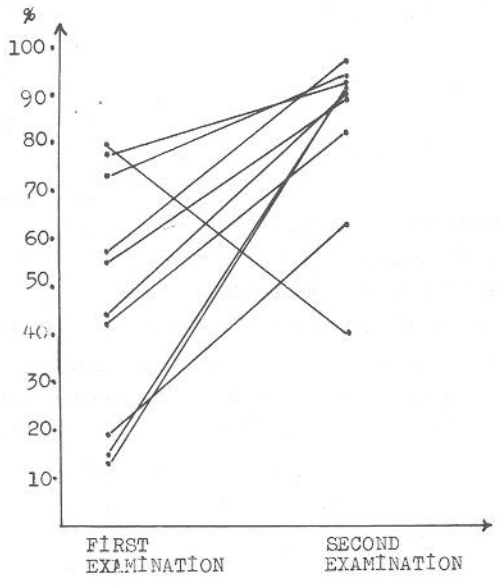

Fig. 4

erythrocytes more than 80 %, the diameters of the erythrocytes revealed excessive variation.

Comment

Addis [1], was the first author describing dysmorphic erythrocytes in the urinary sediments, but he did not point out the importance of this finding. Birch and Fairley [2], reported a relationship between glomerular hematuria and dysmorphic erythrocytes. Authors have noted the uniform appearence of erythrocytes in nonglomerular hematuria. Another author Chung [3], first suggested that urinary sediments could be stained with Wright's technic, in the absence of phase contrast microscopy, and this method would also be valuable in differential diagnosis of hematuria.

The pathogenesis of dysmorphic erythrocyte formation is unclear. It has been shown that neither osmolarity, pH, NaCl content of the urine, nor the time period between voiding and examination affects erythrocyte morphology [10]. It has also been suggested that dysmorphism might be due to mechanical trauma of the erythrocytes, during their passage through the pores of basement membrane [7].

The exact rates of dysmorphic erytrocytes which would identify glomerular and nonglomerular hematuria is another controversial issue. Fasset et al [6], have proposed figures more and less than 80 % for glomerular and nonglomerular hematuria, respectively. Smilarly, Fairley and Birch [4], have suggested that, dysmorphic erhyrocyte rates less than 20 % typically indicates nonglomerular origin. These authors have shown the existence of dysmorphic erytrocytes in the urinary sediments of healthy people and have claimed that all hematurias do contain dysmorphic erythrocytes. Rizzoni et al [9], have reported different figures; they proposed that morphic erythrocyte rates above 90 % were indicative for nonglomerular origin, while dysmorphic erythrocyte rates above 40 % would indicate glomerular hematuria. On the other hand, Stapleton [10], has assumed glomerular hematuria if the rate of dysmorphic erythrocytes exceed 10 %.

Our results show that it is possible to identify the localisation of hematuria with a risk of 20 % misdiagnosis if dismorfism figure is taken as 80 %. If the rates is decreased to 40 %, this would cover all of our glomerular hematurias, but criteria would also indicate 5 nonglomerular hematuric sediments as glomerular ones.

Existence of dysmorphic erythrocytes (up to 40 % - 60 %) in the urinary sediment of patients with urolithiasis have been described in the literature [6,9]. Similarly, we found 74 % and 40 % erythrocytes in 2 patients' urinary samples known to have urinary stone disease.

Van Isegham et al [11], have followed a patient with acute glomerulonephritis prospectively and examined erythrocyte morphology 12 times with an interval of few days. They have found dysmorphism rates less than 10 %, more than 70 % and 95 % in 5., 10. and 15. days of the disease, respectively. We also noted an increase in the rate of dysmorphic erythrocytes, during the progression of the disease.

As a result examination of the erythrocyte morphology in hematuric children seems to be a simple and practical method for differential diagnosis. Dysmorphic erythrocytes more than 80 % show

glomerular hematuria while the same erythrocytes less than 20 % is indicative for nonglomerular hematuria. Dysmorphism between these figures makes various further investigations necessary. Repeating the examination for many times during the disease period gives more accurate results.

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