The Interesting Case

Don’t forget sickled cells in the urine when investigating a patient for haematuria

G. B. Fogazzi, S.-O. Leong* and J. S. Cameron
Department of Nephrology, Guy’s Hospital, London, UK

Abstract
Haematuria is a well-known complication of sickle cell disease. A South African coloured patient with repeated episodes of gross haematuria is described in whom the diagnosis of sickle cell disease was suggested after the finding of sickled erythrocytes in the urine sediment. The diagnosis was then confirmed by haemoglobin electrophoresis, which revealed sickle cell trait (Hb-AS). It is concluded that sickled erythrocytes must be looked for when urine is microscopically scrutinized to determine the source of a haematuria.

Introduction
Since the first report of Abel and Brown in 1948 [1] haematuria has been a well-known complication of sickle cell disease [2–4]. Electrophoresis of haemoglobin and the demonstration of sickled cells in the peripheral blood are clues to the diagnosis. In only a few cases so far have sickled erythrocytes been described in the urine. Herein we report a case in whom it was the finding of sickled cells in the urine that suggested the diagnosis of sickle-cell carrier status, which was then confirmed by haemoglobin electrophoresis.

Case report
A 16-year-old coloured South African male born in Cape Town of parents born locally was evaluated for painless gross haematuria. He presented a year previously with the problem after a upper respiratory tract infection. Since then he has had recurring episodes of gross haematuria, occurring particularly after physical exercise. The haematuria was not accompanied by dysuria, frequency, or other urinary symptoms. Microscopic haematuria was also noted by his doctor in between these episodes. He has been a healthy lad without any significant past medical history and his family history was negative with respect to renal or haematological diseases. Physical examination was unremarkable, and blood pressure was 120/75 mmHg.

Urine was grossly bloody and showed trace albuminuria on dipstick testing (Multistix 10 SG, Ames Inc. USA). After centrifugation of a 10-ml aliquot at 2000 r.p.m. for 10 min, phase-contrast microscopy at 400 × showed only red blood cells which were too numerous to be counted. They were isomorphic in morphology (spherocytes and crenated cells). Moreover in each microscopic field there were about 15–20 sickled cells (Figure 1). A full blood count revealed Hb of 14.5 g/dl; white count: 6.3 × 10⁹/l; and platelets: 154 × 10⁹/l. Haemoglobin electrophoresis, performed after the urinary findings, revealed Hb-AS (sickle cell trait). Renal function was normal with a GFR of 99 ml/min. Imaging of the urinary tract with intravenous urography, ultrasonography and flexible cystoscopy were all normal.

A diagnosis of haematuria associated with sickle-cell trait was made and patient was treated conservatively.

Discussion
Haematuria occurs in 3–4% of patients with sickle cell disease [5]. It is far more common in heterozygotes with sickle cell trait than in homozygotes with sickle cell anaemia, the reason being that the trait is 30–40 times more frequent than the disease. Young adult black people of North America and Africa are the typical patients. However, Afro-Caribbean patients in the West Indies [6] and white patients in different parts of the world, including Europe [6–10], as well as children have also been described [11,12]. Haematuria is typically macroscopic, of variable duration, recurrent, and asymptomatic or associated with pain caused by the passage of clots. More frequently it is unilateral, originating from the left side. Microscopic haematuria is less common, and at times is found between one episode of gross haematuria and another [5,13].
sickling of erythrocytes within the hypoxic, hypertonic, and acidic renal medulla is considered the initiating mechanism which leads to haematuria [14–16]. Sickling in fact causes stasis within the peritubular capillaries, which is followed by interstitial haemorrhages with invasion into the tubular lumina [17]. However, papillary necrosis and haemorrhages secondary to erythrocyte sickling within the vessels of the pelvis or the ureter are other possible sources of bleeding [18–20].

The finding of sickled erythrocytes in the urine of our patient was the clue to the diagnosis of sickle cell disease. They appeared as sickles, crescents, ‘holly-leaf’ shaped cells, or cells with ‘pecked’ contours, and clearly differed in morphology from the other erythrocytes which may be found in haematuria of either glomerular, renal, or postrenal origin [21–23]. The only possible confusion is the differentiation of sickled erythrocytes with isomorphic crenated cells, which, however, have more regular and smaller protrusions (Figure 1). Instead, urinary sickled cells are identical to sickled cells found in the peripheral blood and in the vessels of the renal medulla [13,17].

Sickled cells in the urine have rarely been reported so far. In fact in a review of the international English literature containing information on the urinary sediment findings in about one hundred patients with haematuria and sickle cell disease, we were able to identify only five papers in which sickled cells had been observed in the urine, in a total of seven patients only [9,13,15,16,24] (Table 1). In addition, in only one of these studies was the potential diagnostic role of these cells considered [9]. In that paper sickled cells were found in the urine of a Greek patient, and were confirmed in two subsequent analyses, the second being performed after gross haematuria subsided into microscopic haematuria. While Savige et al. [9] also found urinary dysmorphic erythrocytes in association with sickled cells, we only found isomorphic erythrocytes. This finding, together with the lack of other elements such as erythrocyte or haemoglobin casts, suggested that there was no glomerular bleeding in our patient. This was also supported by the presence of only trace amounts of albuminuria.

In conclusion, we suggest that sickled cells must be looked for when urine erythrocytes are microscopically scrutinized to determine the source of a haematuria. In the case of a positive finding the appropriate blood tests must be carried to confirm the diagnosis of a sickle cell disease.

Table 1. Patients with haematuria associated with sickle cell disease and sickled erythrocytes in the urine

<table>
<thead>
<tr>
<th>Author [Ref.]</th>
<th>Patients with urine sediment described</th>
<th>Patients with sickled cells in urine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goodwin et al. [13]</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Crone et al. [24]</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>Knochel [15]</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Marynick et al. [16]</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Savige et al. [9]</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

References

1. Abel MS, Brown CR. Sickle cell disease with severe haematuria simulating renal neoplasm. *JAMA* 1948; 136: 624–625
Sickled cells in the urine in haematuria


Received for publication: 29.8.95
Accepted: 6 9.95