Urokinase, a Scavenger of Affected Tubules in Acute Worsening during Macroscopic Hematuria of IgA Nephropathy?

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Dear Sir,

Acute deterioration of renal function often follows the occurrence of macroscopic hematuria in patients with IgA nephropathy [1]. The degree of the deterioration ranges from mild to severe enough to need dialysis. A possible cause of the deterioration is tubular damage and obstruction by red blood cell casts [1]. In such circumstances, a scavenger of the affected tubules, if any, may lead to a rapid improvement of renal function.

We describe here in brief a 9-year-old girl with IgA nephropathy in whom macroscopic hematuria lasting for 4 weeks dramatically disappeared and the reduced renal function also rapidly improved by a combination of heparin and urokinase. The patient was admitted on October 8, 1988, because macroscopic hematuria developed late in September without any promoting event and continued. Since that time, she had got out of bed twice for passing urine. Urinary abnormalities had not been noticed at the annual urine screening for schoolchildren.

Significant laboratory studies showed reduction of renal function (table 1) and hypercoagulability (table 2). Renal biopsy revealed mild mesangial proliferative glomerulitis on light microscopy. One of 15 glomeruli checked had a cellular crescent and another glomerulus showed adhesion to Bowman’s capsule. In some of the tubules, red blood cell casts or clots of blood were seen in the lumina, even in the lumina of the proximal tubules. The tubules were swollen and had flattened epithelial cells. A diminished number of the lining tubular cells was also seen. On direct immunofluorescence, glomerular deposition of IgA was 2+, IgG 1+, IgM ±, IgE- C, q2, C3 3+1, C4-, and fibrinogen/fibrin 2+.

Table 1. Laboratory data on renal function before and after treatment

<table>
<thead>
<tr>
<th>Date</th>
<th>Creatinine (mg/dL)</th>
<th>Serum Urea (mg/dL)</th>
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</thead>
<tbody>
<tr>
<td>October 28</td>
<td>2.5</td>
<td>26</td>
</tr>
<tr>
<td>October 29</td>
<td>2.3</td>
<td>25</td>
</tr>
<tr>
<td>November 1</td>
<td>1.8</td>
<td>18</td>
</tr>
<tr>
<td>November 2</td>
<td>1.7</td>
<td>17</td>
</tr>
</tbody>
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Since October 28, 3,500 IU/day heparin were infused intravenously for 4 days. 120 × 103 IU/day urokinase were also administered intravenously for 7 days, although half was infused by one shot over 30 min. Prednisolone, aspirin and dipyridamole were orally given. Moreover, pulse therapy using methylprednisolone was done for 3 days since November 8. The macroscopic hematuria

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lasting for 4 weeks changed from Coke-colored to red wine-colored at the evening of October 28 and disappeared in the next morning. Serum creatinine level on November 7 decreased to 0.9 mg/dl. Laboratory data on November 14 revealed an improvement of renal function (table 1). Thereafter, prednisolone on alternate days and aspirin and dipyridamole every day were prescribed. Almost normal urinalysis has continued.

Molecular weight of urokinase is 54,000 and its pI is 8.4–8.7. Therefore, urokinase administered intravenously is readily filtered out from the glomeruli, especially from the affected glomeruli, into the tubular lumina. Thus, not only the glomerular fibrin but also the red blood cell casts or clots of blood in the tubular lumina would be lysed by the urokinase administered, leading to recanalization of the affected tubules. Moreover, heparin prevents formation of new fibrin or clots of blood. These are thought to have brought about the rapid improvement of renal function.

Dramatic disappearance of the macroscopic hematuria is curious. We have no explicit explanation for its mechanism, although a combination of urokinase and heparin may have improved the intracapillary blood flow of the glomeruli.

A massive dose of urokinase may become a scavenger of the affected tubules in acute worsening during episodes of macroscopic hematuria of IgA nephropathy.

Reference