Renal vein thrombosis in Chinese patients with systemic lupus erythematosus

Ning-Sheng Lai, Joung-Liang Lan

Abstract

Objectives—To evaluate the risk factors associated with renal vein thrombosis (RVT) in Chinese patients with systemic lupus erythematosus (SLE).

Methods—Data on clinical symptoms, renal biopsy, antiphospholipid antibody syndrome profile, and serological examinations of lupus features were examined retrospectively in six patients with RVT confirmed by angiography from a total of 625 patients with SLE over a 14 year period (1982–1996).

Results—The lupus patients with RVT did not have acute symptoms of severe flank pain, haematuria, and oliguria. In contrast, most patients were suspected to have RVT because of peripheral oedema and worsening proteinuria. Roentgenological examinations ^5 (including renal sonography, renal computer tomography, or renal Doppler, or all three) were positive only in some patients. Positive antiphospholipid antibody profiles were found in four of six lupus patients. By renal biopsy, only two samples were confirmed as World Health Organisation (WHO) class V lupus membranous glomerulonephritis. The others were class IV in three patients, and class III in the remaining one. No RVT was found in lupus patients without nephrotic syndrome. Peripheral thrombophlebitis was, however, noted in only one patient.

Conclusion—Nephrotic syndrome could be a distinct risk factor in the development of RVT in Chinese SLE patients, in contrast with that reported in white populations in whom the peripheral thrombotic events were recognised as a determining factor.

(Ren Fail 1992;5:562–564)

Renal vein thrombosis (RVT) in systemic lupus erythematosus (SLE) is rare and its pathogenesis is still to be determined. Multiple factors might be indicated, including nephrotic syndrome,^2 membrane glomerulonephritis,^3 hypercoagulation status,^4 and antcardiolipin antibody (ACA).^5 Antecedent thrombophlebitis was considered to be a high risk in developing RVT or inferior vena cava thrombosis in white patients with lupus. It is of interest that thrombophlebitis has been less frequently observed in Chinese lupus patients. Moreover, the frequency of postoperative and oestrogen related thrombophlebitis in Chinese patients is rare, compared with those in a white population (unpublished data in Taichung and ChiaYi Veterans General Hospital). In this study, we observed a distinct pattern of risk factors in developing RVT in Chinese patients with SLE. No RVT was found in SLE patients without nephrotic syndrome. In contrast, only one patient had a previous history of deep vein thrombosis. Although rare in the prevalence of RVT in SLE, clinicians should be aware of this potentially treatable disease by knowing the associated risk factors, especially the relevant factors in the local area.

Methods

PATIENTS

Patients were selected retrospectively from the patient database in the rheumatology section. It was noted that there were six angiographically confirmed RVT cases from a total 625 lupus patients (0.96%) over a 14 year period (1982–1996).

STUDY DESIGN

Clinical symptoms, antiphospholipid antibody profile (including ACA, thrombocyte count, activated partial thromboplastin time, and rapid plasma reagin) and serological data (complete blood count, blood urea nitrogen, creatinine, cholesterol, C3, C4, CH50, anti-dsDNA, creatinine clearance, and 24 hour urine protein) were collected and analysed. Patients received renal sonography, renal computed tomography, or Doppler evaluation of RVT, or all three, before angiographic evaluation. Renal biopsy was performed for WHO classification and evaluation of active and chronic index of lupus nephritis (active index: cellular proliferation, leucocyte infiltration, hyaline thrombus, necrosis/karyorrhexis, cellular crescent, and interstitial mononuclear cell infiltration. Chronic index: glomerular sclerosis, fibrous crescent, tubular atrophy, and interstitial fibrosis).^5

Results

RVT was suspected in most patients because of the presence of recent development of heavy proteinuria, peripheral oedema, or concomitant antiphospholipid antibody syndrome symptoms, or all three (table 1). No obvious clinical symptoms were detected except very mild flank soreness and knocking pain in two patients during the physical examination. At the time of RVT development, active lupus features (pleural effusion, arthritis, haemolytic anaemia, vasculitis, malar rash, pericardial effusion) and/or active lupus nephritis were noted in clinical evaluation. Characteristically,
Table 1  Clinical and laboratory data in six patients with renal vein thrombosis

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (y)</th>
<th>LN</th>
<th>Clinical symptom</th>
<th>APS profile</th>
<th>NS</th>
<th>Initial renal function</th>
<th>Previous APS symptom</th>
<th>Lupus features at time of RVT diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>20</td>
<td>Class IV</td>
<td>Peripheral oedema</td>
<td>ACA:3.65, PLT: 209</td>
<td>(+,4m)</td>
<td>Transient GFR↓, ERPF↓, Cr↓, TP: 3.8 g</td>
<td>Pulmonary HT</td>
<td>Active lupus nephritis</td>
</tr>
<tr>
<td>2</td>
<td>30</td>
<td>Class III</td>
<td>Flank soreness</td>
<td>ACA:56, PLT: 112</td>
<td>(+,4m)</td>
<td>BUN/Cr: normal, TP: 4.1 g</td>
<td>Raynaud, CRAW, skin ulceration, AVN, digital gangrene</td>
<td>Pleural effusion, arthritis, haemolytic anaemia and vasculitis</td>
</tr>
<tr>
<td>3</td>
<td>40</td>
<td>Class II</td>
<td>Peripheral oedema</td>
<td>ACA:26.2, PLT: 75</td>
<td>(+,2m)</td>
<td>Creatinine↑, TP: 4.4 g</td>
<td>Pulmonary HT, AVN, deep vein thrombosis, repeated abortion</td>
<td>Arthralgia, malar rash with rapid increase of proteinuria</td>
</tr>
<tr>
<td>4</td>
<td>35</td>
<td>Class IV</td>
<td>Peripheral oedema</td>
<td>ACA:310, PLT: 60</td>
<td>(+,4m)</td>
<td>BUN/Cr: normal, TP: 5.3 g</td>
<td>Repeated abortion, brain atrophy</td>
<td>Malar rash, pericardial effusion, haemolytic anaemia</td>
</tr>
<tr>
<td>5</td>
<td>43</td>
<td>Class IV</td>
<td>Peripheral oedema</td>
<td>ACA:22.4, PLT: 43</td>
<td>(+,2m)</td>
<td>Cr: 6.2, Acute renal failure, TP: 4.1 g</td>
<td>Old lacunar infarction</td>
<td>Synovitis, fever, malar rash</td>
</tr>
</tbody>
</table>

Table 2  Roentgenological evaluation and treatment in six patients with renal vein thrombosis

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (y)</th>
<th>Renal sonography</th>
<th>Renal CT</th>
<th>Renal Doppler</th>
<th>RVT*</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>20</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal Bilateral C</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>30</td>
<td>Normal</td>
<td>Normal</td>
<td>Left H+C</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>25</td>
<td>Left†</td>
<td>Left</td>
<td>C, Urokinase</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>35</td>
<td>Left†</td>
<td>Right</td>
<td>C</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>34</td>
<td>Normal</td>
<td>Normal</td>
<td>Left H+C</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>39</td>
<td>Normal</td>
<td>Normal</td>
<td>Bilateral C</td>
<td>C</td>
<td></td>
</tr>
</tbody>
</table>

NP: not performed; C: coumadin 5 mg daily; H: heparin; urokinase: 10 000 U/h for continuous 120 h; RVT: renal vein thrombosis. *Angiography finding: bilateral cortical filling defect in proximal small vein in patient 1; post-capillary venous obstruction over upper pole of left kidney in patient 2; multiple filling defects over lower pole of left kidney in patient 3; post-thrombotic obstruction over lower pole of right kidney in patient 4; left renal vein thrombosis with engorged collateral left ovarian vein in patient 5; bilateral renal vein thrombosis in patient 6. (Unilateral renal size enlargement, 138 mm, 142 mm in patient 3 and patient 4, respectively.)
occur frequently and are a singularly important factor in determining whether glomerulosclerosis develops subsequently. Although rare, the intrarenal vascular changes may be responsible for the sudden deterioration of renal function in some lupus patients, factors that cannot be explained by the presence of lupus glomerulonephritis alone. Clinically, early reports of RVT emphasised the presence of flank pain, microscopic haematuria, flank tenderness, rapid deterioration of renal function, and worsening of proteinuria. However, Harrison et al in 1956 described two groups of patients with RVT. The first group had a sudden onset of the above mentioned symptoms, while the second group had only the nephrotic syndrome and absence of any acute symptoms. The only clinical manifestation in these patients was peripheral oedema. Our patients belonged to the second group of RVT, with predominant clinical symptoms of nephrotic syndrome as classified by Harrison et al. High suspicion is essential for early diagnosis of this potentially treatable condition.

In a large scale evaluation of the risk factors in developing RVT in SLE patients,\(^5\) the results showed that SLE patients with peripheral thrombophlebitis had a high risk of developing RVT (61.5%). Patients with nephrotic syndrome have a smaller risk (27%). In their study, RVT in SLE patients who have nephrotic syndrome is just as frequent as in patients who have nephrotic syndrome of other aetiology. Our data, on the contrary, delineate a different clinical picture in Chinese SLE patients with RVT. It might be indicated that RVT in SLE patients was related to nephrotic syndrome, regardless of renal histopathological type. Furthermore, four patients had a positive antiphospholipid antibody syndrome profile at the time of diagnosis of RVT. Whether or not these ACA played a part in the development of RVT was not confirmed definitely. The reason for this disparity is still unknown, but ethnic difference (white versus Chinese), study design (prospective versus retrospective) are all possible.

RVT is frequently reported to be associated with membranous glomerulonephritis.\(^1\) The earliest findings showing that RVT occurred only in membranous glomerulonephritis led to the suggestion that RVT was the primary event in causing membranous glomerulonephritis and nephrotic syndrome by releasing renal tubular antigens. In contrast with this view, after a review of all the cases with nephrotic syndrome, Dr Zucchelli provided the tentative conclusion that RVT does not occur exclusively with membranous glomerulonephritis,\(^1\) even though the prevalence seems to be more common in membranous glomerulonephritis. In this study, RVT was found both in WHO class V, class III, and class IV lupus nephritis. Therefore, in agreement with Zucchelli, our data suggest that RVT is caused by nephrotic syndrome, particularly when complicated with increased blood viscosity, hypercoagulation state resulting from nephrotic syndrome (increased protein synthesis, including coagulation factors, and/or increased urinary loss of anti-thrombotic proteins such as antithrombin III during nephrotic syndrome),\(^2\) intravascular volume depletion, and other treatments such as high dose corticosteroid use. Although the retrospective nature of the study and the lack of detail information about the background SLE and RVT population weakens conclusions made about pathogenesis of RVT in this population, it is important to recognise these triggering factors in the treatment of RVT in SLE patients.

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