Introduction

Systemic lupus erythematosus (SLE) is an autoimmune disease of unknown etiology in which tissues and cells are damaged by immune complexes and pathogenic autoantibodies. Renal involvement in SLE is called lupus nephritis, which is one of the most serious and common complications of SLE (1-3). It occurs in 60% of the patients and is accompanied by infection. It is the leading cause of mortality in the first decade of the disease. Lupus nephritis is a progressive disease with exacerbations requiring treatment after many years of therapy.

Pathological changes in lupus nephritis may be found in the glomeruli, tubules, blood vessels, or renal interstitium, and renal biopsy plays an important role in the diagnosis and control of the disease (4-10). CD34, a glycosylated single-chain protein with an approximate weight of 116 kDa (11), is one of the single-pass transmembrane sialomucin proteins and intercellular adhesion factors. It is expressed in the membrane of some cell types including hematopoietic cells, endothelial cells, muscle satellite cells, hair follicle stem cells, and fibroblasts. Recent studies have shown that CD34 positive cells can cause changes in the adhesion and migration of bone marrow cells (12-14). Moreover, these cells may increase proliferation and prevent differentiation of progenitor cells, increase lymphocyte adhesion, and, in some cases, such as kidney podocytes, can prevent cell adhesion (15). Multipotency of CD34-presenting cells has made them useful agents for various therapeutic purposes, such as cancer, diabetes, cardiovascular diseases, and autoimmune disorders (16). The role of CD34-presenting cells has been studied in some recent studies, but the results show some controversies. One study showed that patients with more severe nephrosclerosis exhibit lower expression of CD34 in the tubulointerstitium (17). In contrast, another study examined 47 patients for alpha-smooth muscle antibody and CD34 and found that CD34 positivity...
CD34 expression is significant.

<table>
<thead>
<tr>
<th>CD34 expression</th>
<th>SBP (mm Hg)</th>
<th>p</th>
<th>WBC (count/µL)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>1+</td>
<td>124.7±23.2</td>
<td>0.03</td>
<td>9.21±4.42</td>
<td>0.04</td>
</tr>
<tr>
<td>2+</td>
<td>111.5±20.7</td>
<td>9.81±8.24</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3+</td>
<td>131.7±19.2*</td>
<td>6.12±2.59*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>124.17±22.2</td>
<td>8.21±5.27</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

SBP: systolic blood pressure; WBC: white blood cell

*p<0.05 is significant

Methods

In the present study, 73 paraffin-embedded blocks of kidney needle biopsy samples of patients with lupus nephritis collected by the International Society of Nephrology/Renal Pathology Society classification (19). Suboptimal samples (<8 glomeruli or <0.5 cm sample length) were excluded from the study. Then, suitable blocks were selected for immunohistochemical staining. A 4 µm section was prepared from the selected blocks, and IHC staining for CD34 antigen was performed according to the manufacturer’s instructions (Dako Corporation, Glostrup, Denmark).

Briefly, after deparaffinization and re-hydration, endogenous peroxidase activity was blocked using hydrogen peroxide. Primary antibody for CD34 (Dako Corporation, Glostrup, Denmark) was added after antigen retrieval and incubated for 45 min. Then, the antibody was washed, and the slides were incubated with envision (Dako Corporation, Glostrup, Denmark). Diaminobenzidine tetrahydrochloride was used for visualization. The membranous staining pattern in interstitial cells was considered as positive. The semi-quantitative method was used for examination, and scoring was as follows: 0=no reaction, 1=mild reaction, 2=moderate reaction, and 3=strong reaction (20). A negative control was applied on one of the samples by the secondary antibodies removal. Control samples were stained with the same method.

Patients’ clinical data including age, gender, systolic and diastolic blood pressure (SBP and DBP), blood count indices (WBC and platelet count), erythrocyte sedimentation rate, serum urea and creatinine levels, and serological markers, such as antinuclear antibody, dsDNA, anti-cardiolipin, β2-glycoprotein, and complement levels, were also obtained from their medical records for further evaluation.

The ethics committee of Urmia University of Medical Sciences approved the study. Written informed consent was obtained from the patients.

Results

The mean age of the patients was 29.63±11.3 years. Of the patients, 83.6% were females. Tables 1 and 2 show the clinical data and also the serological findings. Our results showed that CD34 expression was correlated with patients’ WBC count and SBP. Patients with a strong (score 3) CD34 expression had higher SBPs and lower WBC counts (p=0.03 and 0.04, respectively).
Most of the recent studies on CD34 have evaluated the relationship between CD34 and GN with etiologies other than SLE. Most of them have shown different results. For example, in one study, only 27% of the patients were CD34 positive (20), but another study showed 77% positivity for CD34 (21). In addition, in one study, 96.66% of the patients with interstitial fibrosis were CD34 positive (22).

The relationship between CD34 expression and activity indices was also explored previously, but the results were not similar (21, 23). Some studies have found no relationship, whereas others have found a significant relationship between CD34 expression, disease activity, and also prognosis in patients with various types of GN, claiming that proliferative GN had higher expression of CD34 than non-proliferative GN and control groups. As previously mentioned, most of these studies have evaluated various GNs other than SLE, and data on lupus nephritis is inconclusive.

We found a significant relationship between CD34 expression and activity index, as patients with lower activity index had higher CD34 expression, suggesting that CD34 positive mesenchymal cells may have a protective role in lupus nephritis.

The relationship between CD34 expression and clinical and serological data was also studied in various types of GNs other than lupus nephritis, but no significant relationship was found (24).

Data on the relationship between CD34 expression and disease chronicity are controversial. Some studies have found significant relationships (either positive or negative) (17, 18), whereas others have shown no correlation between them (21, 23). In the present study, we did not find any significant relationship between chronicity index and CD34 expression (p=0.139). Overall, we found that CD34 was expressed in all of our lupus nephritis samples. We also found a reverse correlation between activity index and CD34, as patients with higher and stronger CD34 expression had lower activity index. We concluded that CD34 expression could play a protective role, and a weak expression of CD34 should raise the possibility of higher activity index in lupus nephritis. We also found...
that patients with higher SBP and lower WBC count showed a strong expression of CD34. This was a novel finding in these patients that has not been expressed before. Some studies have shown that autologous transplantation of CD34 positive cells can induce remission and reduce severity of symptoms in lupus nephritis (25-27). Considering these findings, we suggest that a thorough investigation of CD34 functions in the kidney may introduce new methods in the treatment of patients presenting with active symptoms of renal involvement during SLE.

Ethics Committee Approval: Ethics committee approval was received for this study from the Urmia University of Medical Sciences Ethics Committee.

Informed Consent: Written informed consent was obtained from all the patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - FN; Design - LM; Supervision - FN, AA; Materials - KM; Data Collection and/or Processing - LM, FHG; Analysis and/or Interpretation - AA, LM; Literature Review - FHG, KM; Writing Manuscript - LM, AA; Critical Review - LM, FN, AA.

Conflict of Interest: The authors have no conflict of interest to declare.

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References