INTRODUCTION

Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by the increased production of autoantibodies by systemic clinical manifestation and damage to multiple organs. This study aimed at analysing the relationship between serum levels of macrophage-derived chemokine (MDC), and matrix metalloproteinase-9 (MMP-9), and to determine the relationship between serum levels and the disease activity of SLE.

METHODS

Subjects: Diagnosis of SLE was established according to the 1997 revised American Rheumatism Association Criteria, and disease activity was
evaluated by the SLEDAI (SLE Disease Activity Index). The patients with SLE (32 women and 4 men, aged 11-61 yrs) were divided into 2 groups: 13 SLE patients with renal disease and 23 SLE patients without renal disease according to proteinuria (++↑ or >0.5g/d); 23 active course patients and 13 inactive course patients were evaluated using the SLEDAI standard, and active disease was indicated by SLEDAI score of more than 8 points; 23 SLE patients with arthritis and 13 without the lesion according to articular damage. 30 sex and age matched healthy volunteers were recruited as controls.

Serum: Three milliliters of venous peripheral blood were collected from each subject, centrifuged to get serum, and then stored at -80ºC. Nine serum samples were collected from patients taking corticosteroid three or four weeks later. The concentrations of MDC and MMP-9 were measured by ELISA respectively. ELISA kits for HGF, MDC and MMP-9 were purchased from R&D Systems Inc (Catalog No: DMD00, DMP00). Assays were performed according to the manufacturer’s instructions.

Statistical analysis: All the results were presented as mean±standard deviation. The differences were tested for statistical significance by Student’s t test and relative risk. A probability (P) less than 0.05 was considered as significantly different.

RESULTS

Significantly decreased serum levels of MDC and MMP-9 was found in SLE patients as compared to those in controls, 450.95±76.76 pg/ml vs 606.23±23.71 pg/ml (P<0.001) and 108.52±113.23 ng/ml vs 352.25±155.01 ng/ml (P<0.001) respectively. Serum levels of MDN and MMP-9 were markedly lower in active patients than those with inactive disease, namely 393.98±53.73 pg/ml vs 555.40±196.07 pg/ml (P<0.001), and 71.70±66.24 ng/ml vs 165.80±145.82 ng/ml (P<0.05) respectively. Serum levels of MDC and MMP-9 were decreased in patients with renal damage than those without the damage, 366.81±56.25 pg/ml vs 496.85±114.55 pg/ml (P<0.001), and 72.08±56.31 ng/ml vs 141.93±140.55 ng/ml (P<0.05) respectively. Markedly lower serum level of MDC was found in patients with arthritis than those without the damage, 386.43±48.79 pg/ml vs 569.25±199.47 pg/ml (P<0.01), but serum level of MMP-9 has no significant difference in these two groups (P>0.05). Relative analysis showed that no positive correlation was found among the serum level of MDC and SLEDAI (r=0.205 P>0.05), but serum level of MMP-9 showing a negative correlation with SLEDAI (r=−0.41 P<0.01), as Table-I and Table-II.

DISCUSSION

SLE is a complicated autoimmune disease characterized by various immunological abnormalities, including polyclonal activation of circulating B lymphocyte that produce a large quantity of autoreactive antibodies, the abnormality of T lymphocyte and IC deposition. During the process, many chemokines and their receptors play an important regulating role. If monocyte/macrophage releases IL-10 continuously, it will result in division of Th cell to Th2 cell. If monocyte/macrophage releases IL-12 continuously, it will promote transformation of Th cell to Th1 cell. So we focus on cytokines derived from monocyte/macrophage and this will demonstrate the role of chemokines in SLE pathogenesis.

MDC, a CC chemokine, is a potent chemoattractant which activated Th2 lymphocytes via the chemokine receptor CCR4, and its receptor CC chemokine receptor 4 (CCR4) preferentially

Table-I: The comparison of serum level of MDC between SLE patients and controls

| Group                | n   | $\bar{x}$±s (pg/ml) | t value | P value |
|----------------------|-----|---------------------|---------|---------|
| Controls             | 30  | 606.23±23.71        | 10.63   | <0.001  |
| SLE patients         | 36  | 450.95±76.76        |         |         |
| Renal damage         | 13  | 366.81±56.25        | 3.68    | <0.001  |
| No renal damage      | 23  | 496.85±114.55       |         |         |
| Active               | 23  | 393.98±53.73        | 3.72    | <0.001  |
| Inactive             | 13  | 555.40±196.07       |         |         |
| SLEDAI>8             | 23  | 389.46±57.88        | 3.69    | <0.001  |
| SLEDAI≤8             | 13  | 538.81±168.29       | 4.13    | <0.001  |
| Arthritis            | 23  | 386.45±48.79        |         |         |
| No arthritis         | 13  | 569.25±199.47       |         |         |
| Before treatment     | 9   | 163.91±48.36        | 6.72    | <0.001  |
| After treatment      | 9   | 452.78±102.99       |         |         |
expressed on Th2 cells. Th2 type cytokines IL-4 and IL-13 downregulated the production of MDC. This may partially contribute to maintaining Th1/Th2 balance.\textsuperscript{5} Dendritic cells, B lymphocytes and macrophages all produced MDC constitutively, while NK cells, monocytes, and CD4\textsuperscript{+} T lymphocytes produce MDC upon stimulation. IFN-\(\gamma\) can also suppress MDC expression in monocyte, macrophage, and dendritic cells.\textsuperscript{6} Because many immune cells can produce MDC and MDC can chemoattract many immune cells, MDC may be essential in SLE pathogenesis. Serum level of MDC in 36 SLE patients was tested and it was discovered that serum level of MDC was significantly decreased in patients as compared to those in controls, and markedly decreased in patients with active disease than those without the disease. So MDC and MMP-9 may be involved in the pathogenesis of lupus nephritis and seemed to be markers of renal damage, and MDC may be involved in the pathogenesis of arthritis and seemed to be a new sensitive marker of articular damage. As Garcia\textsuperscript{a} and his colleagues reported, they found that MDC was critically involved in the development of anti-GBM GN from acute glomerular injury to irreversible tissue damage. Sato\textsuperscript{10} and his colleagues investigated the serial changes of glomerular metalloproteinase activity in antithymocyte-induced glomerulonephritis in rats and found attenuated glomerular MMP-9 activity.

Table-II: The comparison of serum level of MMP-9 between SLE patients and controls.

| Group               | n   | \(\bar{x}\)±s (ng/ml) | t value | P value |
|---------------------|-----|------------------------|---------|---------|
| Controls            | 30  | 352.25±155.01          | 7.92    | <0.001  |
| SLE patients        | 36  | 108.52±113.23          |         |         |
| Renal damage        | 13  | 72.08±56.31            | 2.17    | <0.05   |
| No renal damage     | 23  | 141.93±140.55          |         |         |
| Active              | 23  | 71.70±66.24            | 2.98    | <0.05   |
| Inactive            | 13  | 165.80±145.82          | 2.20    | <0.05   |
| SLEDAI>8            | 23  | 80.29±71.61            |         |         |
| SLEDAI<8            | 13  | 152.45±149.80          |         |         |
| Arthritis           | 23  | 103.37±126.35          | 0.40    | >0.05   |
| No arthritis        | 13  | 117.32±89.40           |         |         |
| Before treatment    | 9   | 114.41±92.40           | 2.00    | <0.05   |
| After treatment     | 9   | 245.64±196.57          |         |         |

SLE tends to damage multiple organs, including the kidney and articule. Our test showed the serum levels of MDC and MMP-9 were decreased in patients with renal damage than those without the damage, and the serum level of MDC was markedly decreased in patients with arthritis than those without the damage. MMP-9 was involved in inflammation and immune system dysfunctions. Besides immunologic abnormalities, SLE also presents chronic inflammatory components. Therefore, a role of MMP-9 in SLE pathology might be suspected.\textsuperscript{8} Serum level of MMP-9 in 36 SLE patients was tested and it was discovered that serum level of MMP-9 was significantly decreased in patients as compared to those in controls, and was lower in patients with active disease than those with inactive disease. A negative relation between serum level of MMP-9 and SLEDAI was found, which may reflect dynamic change of SLE.

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airway inflammation by impairing the recruitment of DCs into airways and the local production of DC-derived chemokines. At present, DCs are the most powerful antigen presenting cells and the main resource of MDC. The functional disorder antigen presenting cells and the reduced DCs are in existence in patients with SLE has been reported and the proportion of DCs in peripheral blood showed a negative correlation with disease activity. From the proportion of DCs in peripheral blood showed existence in patients with SLE has been reported and accumulation of clinical researches involved in SLE pathogenesis, it depends on further SLE patients. Whether this mechanism may also be involved in SLE pathogenesis, it depends on further accumulation of clinical researches.

CONCLUSION

SLE is an autoimmune disease. The useful measurement to cure this disease is Prednisone. When symptom ease, the dosage of Prednisone should be reduced. At this time, patient’s condition prefers to relapse, especially during 10-15mg a day to take. So the combing between Traditional and Western medicine is very important. The combination can control its deterioration and reduce its relapse so it is better to cure it.

Limitations of the Study: Small sample size was one of the important limitations of this study.

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