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Expression of IL-2 and IL-11 and its significance in patients with ankylosing spondylitis

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ABSTRACT

Objective: To explore the expression of IL-2 and IL-11 and its significance in patients with ankylosing spondylitis (AS). **Methods:** A total of 48 active AS patients in our hospital and 40 normal control subjects were selected in our study. Bath ankylosing spondylitis disease activity index (BASDAI), Bath ankylosing spondylitis functional index (BASFI), Bath ankylosing spondylitis metrology index (BASMI), ESR and CRP expression levels were compared before treatment, 12 h after treatment and 24 h after treatment. IL-2 and IL-11 expression were also compared between these two groups. **Results:** The BASDAI score, BASFI score and BASMI score of the AS patients before treatment significantly decreased compared with those 12 weeks and 24 weeks after treatment ($P<0.05$). ESR and CRP levels of the AS patients 12 weeks and 24 weeks after treatment significantly decreased compared with those before treatment ($P<0.05$). Difference was significant in serum IL-2 and IL-11 levels between 12 weeks and 24 weeks after treatment and before treatment ($P<0.05$). And no statistically significance was observed for serum IL-2 and IL-11 levels between normal control group and those of patients in AS group 24 weeks after treatment ($P>0.05$). Pearson's linear-correlation analysis showed that serum IL-2 level had a positive correlation with BASDAI, BASFI, BASMI, ESR and CRP ($r=0.661,0.547,0.474,0.362,0.416$, $P<0.05$) and serum IL-11 level had a negative correlation with BASDAI, BASFI, BASMI, ESR and CRP ($r=-0.629$, -0.412, -0.422, -0.387, -0.408, -0.315, $P<0.05$). **Conclusions:** Serum levels of IL-2 in active AS patients significantly increase and will decrease after treatment. However, serum levels of IL-11 significantly decrease and will increase after treatment, which indicates that serum IL-2 has a positive correlation with the degree of AS and serum IL-11 has a negative correlation with the degree of AS, both of which are correlated closely with the onset of AS.

1. Introduction

Ankylosing spondylitis (AS) is a chronic inflammatory disease at peripheral joints, sacroiliac joints and insertion of tendons, which is commonly seen in adolescent males. 90% of patients with AS are HLA-B27 positive. In China, the prevalence of ankylosing spondylitis is about 0.3%, with its main manifestations in the early stage including lesions at insertion sites of the ligament and synovitis. Spinal ankylosis caused by ligament calcification may occur at late stage, which may lead to disability, seriously influencing the patient's quality of life. However, up till now, the etiology of AS is still not clear. It may be related to environmental factors, genetic susceptibility factors, infection, disorders of the immune system and other factors[1,2].

2. Materials and methods

2.1. General information

Between January 2009 and January 2012, 48 active AS patients in our hospital were selected in our study. All patients are diagnosed based on the modified New York criteria of 1984[3]. There were 45 male and 3 female with a mean age of (34.5±10.6) years (range, 17-61 years). The mean duration of illness was 6.8 months (range, 0.5-27 months)

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with HLA-B27 positive in 42 cases and HLA-B27 negative in 6 cases. Patients were excluded if they had a history taking methotrexate and other drug use history. Those who had infection and other connective tissue diseases were also excluded. In addition, 40 healthy subjects were selected from our hospital employees as a control group. All the patients in the control group had no history of chronic low back pain or joint disease. Systemic infection and connective tissue disease were also excluded.

2.2. Treatment and detection index

All active AS patients were given nonsteroidal anti-inflammatory drugs and drugs of chronic effects such as methotrexate and sulfasalazine. A detailed and thorough examination was given to the selected objects. Bath ankylosing spondylitis disease activity index (BASDAI), Bath ankylosing spondylitis functional index (BASFI) and Bath ankylosing spondylitis metrology index (BASMI) were measured before treatment, 12 weeks and 24 weeks after treatment, respectively. Meanwhile, blood samples were drawn at eight in the morning during fasting conditions for measuring CRP, ESR, blood routine examination, hepatic and renal function. Fasting blood samples of all subjects were taken at 8 in the morning, which were collected and stored at -30℃ and serum IL-2, IL-11 levels were measured using double antibody sandwich enzyme linked immunosorbent assay.

2.3. Statistical analysis

Statistical analysis was performed using SPSS16.0 software. Data were expressed as mean ± standard deviation. Statistical comparisons were by t test and correlation analysis. It was considered statistically significant if the P value was less than 0.05.

3. Results

3.1. Comparison of curative effect before and after treatment in patients with AS

The curative effect before and after treatment in patients with AS showed that the BASDAI score, BASFI score and BASMI score of the AS patients 12 weeks and 24 weeks after treatment significantly decreased compared with those before treatment (P<0.05), which indicated the effectiveness of the treatment(Table 1).

Table 1
Curative effect before and after treatment in patients with AS.

Period	BASDAI	BASFI	BASMI
Before treatment	3.4±2.0	2.8±1.8	3.4±2.1
12 weeks after treatment	2.4±1.7*	2.2±1.5*	2.7±1.4*
24 weeks after treatment	1.7±1.2*	1.6±1.3*	1.7±1.2*

*: P<0.05, compared with before treatment.

3.2. ESR and CRP levels before and after treatment in patients with AS

ESR and CRP levels before and after treatment in patients with AS showed that ESR and CRP levels of the AS patients 12 weeks and 24 weeks after treatment significantly decreased compared with those before treatment (P<0.05) (Table 2).

Table 2
Comparison of ESR and CRP levels before and after treatment in patients with AS.

Period	ESR(mm/h)	CRP(mg/L)
Before treatment	34.6±9.8	28.1±6.9
12 weeks after treatment	26.2±8.7*	17.2±5.3*
24 weeks after treatment	21.1±6.8*	12.4±4.1*

*: P < 0.05, compared with before treatment.

3.3.Expression of serum IL-2 and IL-11

Significant difference was noted for serum IL-2 and IL-11 levels between 12 weeks and 24 weeks after treatment and before treatment (P<0.05). And no statistically significance was observed for serum IL-2 and IL-11 levels between normal control group and those of patients in AS group 24 weeks after treatment (P>0.05) (Table 3).

3.4. Correlation detection

Pearson's linear-correlation analysis showed that serum IL-2 level had a positive correlation with BASDAI, BASFI, BASMI, ESR and CRP (r=0.661, 0.547, 0.474, 0.362, 0.416, P<0.05) and serum IL-11 level had a negative correlation with BASDAI, BASFI, BASMI, ESR and CRP(r=-0.629, -0.412, -0.422, -0.387, -0.408, -0.315, P<0.05).

4. Discussion

AS is a chronic inflammatory disease which involves

Table 3
Expression of serum IL-2 and IL-11.

Group		IL-2(pg/L)	IL-11(pg/L)
AS group	Before treatment	156.3±48.9	116.2±37.6
	12 weeks after treatment	101.2±35.3	146.5±39.2
	24 weeks after treatment	64.8±11.2	168.3±41.4
Normal control group		56.6±8.9	178.7±45.7

the spine and the peripheral joints to different extent. The incidence of AS is closely related to HLA-B27. It is commonly seen in China with a high incidence ranging in age from 10 to 30 years[4]. No obvious symptoms or signs were noted in the early stages of AS. Its early onset may be associated with abnormal bone metabolism, enhanced bone resorption and relative lack of bone formation. With the development of lesions, rigid peripheral joints and the spine may occur, which will lead to deformity or disability. Traditional therapies include nonsteroidal anti-inflammatory drugs or adrenal cortical hormones, but they can only alleviate the symptoms but cannot improve symptoms[5,6]. In our study, drugs such as methotrexate and sulfasalazine were used to treat the patients and the results showed that the BASDAI score, BASFI score and BASMI score of the AS patients 12 weeks and 24 weeks after treatment significantly decreased compared with those before treatment ($P<0.05$). It showed that methotrexate and sulfasalazine could largely achieve a therapeutic purpose for AS patients.

Recently, cytokine mediated effects attract more and more attention. IL-2 is one of the most important lymphokines ever known in the occurrence and development of joint disease with a molecular mass of 15 kD, which is produced by mitogen, antigen or T cells activated by T cell antigen receptor monoclonal antibody[7]. Almost all activated T cells can secrete IL-2, among which helper T cells account for 80%. Therefore, IL-2 expression mainly reflects TH function. IL-2 can maintain long-term growth potential *in vitro*, activate T cells, NK cells and promote the functional expression and proliferation of B-cells. Therefore, IL-2 plays an important regulatory role in humoral and cell-mediated immunity.

The results of this study showed that the expression of IL-2 in AS patients was significantly higher than that in the normal group, which indicated that there might be an abnormal increase in activated immune cells in the peripheral blood in AS patients.

Increased IL-2 secretion reflected the increased exogenous activation on the body and the enhanced TH function. In addition, the results showed that the serum IL-2 level had a positive correlation with BASDAI, BASFI, BASMI, ESR and CRP. After treatment, the IL-2 levels gradually decreased, indicating that the IL-2 level could reflect the disease activity of AS, which played an important role in the pathogenesis of AS.

IL-11 belongs to IL-6 cytokine family, secreted by cells of stromal cell lines, which is a multifunctional cytokine[8,9]. The local IL-11 in bone is secreted by osteoblasts, which also plays an important role on osteoclasts, however. On one hand, it can inhibit the activity of osteoblasts and inhibit bone formation. On the other hand, it can stimulate proliferation of osteoclasts and thereby promote bone resorption. Recent studies have shown that, some systemic or local factors can produce IL-11 by stimulating osteoblasts to influence osteoblasts and osteoclasts, regulating bone metabolism. The study of Shinohara *et al*[10] showed that in the presence of IL-11, osteoclasts had the function of bone resorption, indicating that IL-11 was an important regulatory factor in both physiological and pathological conditions for regulation of bone mineral density. Our study showed that the serum level of IL-11 in AS patients was lower than that in normal control group. The possible reason was that the local or systemic inflammation inhibited the activity of osteoblasts, so as to reduce the secretion of IL-11. In addition, inflammation also stimulated osteoclasts to enhance their activity and bone resorption, thus played a role in the negative feedback regulation of IL-11 production, which reduced the IL-11 production. The reduction of IL-11 caused a decrease in the inhibition of osteoblast. The overexpression of osteoblast finally led to local osteophyte formation. But this study showed that serum IL-11 level had a negative correlation with BASDAI, BASFI, BASMI, ESR and CRP. After treatment serum IL-11 level gradually started to rise, showing that serum IL-11 in AS patients correlated negatively with the degree of AS and correlated closely with the onset of AS.

Conflict of interest statement

We declare that we have no conflict of interest.

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