Correlation between activity of rheumatoid arthritis and severity of "oketsu" syndrome

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Abstract

To investigate the relationship between the "oketsu" syndrome, which is characterized by blood stagnation, and rheumatoid arthritis (RA), we assessed the prevalence and severity of oketsu in 78 patients with RA in April 1996. The prevalence of oketsu was 53.8 % using Terasawa's criteria. The severity of oketsu was significantly correlated with the activity of RA, assessed by Lansbury's activity index ($rs=0.26$, $p=0.025$). Six months later, 64 of the 78 patients were re-evaluated. The 15 patients who no longer exhibited the oketsu syndrome showed a tendency toward a decrease in Lansbury's activity index ($p=0.083$). A significant increase in Lansbury's activity index ($p=0.043$) was seen in 5 patients who developed the oketsu syndrome over the 6-month period. Findings suggest that a clinically meaningful relationship exists between the severity of oketsu and the activity of RA.

Key words "oketsu" syndrome, rheumatoid arthritis, Kampo medicine.

Abbreviations RA, rheumatoid arthritis ; Toki-shakuyaku-san (Dang-Gui-Shao-Yao-San), 当帰芍薬散 ; Ji-daboku-ippo (Zhi-Da-Pu-Yi-Fang), 治打撲一方.

Introduction

According to Kampo medicine, or Japanese Oriental medicine, the "oketsu" syndrome is characterized as a state of blood stagnation. There is a broad consensus among Kampo practitioners that a relationship exists between the presence of the oketsu syndrome and rheumatoid arthritis (RA), but there are few reports of the prevalence of oketsu syndrome in RA patients. Whether oketsu influences the activity of RA is unclear. The present study attempted to clarify the relationship between these disorders by investigating the prevalence of oketsu syndrome in patients with RA using the diagnostic criteria of Terasawa.[1] We investigated the possible correlation between the oketsu score and the disease activity of RA that was rated according to Lansbury's activity index.[2] Six months later, we obtained repeat measurements of oketsu scores and RA disease activity for some of the patients.

Patients and Methods

Patients : We evaluated 78 Japanese patients with RA (4 men and 74 women aged 38 to 83 years, mean 62.3±8.8 (S.D.) years) who visited the Department of Japanese Oriental Medicine, Toyama Prefectural Central Hospital, in April 1996. All patients met the American College of Rheumatology 1987 criteria for the diagnosis of RA.[3]

Methods : The diagnosis of the oketsu syndrome was made according to the criteria set forth by Terasawa.[1] Symptoms include dark-rimmed eyes ; areas of dark pigmentation of facial skin ; livid lips, gingiva, and tongue ; telangiectasis ; subcutaneous

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Table I System for scoring the oketsu syndrome in males and females

Symptom	Score	
	male	female
Dark-rimmed eyes	10	10
Areas of dark pigmentation of facial skin	2	2
Rough skin	2	5
Livid lips	2	2
Livid gingiva	10	5
Livid tongue	10	10
Telangiectasis/vascular spiders	5	5
Subcutaneous hemorrhage	2	10
Palmar erythema	2	5
Resistance and tenderness on pressure of the left para-umbilical region	5	5
Resistance and tenderness on pressure of the right para-umbilical region	10	10
Resistance and tenderness on pressure of the umbilical region	5	5
Resistance and/or tenderness on pressure of the ileo-cecal region	5	2
Resistance and/or tenderness on pressure of the sigmoidal region	5	5
Resistance and/or tenderness on pressure of the subcostal region	5	5
Hemorrhoids	10	5
Dysmenorrhea	–	10

A total score of 21 points or higher indicates a diagnosis of oketsu syndrome ; a score of 40 points or higher indicates severe oketsu syndrome. Mild symptoms are denoted by half points. (Terasawa, 1983)

hemorrhage ; and palmar erythema. Table I lists the symptoms and the scoring system for the oketsu syndrome in males and females. Mild symptoms are designated by half points. A total score of 21 points or higher indicates the presence of oketsu syndrome, and a score of 40 points or higher indicates severe oketsu syndrome.

The activity of RA was evaluated by means of Lansbury's activity index, which scores the duration of morning stiffness, grip strength, articular index, and the erythrocyte sedimentation rate (ESR).

Patients were followed for 6 months at our outpatient clinic. All of them were treated with Kampo medicines,[4] and some received concomitant nonsteroidal anti-inflammatory drugs (NSAIDs), glucocorticoids, or slow-acting antirheumatic drugs (SAARDs) such as gold compounds and bucillamine. Six months later, in October 1996, we re-evaluated the oketsu scores and Lansbury's activity indexes in 64 of the 78 patients. Regarding the other 14 patients living some distance away, we could not re-evaluate them in October 1996, because clinic visits were inconvenient for them. Based on changes in the oketsu scores between April and October, patients were classified as follows, with (+) referring to the presence of oketsu and (-), to the absence of oketsu : (+) → (-) ; (-) → (+) ; (+) → (+) ; and (-) → (-). For each group, the activity of RA in April was compared with that of October.

Statistical analysis : Data are reported as mean± S.D. Statistical analyses were performed using Spearman's rank correlation coefficient or Wilcoxon's signed-rank test. A level of $p<0.05$ was accepted as statistically significant.

Results

Prevalence of oketsu syndrome in RA

A total of 42 of the 78 patients with RA (53.8 %) were diagnosed as having the oketsu syndrome. Table II shows that the prevalence of oketsu ranged from 45.8 - 60.0 % at each stage and duration of RA. The mean age was 61.6±8.0 (S.D.) in the 42 oketsu patients ; 62.3±9.9 (S.D.) in the 36 non-oketsu patients. Glucocorticoids had concomitantly been used in 8 (19.0 %) of the 42 oketsu patients ; in 5 (13.9 %) of the 36 non-oketsu patients. Oketsu-improving Kampo medicines had been used in 17 (40.5 %) of the

Table II Prevalence of oketsu syndrome in 78 patients with RA

RA	Number of patients		Prevalence of oketsu
	Oketsu syndrome	No oketsu syndrome	
Stage			
I	3	2	60.0 %
II	18	14	56.3 %
III	10	7	58.8 %
IV	11	13	45.8 %
Disease duration			
<10 yrs	27	20	57.4 %
≧10 yrs	15	16	48.4 %

RA=Rheumatoid arthritis

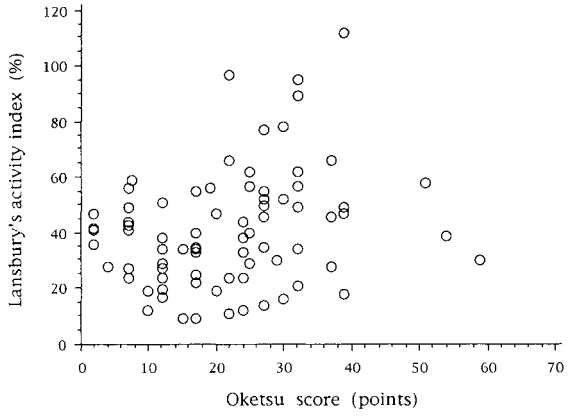

Fig. 1 Correlation between oketsu score and Lansbury's activity index for RA in 78 patients. Statistical analyses were performed using Spearman's rank correlation coefficient. The oketsu score was significantly correlated with Lansbury's activity index (rs=0.26, p=0.025).

Table III Changes in oketsu syndrome and in Lansbury's activity index in 64 patients between April-October 1996

Change in oketsu syndrome April→October	No. of patients	Change in Lansbury's activity index (%) April Mean (S.D.)	October Mean (S.D.)	p-Value
(+) → (−)	15	50.5 (22.9)	45.4 (19.6)	0.083
(−) → (+)	5	36.0 (16.4)	44.6 (22.7)	0.043
(+) → (+)	18	48.7 (27.6)	48.2 (18.6)	0.449
(−) → (−)	26	32.9 (13.9)	31.2 (17.5)	0.809

Data are presented as mean±S.D. Statistical analyses were performed using Wilcoxon's signed-rank test.
(+)=present (−)=absent

42 oketsu patients ; in 9 (25 %) of the 36 non-oketsu patients.

Correlation between oketsu score and Lansbury's activity index

The oketsu score correlated significantly with Lansbury's activity index (rs=0.26, p=0.025) (Fig. 1).

Change in Lansbury's activity index (Table III)

At the 6-month follow-up in October 1996, the 15 patients who no longer had oketsu showed a tendency toward a decrease in Lansbury's activity index (p=0.083). The 5 patients who developed oketsu over the 6-month period showed a significant increase in Lansbury's activity index (p=0.043).

Discussion

There is a broad consensus among Kampo practitioners that a relationship exists between the presence of the oketsu syndrome and rheumatoid arthritis (RA), but there are few reports of the prevalence of oketsu syndrome in RA patients. Whether oketsu influences the activity of RA is unclear. To clarify the relationship between these disorders, we investigated the prevalence of oketsu syndrome in patients with RA using the diagnostic criteria of Terasawa.[1] We investigated the possible correlation between the oketsu score and the disease activity of RA that was rated according to Lansbury's activity index.[2] Six months later, we obtained repeat measurements of oketsu scores and RA disease activity for some of the patients.

Of the 78 patients with RA who visited our outpatient clinic in April 1996, 42 (53.8 %) had the oketsu syndrome. A previous study reported that Kampo medicines prescribed to improve the oketsu syndrome had been used in 55 % of the RA patients who showed a marked improvement ;[5] this incidence is consistent with the 53.8 % incidence found in the present study. Based on these findings, we estimate that about 50 % to 60 % of the RA patients living in Japan (especially in the Hokuriku region) have the oketsu syndrome in spring.

Our group previously reported that the viscosity of the plasma in patients with oketsu exceeds that in healthy volunteers,[6] and that oketsu is closely related

to abnormalities of the microcirculation of the bulbar conjunctiva.[7] Hanada *et al.*[8] compared the bulbar conjunctival venules of RA patients with those of healthy volunteers and found the hemodynamic status of the microcirculation to be less stable in RA patients; they also reported that the plasma viscosity was correlated with Lansbury's activity index and was higher in RA patients than in healthy volunteers. Our data demonstrated that the higher the oketsu score, the more severe the activity of the RA. Follow-up assessment indicated that when the oketsu syndrome improved, the RA activity also improved. In other cases, both the oketsu severity and the RA activity worsened. These findings suggest there exists a clinically meaningful relationship between the severity of oketsu and the activity of RA. However, it remains unclear whether the oketsu syndrome enhances disease activity in RA, or results from an increase in such activity.

Our group previously reported a patient with RA who was effectively treated with Toki-shakuyaku-san (Dang-Gui-Shao-Yao-San), a medicine commonly used to alleviate the symptoms of oketsu.[9] We have also reported the beneficial effects of the supplemental administration of Ji-daboku-ippo (Zhi-Da-Pu-Yi-Fang) in patients with RA.[10] These findings and the present results suggest that medications that improve the symptoms of oketsu may also be beneficial in patients with RA.

和文抄録

血液の流れのうっ滞として特徴づけられる瘀血症候群と慢性関節リウマチ(RA)との関連性を調べるために，1996年4月に受診したRA患者のうち78名の瘀血有病率とその重症度を評価した。寺澤らの瘀血診断基準を用いたところ，瘀血の有病率は53.8％であった。また，瘀血の重症度は有意にRAの活動性（ランスバリー活動性指数）と相関していた（rs＝0.26, p＝0.025)。78名中64名については，6ケ月後の経時的変化を評価することができた。6ケ月後に瘀血から非瘀血へと改善した15例はランスバリー指数の減少傾向を示した（p＝0.083)。6ケ月後に非瘀血から瘀血へと増悪した5例では有意なランスバリー指数の増加を認めた(p＝0.043)。これらの所見から，瘀血の重症度とRAの活動性との間に臨床的に意味のある関連性が存在することが示唆された。

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