

## The characteristics of the microcirculation of bulbar conjunctiva in "oketsu" syndrome

Katsutoshi TERASAWA,\* Takashi ITOH, Yumi MORIMOTO, Yukitaka HIYAMA and Hiroyori TOSA

*Department of Japanese Oriental Medicine, Toyama Medical and Pharmaceutical University*

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### Abstract

In order to elucidate the characteristics of microcirculation in "oketsu" (blood stagnant) syndrome, 20 patients and 35 volunteers were evaluated by using a video-microscope system. According to "Terasawa" diagnostic criteria, patients and volunteers were classified into 3 groups: non-"oketsu", mildly affected and severely affected with "oketsu" syndrome. Then the correlations between the "oketsu" state and the presence of abnormal findings were analyzed statistically. The results showed that intravascular erythrocyte agglutination associated with sludging and/or stasis of blood significantly correlated with the "oketsu" syndrome. This syndrome was also correlated with such architectural changes as meandering, narrowing, microaneurysms and proliferation of microvessels. These abnormal findings in bulbar conjunctiva have been reported in arteriosclerotic and diabetic diseases; however, this investigation suggested that these abnormalities also appear without such diseases. It is thought that this study provides the empirical concept of the "oketsu" syndrome with concrete scientific evidence regarding the abnormalities of microcirculation.

**Key words** oketsu syndrome, blood stasis syndrome, microcirculation, bulbar conjunctiva.

**Abbreviations** AAS, architectural abnormality score; BFS, blood flow score; IEA, intravascular erythrocyte agglutination; oketsu, 瘀血.

system.

### Introduction

"Oketsu," blood stasis or stagnant syndrome, is one of the pathological and physiological concepts existing only in traditional Chinese medicine.<sup>1,2)</sup> In traditional Chinese medicine, "ketsu" (blood) means human red body fluid containing life energy, that circulates in the body. A pathological state induced by circulatory failure of this "ketsu" is called "oketsu." This empirical concept, however, has not been established on the basis of scientific observation of blood circulation. The present report was undertaken in an attempt to elucidate the abnormalities of blood microcirculation in bulbar conjunctiva in the "oketsu" syndrome by using a video-microscope

### Subjects and Methods

**Subjects** : Twenty patients (male, 22-74 y.o.) admitted to the Department of Japanese Oriental Medicine, Toyama Medical and Pharmaceutical University, during the study period were evaluated in this study (Table I). Thirty-five volunteers (male, 19-57 y.o. staff members and students of this university) consisted of 15 myopes with glasses and 20 of normal visual acuity were also investigated in this study. The degree of the "oketsu" state was standardized according to the diagnostic criteria of Terasawa *et al.*<sup>3)</sup>

**Observation of blood flow** : Microcirculation of the bulbar conjunctiva in the left eyeball (lat-

\*〒930-01 富山市杉谷2630  
富山医科薬科大学附属病院和漢診療部 寺澤捷年  
2630, Sugitani, Toyama 930-01, Japan

Table I

No.	age	Diagnosis	glasses	visual acuity	"Oketsu"	BFS	AAS
1.	76	irritable bowel synd.	+(+D)	0.3 /0.2	mild	9	2
2.	38	multiple sclerosis	+(-D)	0.2 /0.07	mild	16*	2
3.	63	Brown-Sequard synd.	-	1.0 /1.0	mild	6	2
4.	56	diabetes mellitus	-	1.5 /1.5	mild	22*	2
5.	33	Burger disease	+(-D)	0.04/0.06	mild	6	1
6.	32	chemical diabetes	-	1.5 /1.5	mild	7	4
7.	22	polyneuritis	-	1.5 /1.5	mild	6	2
8.	54	diabetes mellitus	+(-D)	0.05/0.07	mild	16*	4
9.	59	intermittent claudication	-	0.7 /1.2	severe	7	2
10.	74	cerebral infarction	+(+D)	0.5 /0.4	severe	12	2
11.	44	anterior spinal artery synd.	-	0.8 /0.5	severe	9	4
12.	65	diabetes mellitus	-	0.9 /0.9	severe	22*	4
13.	64	diabetes mellitus	+(+D)	0.4 /10 cm	severe	22*	4
14.	60	multiple sclerosis	-	0.7 /0.9	severe	22*	3
15.	61	cerebral infarction	-	0.8 /0.7	severe	22*	4
16.	56	carcinoma of the lung	+(+D)	0.4 /0.4	severe	6	2
17.	60	rheumatoid arthritis	-	1.0 /0.9	severe	7	3
18.	53	chronic hepatitis	-	1.5 /1.5	severe	7	3
19.	41	Ménière's disease	-	2.0 /2.0	severe	6	2
20.	50	thrombosis of basilar artery	-	2.0 /2.0	severe	17*	4

Note : glasses +/- means wear or not wear, (+/-D) indicates + or - diopter.

Visual acuity, right/left. \*in BFS indicates presence of blood stasis.

None of the cases has a past history of severe conjunctivitis.

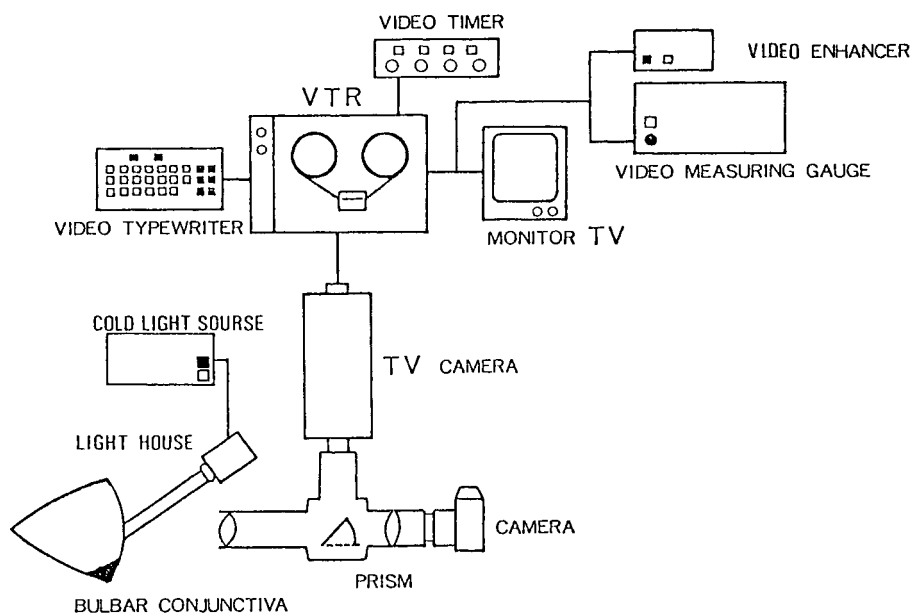


Fig. 1 System diagram of the video-microscope system.

eral-upper part) was observed by using a video-microscope system<sup>4)</sup> developed by Dr. Nobuko Tsushima of the National Cardiovascular Center, Osaka, Japan (Fig. 1): The light source is a halogen lamp (6 V, 30 W), and the light is led to a lamp house by glass fibers. The projection gate of the lamp house has variable slits in both horizontal and vertical directions. Observation of bulbar conjunctiva is made with an objective lens of five magnifications. By using a prism chamber, it is possible to observe the conjunctiva with a camera (Nikon MD-4) or a video camera (Victor KY-M280). The pictures passing through the video camera are recorded by videotape recorder (Victor CR-6600) and monitored by a 20-inch TV monitor. The final magnifications are  $\times 30$  and  $\times 175$  in the camera film and the TV monitor, respectively. The internal diameters of the vessels observed in this study ranged from 5 to 30  $\mu\text{m}$ , corresponding to precapillaries, true capillaries and postcapillaries by anatomical classification of Zweifach.<sup>5)</sup>

*Evaluation of blood flow abnormalities*: The following findings of microcirculation were evaluated; rouleau phenomenon, intravascular erythrocyte agglutination (IEA), sludging of blood and blood stasis. Then a blood flow score (BFC) was given to each subject using the following equation:

$$\text{BFC} = \text{rouleau} \times 1 + \text{IEA} \times 2 + \text{sludge} \times 3 + \text{stasis} \times 10$$

*Evaluation of architectural changes in small vessels*: Architectural abnormalities were observed in the following items; meandering, proliferation, segmental dilation, segmental narrowing and micro-aneurysm of the microvessels. These findings were classified into four grades (0=none, 1=slight, 2=moderate, and 3=remarkable), then

an architectural abnormality score (AAS) was given to each subject according to the arithmetic sum of the items.

*Evaluation of arteriosclerosis*: The vessels of the ocular fundi were observed by direct fundoscopy, and then classified into five grades by Scheie's criteria.<sup>6)</sup>

*Statistical analysis*: In case of intravascular agglutination with the sludge phenomenon, the statistical evaluation was performed by the Chi square test between the three group of "oketsu" score and the prevalence of abnormal findings. For the analyses of blood stasis vs. "oketsu" state, BFC vs. "oketsu" state, and AAC vs. "oketsu" state, the Student's *t*-test was used.

## Results

### *Correlation between the "oketsu" syndrome and retinal arteriosclerosis and concomitant diseases*

As shown in Table I, the present study included several diabetics and patients with arteriosclerosis, but there was no significant correlation between the degree of the "oketsu" state and arteriosclerosis of the retinal arteries (Table II), and concomitant diseases.

### *Intravascular erythrocyte agglutination (IEA) with the sludge phenomenon*

A typical case of this abnormal finding is presented in Fig. 2. As shown in Table III, this abnormal finding was significantly correlated with the "oketsu" state.

### *Blood stasis*

In this study, we evaluated blood stasis in a condition such as when there was cessation of blood flow for at least one minute. In cases of volunteers, there was no evidence of blood stasis even in those with severe "oketsu" syndrome. In

Table II Correlation between "oketsu" state and degree of retinal arteriosclerosis.

	Normal	S1	S2	S3
Non-"oketsu" group	15	0	0	0
Mildly affected group	20	3	0	0
Severely affected group	8	6	2	1

Note: S1-S3 represent Scheie's classification of retinal arteriolar sclerosis.

Table III Correlation between "oketsu" state and intravascular erythrocyte agglutination (IEA).

	IEA (-)	IEA (+)	IEA (++)
Non-"oketsu" group	5	7	3
Mildly affected group	4	5	14
Severely affected group	0	2	15

IEA vs. "oketsu,"  $p < 0.005$



Fig. 2 Example of intravascular erythrocyte agglutination with sludge phenomenon. Photograph from TV monitor ( $\times 175$ ).



Fig. 3 Blood flow abnormalities in "oketsu" syndrome : Intravascular erythrocyte agglutination ( ++ ), sludging of blood ( ++ ), blood stasis (arrow) and meandering of microvessels.

patients, however, blood stasis was observed in 3 of 8, and in 5 of 12 in mildly affected and severely affected cases of "oketsu" syndrome, respectively (marked \* in Table I).

#### Blood flow score (BFS)

Blood flow scores, which represent abnormalities of blood flow in microcirculation as a whole, were significantly different between the three groups;  $1.9 \pm 2.3$  (mean  $\pm$  S.D.),  $6.2 \pm 2.4$  and  $11.2 \pm 3.7$  in the non-"oketsu" group, mildly affected group and severely affected group, respectively. Examples of the abnormal findings of the microcirculation in bulbar conjunctiva are given in Fig. 3.

#### Architectural abnormality score (AAS)

AAS, representing architectural abnormalities in microvessels, was also significantly different between the three groups;  $0.9 \pm 0.7$  (mean  $\pm$  S.D.),  $1.9 \pm 0.9$ , and  $2.8 \pm 0.8$  in the non-"oketsu" group, mildly affected group, and severely affected group, respectively.

#### Ophthalmological effects of video-microscopic observations

There was no ophthalmological evidence such as blurred vision, itching or dryness of the eyeball following the video-microscopic observation.

## Discussion

Recently, Hayashi *et al.*<sup>7)</sup> reported on the pharmacological effects of a Kampo formula (Keisi-bukuryō-gan) on the microcirculation of bulbar conjunctiva. Keisi-bukuryō-gan is one of the most popular Kampo formulas for treating the "oketsu" syndrome. However, there has been no report concerning the correlation between the "oketsu" syndrome and characteristics of the microcirculation.

The results obtained in this study suggest that the "oketsu" syndrome is closely correlated with the abnormalities of the microcirculation of bulbar conjunctiva. Concerning such abnormalities, Davis and Landau<sup>8)</sup> and Isogai<sup>9)</sup> have reported on arteriosclerosis and diabetes mellitus, respectively. The present study includes 5 diabetic and 5 arteriosclerotic patients. As shown in Table I, there is a pronounced tendency for arterio-

sclerotic and diabetic patients to have more abnormalities in relation to the blood flow of microvessels. In agreement with the report of Yukimura *et al.*,<sup>10)</sup> all diabetic patients in this study were also evaluated as "oketsu" state patients by the "Terasawa" diagnostic criteria,<sup>3)</sup> which means that diabetes mellitus in Western medicine is complicated in a high incidence by the "oketsu" syndrome in Kampo medicine.

The results also indicate that abnormalities of the microcirculation appear not only in diabetic and arteriosclerotic diseases but even in a "normal" volunteer. The word "normal" means a subject who has no apparent disorder from the viewpoint of Western medicine. In this study, however, we classified "healthy volunteers" into three groups of the "oketsu" state in order to elucidate the abnormalities of the microcirculation of this syndrome.

Through this investigation, it becomes apparent that "oketsu," a new dimension for microcirculation provided by traditional Kampo medicine, is closely correlated with abnormalities of the blood flow and architecture of microvessels. Further, we believe that the empirical concept of the "oketsu" syndrome is scientifically supported by the findings of this study.

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## 和文抄録

瘀血病態における微小循環障害の実相を検討する目的で眼球結膜血管を顕微鏡ビデオ装置で観察した。対象は患者20例と健常人35人であり、寺澤らの瘀血診断基準を用いてこれらを非瘀血群、軽度瘀血群、重度瘀血群の3群に分類した。血流の異常としては血管内赤血球集合、スラッジ現象、連鎖現象、血流の局所的停止が観察されたが、これらの異常所見は推計学的に有意に瘀血病態と関連した。また血

管構築の異常として血管の蛇行, 狭小化, 小血管瘤, 毛細血管の新生が観察されたが, これらの異常所見も瘀血病態で有意に多く見られた。これらの血流と構築上の異常は動脈硬化性疾患や糖尿病でしばしば観察されるが, 本研究により, 瘀血という新たな指標で相関を検討することの意義が明らかになった。また経験的に血の滞りとされてきた瘀血病態に科学的な事実を提供しえたと考える。

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