J Cardiol 2007 May; 49(5): 217–219

Important Message

Remarkable Efficacy of Thermal Therapy for Sjögren Syndrome

Chuwa TEI, MD, FJCC
Koji ORIHARA, MD
Tsuyoshi FUKUDOME, MD

Key Words
■**Thermal therapy** ■**Heart failure**(**infrared-ray dry sauna**)
■**Cardiomyopathies, dilated** ■**Complications**(**Sjögren syndrome**)
■**Cells**(**monocytes**) ■**Leukocytes**(**human leukocyte antigen-A, B, C**)

We previously provided repeated thermal therapy using an infrared-ray dry sauna evenly maintained at 60°C for patients with chronic heart failure and reported that it improved the hemodynamics and symptoms.[1–4] Furthermore, we previously showed *in vivo* that the advantageous effect is based in part on the up-regulation of the endothelial nitric oxide synthase(eNOS)expression level after repeated thermal therapy.[5,6] In this report, we describe a patient who suffered from Sjögren syndrome with complications of idiopathic dilated cardiomyopathy(DCM), and we demonstrate that repeated therapy using an infrared-ray dry sauna remarkably improved the symptoms of Sjögren syndrome as well as DCM. In addition, we simultaneously observed that this therapy down-regulated the abnormally high level of human leukocyte antigen(HLA)-A, B, C(major histocompatibility complex class I)expression on the monocytes to close to the normal range, regardless of the fact that the medications were left unchanged during the sauna therapy.

A 62-year-old female had been experiencing arthritic pain and dry mouth since April 2001; she was diagnosed to have Sjögren syndrome and had been taking the appropriate medication. Subsequently, she developed the subjective symptom of shortness of breath on effort in 2002, was diagnosed with DCM, and medical follow-up treatment was initiated. She was admitted to our hospital in March 2004. On admission, xerostomia, xerophthalmia and arthritis from Sjögren syndrome were particularly noticable. The severity of cardiac failure was New York Heart Association(NYHA)class Ⅱ–Ⅲ, and the white blood count, C-reactive protein and brain natriuretic peptide(BNP)levels were 4,900 /μl, 1.05 mg/d*l* and 118 pg/m*l*, respectively. Other notable findings were that the anti-RNP antibody and anti-Sm antibody were positive, and the anti-DNA antibody was 3 IU/m*l*. The anti-SSA and anti-SSB antibodies were negative. Ultrasonic cardiography showed the left ventricular diastolic volume(LVDV), left ventricular systolic volume(LVSV)and ejection fraction(EF)were 150 m*l*, 111 m*l* and 26%, respectively.

After 20 times of repeated thermal therapy once each day for 4 weeks, cardiac dysfunction improved(LVDV = 106 m*l*, LVSV = 67 m*l*, EF = 37%, BNP = 40 pg/m*l*, NYHA class Ⅰ–Ⅱ). In addition, the subjective symptoms of Sjögren syn-

鹿児島大学大学院医歯学総合研究科 循環器・呼吸器・代謝内科学〔鄭 忠和，折原弘治，福留 剛〕：〒890–8520 鹿児島県鹿児島市桜ヶ丘8–35–1
Department of Cardiovascular, Respiratory and Metabolic Medicine, Graduate School of Medicine, Kagoshima University, Kagoshima
Address for correspondence: TEI C, MD, FJCC, Department of Cardiovascular, Respiratory and Metabolic Medicine, Graduate School of Medicine, Kagoshima University, Sakuragaoka 8–35–1, Kagoshima, Kagoshima 890–8520; E-mail: tei@m.kufm.kagoshima-u.ac.jp
Manuscript received March 5, 2007; accepted March 27, 2007

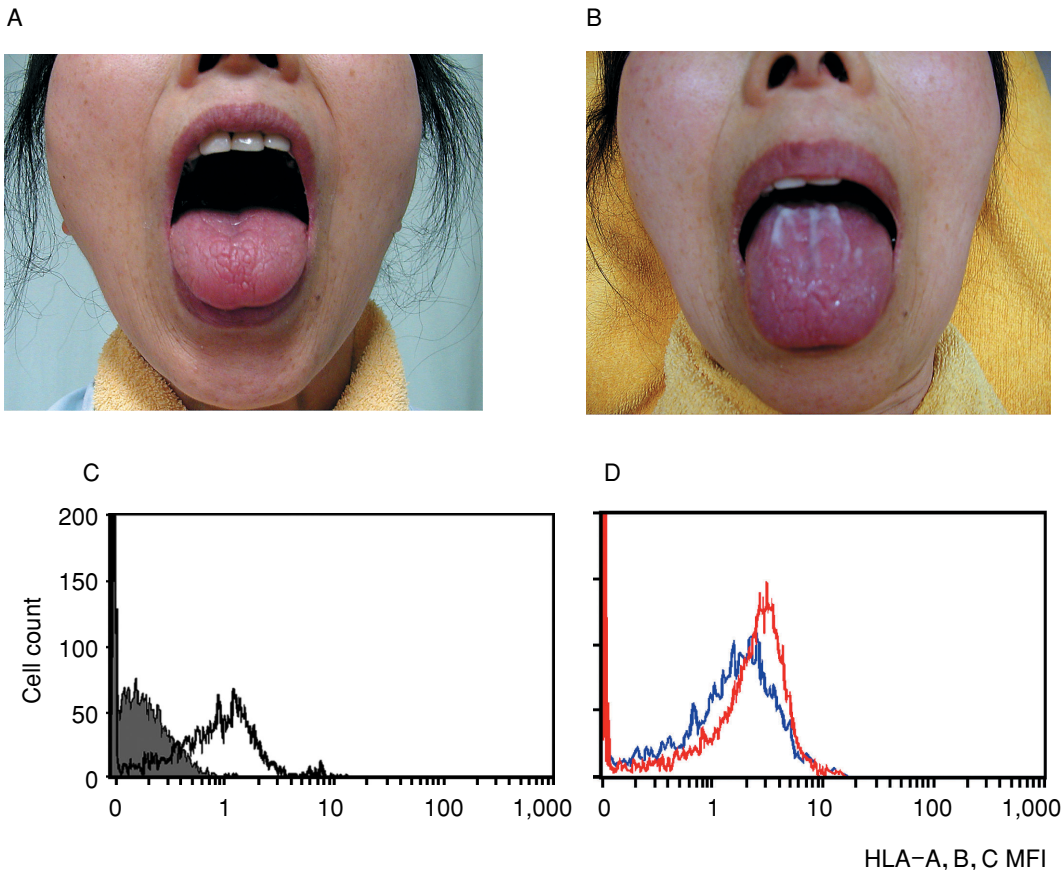

Fig. 1 Alleviation of xerostomia and normalization of the HLA-A, B, C expression level on the monocytes

A: Xerostomia before thermal therapy.

B: Alleviation just after thermal therapy.

C: HLA-A, B, C expression level on the monocytes is represented numerically with values derived from mean fluorescence intensity (MFI) treated with anti-HLA-A, B, C antibody (*black line*) divided by control MFI treated with anti-IgG2a (*gray zone*). The mean ± SD was 3.37 ± 1.31 ($n = 23$).

D: HLA-A, B, C expression level is shown as the *red line* (11.60), and the modulation after 20 sessions of thermal therapy shown as the *blue line* (6.34).

drome, in particular, xerostomia and arthritis, were all dramatically alleviated (**Figs. 1−A, B**). On the other hand, we examined the HLA-A, B, C expression level on the circulating monocytes, which activated the CD8 + cytotoxic T lymphocytes[7,8] and are capable of inhibiting the cytotoxic activity of the NK cells,[9] by flow-cytometry before and after the 20 sessions of repeated thermal therapy. The results showed that she had an HLA-A, B, C expression level which was 3.4 times higher than the mean value of the normal volunteers ($n = 23$) before the thermal therapy, but after the thermal therapy, the level was down-regulated and even approached the normal range (mean ± 2SD, $n = 23$; **Figs. 1−C, D**). We hypothesized that this modulation of HLA-A, B, C on the monocytes may thus be associated with the alleviation of the symptoms of Sjögren syndrome, and our study investigating this mechanism is now currently in progress.

This case shows that thermal therapy may qualify as a treatment for Sjögren syndrome. Furthermore, repeated thermal therapy was found to effectively alleviate the symptoms of three consecutive patients with Sjögren syndrome, in particular the symptoms of xerostomia and arthritis, without any complications.

References

1) Tei C, Horikiri Y, Park JC, Jeong JW, Chang KS, Toyama Y, Tanaka N: Acute hemodynamic improvement by thermal vasodilation in congestive heart failure. Circulation 1995; **91**: 2582−2590
2) Tei C, Tanaka N: Thermal vasodilation as a treatment of congestive heart failure: A novel approach. J Cardiol 1996; **27**: 29−30
3) Tei C: Thermal therapy for congestive heart failure: Estimation by TEI index. J Cardiol 2001; **37**: 155−159
4) Kihara T, Biro S, Imamura M, Yoshifuku S, Takasaki K, Ikeda Y, Otsuji Y, Minagoe S, Toyama Y, Tei C: Repeated sauna treatment improves vascular endothelial and cardiac function in patients with chronic heart failure. J Am Coll Cardiol 2002; **39**: 754−759
5) Ikeda Y, Biro S, Kamogawa Y, Yoshifuku S, Eto H, Orihara K, Yu B, Kihara T, Miyata M, Hamasaki S, Otsuji Y, Minagoe S, Tei C: Repeated sauna therapy increases arterial endothelial nitric oxide synthase expression and nitric oxide production in cardiomyopathic hamsters. Cir J 2005; **69**: 722−729
6) Ikeda Y, Biro S, Kamogawa Y, Yoshifuku S, Eto H, Orihara K, Kihara T, Tei C: Repeated thermal therapy upregulates arterial endothelial nitiric oxide synthase expression in Syrian golden hamsters. Jpn Circ J 2001; **65**: 434−438
7) Chouaib S, Chehimi J, Bani L, Genetet N, Tursz T, Gay F, Trinchieri G, Mami-Chouaib F: Interleukin 12 induces the differentiation of major histocompatibility complex class I-primed cytotoxic T-lymphocyte precursors into allospecific cytotoxic effectors. Proc Natl Acad Sci USA 1994; **91**: 12659−12663
8) Tomiyama H, Akari H, Adachi A, Takiguchi M: Different effects of Nef-mediated HLA class I down-regulation on human immunodeficiency virus type 1-specific CD8(+) T-cell cytolytic activity and cytokine production. J Virol 2002; **76**: 7535−7543
9) Rubio G, Ferez X, Sanchez-Campillo M, Galvez J, Marti S, Verdu R, Hernandez-Caselles T, Garcia-Penarrubia P: Cross-linking of MHC class I molecules on human NK cells inhibits NK cell function, segregates MHC I from the NK cell synapse, and induces intracellular phosphotyrosines. J Leukoc Biol 2004; **76**: 116−124