Clinical Investigation

A Case of Reflex Sympathetic Dystrophy (RSD) Satisfactorily Treated with Uzu-keishi-to

Mosaburo KAINUMA Shoko SENDA Naoki MANTANI
Yutaka SHIMADA Katsutoshi TERASAWA

Department of Japanese Oriental (Kampo) Medicine, Faculty of Medicine, Toyama Medical and Pharmaceutical University, 2630 Sugitani, Toyama 930-0194, Japan

烏頭桂枝湯が奏効した反射性交感神経性 ジストロフィーの1例

貝沼茂三郎 仙田 晶子 萬谷 直樹*
嶋田 豊 寺澤 捷年

富山医科薬科大学医学部和漢診療学講座, 富山, 〒930-0194 富山市杉谷2630

Abstract

We encountered a patient with chronic pain due to reflex sympathetic dystrophy (RSD) that was relieved by Uzu-keishi-to (Wu tou gui zhi tang) therapy. A 69-year-old man was diagnosed with RSD in 1995. Intractable pain of the extremities and trunk persisted despite several therapies such as spinal cord stimulation, local anesthetic blocks, and a variety of conventional medications. The patient was admitted to our hospital in June 2000, and was diagnosed as having stage II RSD. Thermography demonstrated that the left side of the back and the hand were lower in temperature than the corresponding areas of the right side. "Perfusion" images of three-phase bone scintigraphy showed a lower flow in the lower left extremity. Uzu-keishi-to was administered in addition to the Western medicines. After administration of Uzu-keishi-to, the pain was relieved and the value of the face scale decreased from 20 to 11. Moreover, after 16 weeks of Uzu-keishi-to therapy, the decreased blood flow on the left side of the body detected by thermography and three-phase bone scintigraphy increased to a level equal to that of the right side. Uzu-keishi-to is effective not only in reducing the intractable pain of RSD but also in preventing the development of "dystrophy." Further evaluation of Uzu-keishi-to therapy for patients with RSD is warranted.

Key words : reflex sympathetic dystrophy, Uzu-keishi-to, Kampo medicine, thermography, bone scintigraphy

要旨

反射性交感神経性ジストロフィー (RSD) の慢性疼痛に、烏頭桂枝湯が奏効した1例を経験した。患者は69歳男性で、1995年にRSDと診断され、四肢および体幹の頑固な疼痛は、脊髄電気刺激法、神経ブロックや種々の薬剤に抵抗して持続した。2000年6月当科に入院し、RSDのステージIIと診断された。サーモグラフィーでは、左側背部と左側手部～手指の温度が右側と比較して低下しているのが確認され、3相性骨シンチグラフィーの血管相でも左側足部の血流の低下がみとめられた。従来からの西洋薬に加えて烏頭桂枝湯を開始したところ、16週後には疼痛は半減しフェイスケールも20から11点に減少した。さらに、サーモグラフィーや3相性骨シンチグラフィーの血管相でみられた左側の血流低下も、右側と同程度にまで回復した。烏頭桂枝湯は、RSDの頑固な疼痛に有効であるだけでなく、ジストロフィーの進行防止にも有効である可能性が示唆された。RSD患者における烏頭桂枝湯の有効性については、さらなる検討が求められる。

キーワード : 反射性交感神経性ジストロフィー, 烏頭桂枝湯, 漢方薬, サーモグラフィー, 骨シンチグラフィー

Introduction

Reflex sympathetic dystrophy (RSD), corresponding to the complex regional pain syndrome (CRPS) type I¹⁾, is a chronic pain state that sometimes occurs after soft tissue or bone injury^{2,3)}. The pain of RSD is accompanied

with autonomic changes such as sweating or vasomotor abnormalities³⁾, and progression of RSD finally causes atrophy of skin and bone²⁾.

Conventional pain medication, physical therapy, sympathetic blocks, and transcutaneous electrical stimulation

* Corresponding author :

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of nerves have all been used to reduce the intensity of pain caused by RSD, but with generally unfavorable results^{3,4)}. An effective treatment for RSD has not yet been established. In the field of Kampo medicine, Kampo formulae including Uzu (Aconiti-tuber) have been used to treat patients with chronic pain⁵⁾. Here we present a case of refractory RSD satisfactorily treated with Kampo formulae, Uzu-keishi-to (烏頭桂枝湯).

Case

In June 2000, a 69-year-old man consulted our department with a complaint of intractable pain due to RSD. At the age of 64, he fell down stairs and required surgery for cervical bone fracture, the anterior cervical fusion (C 7-Th 1). Post operatively, he developed a pain in the bilateral upper and lower extremities and trunk. The pain, accompanied by allodynia (pain from non-noxious stimulus) of the feet and an incandescent feeling in the trunk, persisted despite treatment with several medications. He was admitted to a university hospital, and diagnosed as

having RSD in 1997. Cervical myelopathy or radiculopathy was negated by orthopedists. In that hospitalized period, he was treated by analgesics, anti-depressant, blockade of nerves including sympathetic nerve block, and spinal cord stimulation, with no improvement. After leaving the hospital, the pain had been persisting, despite treatment with many kinds of therapy. Thereafter, the patient consulted our department.

In June 2000, he was admitted to Toyama Medical and Pharmaceutical University hospital. Physical characteristics on admission were as follows : body height 161 cm, body weight 64.6 kg, blood pressure 120/80 mmHg, and heart rate 80/min. There was no apparent edema of the extremities. The body was extremely moist with sweat. Neurologically, the reflexes of the extremities were diminished, but neither motor weakness nor functional disturbance was observed.

There was no abnormality in the laboratory data except for mild liver disorder and hyperlipidemia. Left-side-dominant bone atrophy in the fingers was found on X-ray films (Fig.1), but there were no spinal canal stenosis finding observed on cervical X-ray. The patient met the diagnostic criteria for RSD established by the International Association for the Study of Pain¹⁾, and also met the criteria established by Kemler et al⁶⁾. We diagnosed the patient as being at stage 2 described by Lankford⁷⁾. Thermography demonstrated that skin temperature of the left hand and the left back was markedly lower than that of the right side (Fig.2 a, 2 b). Three-phase bone scintigraphy was performed following IV injection of technetium-99 m methylene diphosphonate : in the first phase, rapid sequential images of the lower extremities were acquired every 5 seconds for 60 seconds ("perfusion" images), and static images of the extremities were obtained 2 minutes ("blood pool" images) and 3 hours ("bone" images) after injection⁸⁾. Although the uptake on bone scintigraphy was symmetric and did not increase on either

Fig.1 Plain radiograph of both hands, showing osteoporosis, cortical cavitation, and loss of bone substance on the left.

Fig.2 a, 2 b Thermogram, showing lowered skin temperature of left hand (Fig. 2a) and left back (Fig. 2b).

RN-Angiogram
6 -16-0
Tc-HSA
740 MBq
128 *128
22-8345-4
ZOOM X= 1.00
Y= 1.00
MAX =5

1 -32
2 SEC

SCL 18
UP 80
LOW 0

-13-0
99m-Tc-HMDP
740 MBq
128 *128
22-8345-4
ZOOM X= 1.00
Y= 1.00
MAX =14

-32
SEC

L 18
UP 90
LOW 0

Fig.3 a, 3 b Perfusion Images (3-phase bone scintigram) of the lower extremities. A decreased flow in the left lower extremity on admission (Figure 3 a) recovered after 16 weeks of Uzu-keishi-to therapy (Figure 3 b).

side, the “perfusion” images showed a lower flow in the left lower extremity (Fig.3 a).

The western medicines he was receiving on the day of admission were continued unchanged during the hospital-ized period ; 100 mg of amobarbital, 2 mg of clonazepam, 1 mg of etizolam, and 20 mg of imipramine hydrochloride, per day. In addition to these medicines, we administered Uzu-keishi-to (Wu tou gui zhi tang in Chinese) based on Kampo-assessment, “*sho*” (Uzu-keishi-to has been indicated for symptoms such as excess sweating, sleep disturbed by intractable pain, and cold feeling in the exterior layers of the body⁵⁾). The dose of Uzu (Aconiti tuber), contained in Uzu-keishi-to as a component herb, was started from 2.0 g, and adjusted to 4.5 g 3 weeks after admission.

The chronic pain of RSD was reduced gradually after administration of Uzu-keishi-to. After the 16-week period of Uzu-keishi-to therapy, the pain evaluated by visual analogue scale decreased to half, and the value on the facescale⁹⁾ decreased from 20 to 11 (Fig.4). Moreover, thermography showed that the skin temperature of the left hand increased to equal the level of the right hand, and the decreased flow in the left lower extremity observed during the “perfusion” phase of bone scintigraphy recovered after 16 weeks of Uzu-keishi-to therapy (Fig.3 b). Pain relief has persisted to date.

Discussion

In the field of Kampo medicine, Kampo formulae containing Aconiti Tuber have been used to treat patients with chronic pain⁵⁾. Among these formulae, Uzu-keishi-to has been indicated for symptoms such as excessive sweating, sleeplessness due to intractable pain, and cold feeling in the exterior layers of the body, in addition to painful conditions. Uzu-keishi-to may have been used since ancient times to treat some patients with sympathicotonia, since excessive sweating can be caused by sympathicotonia.

In the present case, the 5-year-history of persistent pain was relieved and the values of visual analogue scale and face scale decreased to half after administration of Uzu-keishi-to, which contains Aconiti Tuber (“Uzu” or “Bushu” in Japanese) as an herbal component. Pharmacological mechanism of the analgesic effect of Aconiti Tuber as well as aconitine (a main alkaloid of Aconiti Tuber) have been clarified in several experimental studies¹⁰⁾¹¹⁾. Although we did not attempt to use Aconiti Tuber alone in the traditional manner of Kampo medicine, the analgesic effect shown in the patient may be attributable, at least in a part, to Aconiti Tuber.

Also of particular note in the present case, the decreased blood flow on the left side of the body detected by thermography and 3 phase bone scintigraphy increased to a level equal to that on the right side after 16 weeks of Uzu-keishi-to therapy. It is reported that blood flow in the impaired region increases during stage I RSD, then decreases at stage II¹²⁾¹³⁾. Mashimo reported that improvement of skin temperature on thermography sometimes reflects clinical effectiveness in patients with RSD which is accompanied by autonomic dysregulation with vasomotor and sudomotor changes¹²⁾. Yamaga also reported that thermography in RSD patients is useful to evaluate availability of treatments : a difference in temperature between the impaired side and the intact side of the body was disappeared after effective treatment¹³⁾. The vasodilator effects of *Paoniae Radix*¹⁴⁾ and *Cinnamomi Cortex*¹⁵⁾, both of which are herbal components of Uzu-keishi-to, have been reported in experimental studies. Thus, the improvement of blood flow in the presented case may have reflected the clinical effectiveness of Uzu-keishi-to.

Moreover, it is suggested that the persistence of low blood flow causes the progression of distal tissue atrophy (dystrophy)¹⁶⁾¹⁷⁾. The improvement in low blood flow confirmed by the thermography and 3-phase bone scintigraphy would suppress the progression of dystrophy in

Fig.4 Clinical course

the patient.

It has been reported that chronic RSD or causalgia was satisfactorily treated with Kampo medicines : Gorei-san¹⁸⁾, Keishi-ka-ryojutsubu-to¹⁹⁾, and Touki-shigyakuka-goshu-yu-shokyo-to²⁰⁾. In those reported cases, thermography or 3 phase bone scintigraphy was not performed after administration of Kampo medicines. We are not aware of any reports that described alleviation of RSD after Uzu-keishi-to therapy.

In conclusion, we presented a case of refractory RSD satisfactorily treated with Uzu-keishi-to. After 16 weeks of Uzu-keishi-to therapy, decreased blood flow on the left side of the body detected by the thermography and 3-phase bone scintigraphy increased to a level equal to that on the right side. Uzu-keishi-to may be effective not only in reducing the intractable pain of RSD but also in preventing progression to “dystrophy”. Uzu-keishi-to therapy might be a useful additional or alternative agent for the treatment of RSD.

Supplementary Notes

Uzu-keishi-to contains 6 herbs : Cinnamomi Cortex (4 g), Zingiberis Rhizoma (1 g), Zizyphi Fructus (3 g), Paeoniae Radix (3 g), Glycyrrhizae Radix (2 g), Aconiti Tuber (1-4 g). The 5 herbs except Aconiti Tuber were extracted in boiled water (600 ml) for 40 min, and the extract from 5 herbs was then added to the extract of Aconiti Tuber which was extracted in 40 g of honey for 90 min.

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