Case report J. Trad. Med. 19, 76－80, 2002

A case of pustulotic arthro-osteitis successfully treated with Kampo medicines

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(Received January 11, 2002. Accepted February 19, 2002.)

Abstract

We present a case of pustulotic arthro-osteitis (PAO) successfully treated with a combination of two Kampo formulae, Unkei-to and Keishi-ni-eppi-itto-ka-ryojutsubu. A 38-year-old man developed PAO in 1998. Spontaneous remissions and recurrences of arthralgia occurred repeatedly. In August 2000, the patient consulted our department requesting Kampo therapy. Unkei-to reduced the palmar eruption to 10-20 % of the peak. Keishi-ni-eppi-itto-ka-ryojutsubu was administered in addition to Unkei-to. Thereafter, polyarthralgia decreased to half and spontaneous pain disappeared. C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) values also decreased, and these values remained low for 5 months to date. After the disease activity decreased, gallium scintigram did not show any increase in uptake in the joints throughout the whole body. Keishi-ni-eppi-itto-ka-ryojutsubu and Unkei-to may be a useful additional and alternative agent for the treatment of PPP and PAO.

Key words pustulotic arthro-osteitis, pustulosis palmoplantaris, Kampo medicines, Unkei-to, Keishi-ni-eppi-itto-ka-ryojutsubu.

Abbreviations Unkei-to (Wen-Jing-Tang), 温経湯 ;Keishi-ni-eppi-itto-ka-ryojutsubu (Gui-Zhi-Er-Yue-Bi-Yi-Tang-Jia-Ling-Zhu-Fu), 桂枝二越婢一湯加苓朮附 ; PAO, pustulotic arthro-osteitis ; PPP, pustulosis palmoplantaris.

Introduction

Pustulotic arthro-osteitis (PAO), which occurs in 10-30% of patients with pustulosis palmoplantaris (PPP),[1] is refractory and commonly progressive disease.[2,3] The pain and rigidity in the back and/or the sternocostoclavicular region persists despite treatment with several Western medicines.[1,4] To date, treatment regimens for PAO are chiefly symptomatic. No medicines have proven to prevent the worsening of the arthro-osteitis, and an effective treatment for PAO has not yet been established.

From ancient times, Kampo medicines have successfully been used to treat patients with arthritis.[5,6,7] A recent study has demonstrated that Kampo medicine suppresses the development of arthritis in a mouse model.[8] Here, we present a case of PAO successfully treated with a combination of two Kampo formulae, Unkei-to and Keishi-ni-eppi-itto-ka-ryojutsubu.

Case

A Japanese man initially developed lumbago in June 1998 at the age of 37, then 2 days later developed pustules on the palms and soles. Polyarthralgia simultaneously appeared in the costoclavicular area, back, neck, shoulders and knees. Spontaneous remissions and recurrences of arthralgia occurred repeatedly. He was examined at a nearby hospital by an orthopedic physician, and rheumatoid arthritis and pyogenic spondylitis were ruled out through several examinations including X-ray films, radioisotope, and bone biopsy of the thoracic spine. He was diagnosed as having pustulosis palmoplantaris (PPP) by a dermatologist, and was treated with a steroid ointment. In this way, he was diagnosed with pustulotic arthro-osteitis. From Feb. 2000, etretinate (Tigason) 30 mg/day was administered to treat PPP. However, PPP

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did not improve. C-reactive protein (CRP) value continued between 1.6 and 4.0 mg/dl and erythrocyte sedimentation rate (ESR) value was between 54 and 60 mm/hr against NSAID (loxoprofen sodium 180 mg/day).

In August 2000, the patient consulted our department requesting Kampo therapy. The X-ray film of the spine showed arch-like (Th 9-10) and beak-like (Th 11-12) bridging syndesmophytes of the spine in addition to ankylosing-spondylitis-like spondylosis of the thoracic spine (Figure 1). Cervical spondylitis (C3 to C6) , mild lumbar spondylitis (L3) and abnormal ossification of the spine (L5-S) were also seen. Slight ossification was visible at the left costo-clavicular ligament, but there was no sarco-iliitis. There was no bone erosion of the shoulders, elbows, hands, knees, or ankles. Radioisotope 99mTc bone scintigraphy revealed increased uptakes at the costoclavicular area, left knee joint and the level of C3-7, Th 9-11 and L3-5 in the spine. The finding of sacroiliitis was not observed in bone scintigram or X-ray films. Chest CT did not demonstrate any sign of lymph node swelling or mediastinitis. Amyloid deposition was not detected in specimens of the stomach or duodenum. ESR was 60 mm/hr, and CRP was 1.6 mg/dl. Rheumatoid factor (RF), anti-nuclear antibody and HLA B27 antigen were absent. A2, B60, B48 and Cw3 were found in HLA of A, B and C locus. Electrolytes, liver, kidney, thyroid function tests, and urine analysis were all normal.

Figure 1 Plain radiograph of thoracic spine, showing arch-like (Th 9-10) and beak-like (Th11-12) bridging syndesmophytes.

These findings confirmed the diagnosis of PAO. We initially treated him with Unkei-to (TJ-106 manufactured by Tsumura & Co), which is traditionally used to treat hand eczema (Table I). This resulted in a decrease in the palmar eruption to 10-20 % of the peak (Figure 2 a, b). However, arthralgia persisted to the same degree and swelling in the left knee joint sometimes required puncture. Therefore, Keishi-ni-eppi-itto-ka-ryojutsubu (Table I), which is traditionally used for patients with arthritis, was administered in addition to Unkei-to. Thereafter, polyarthralgia decreased gradually and spontaneous pain disappeared. The patient's articular pain score on 10-cm visual analogue scale was reduced to half the level before the first visit to our department. CRP and ESR values also decreased gradually (Figure 3), and these values remained low for 5 months (CRP 0.8-1.1 mg/dl, ESR 30 - 36 mm/hr) to date. After the disease activity decreased,

Table I Kampo medicines used in treatment for the present patient

Kampo medicines	Components (g)
Unkei-to (TJ-106) (Wen-Jing-Tang)	Ophiopogonis Tuber (4.0) Pinelliae Tuber (4.0) Angelicae Radix (3.0) Glycyrrhizae Radix (2.0) Cinnamomi Cortex (2.0) Paeoniae Radix (2.0) Cnidii Rhizoma (2.0) Ginseng Radix (2.0) Moutan Cortex (2.0) Evodiae Fructus (1.0) Zingiberis Rhizoma (1.0) Asini Gelatinum (2.0)
Keishi-ni-eppi-itto-ka-ryojutsubu (Gui-Zhi-Er-Yue-Bi-Yi-Tang-Jia-Ling-Zhu-Fu)	Atractylodis Lanceae Rhizoma (10.0) Hoelen (5.0) Gypsum Fibrosum (8.0) Zizyphi Fructus (4.0) Cinnamomi Cortex (3.0) Ephedrae Herba (3.0) Paeoniae Radix (3.0) Glycyrrhizae Radix (3.0) Zingiberis Rhizoma (1.0) Aconiti Tuber (1.0)

Medicinal aqua of Keishi-ni-eppi-itto-ka-ryojutsubu was extracted from the mixture of 10 herbs by boiling in 600 ml water for 60 mins. Extracted aqua was divided into three parts, each of which was administered 3 times a day before each meal.

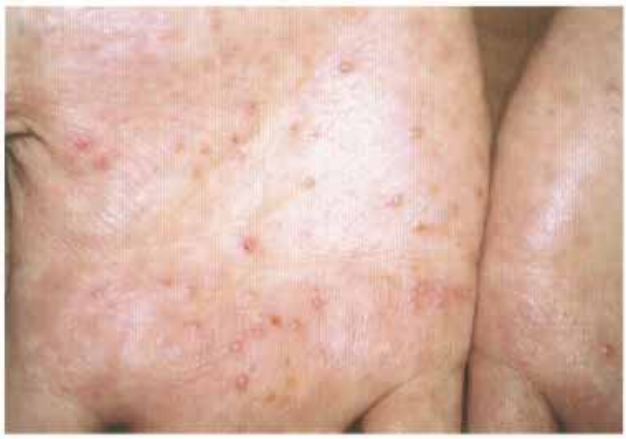

Figure 2a

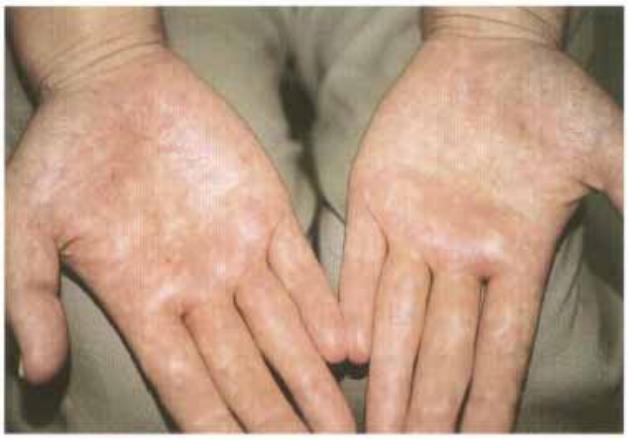

Figure 2b

Figures 2a and 2b Pustulosis palmoplantalis before (Fig.2a) and after (Fig. 2b) Unkei-to therapy.

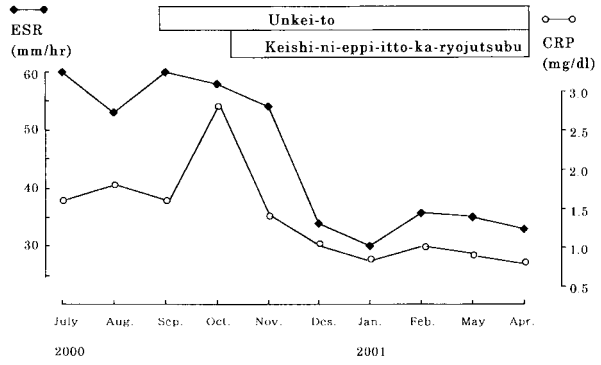

Figure 3 Clinical course and serological data after July 2000.
ESR : Erythrocyte sedimentation rate, CRP : C-reactive protein

bone scintigraphy and gallium scintigraphy were performed. Bone scintigram showed increased uptake at the same regions as shown on the last bone scintigram (Figure 4). However, gallium scintigram did not show any increase in uptake in the joints throughout the whole body (Figure 5).

Discussion

For this patient, the existence of pustulosis palmoplantaris, sternocostoclavicular lesion, and syndesmophyte formation in the spine were observed. Based on the presence of these findings and exclusion of other diseases, the patient was diagnosed with pustulotic arthro-osteitis (PAO). The arthritis had persisted for 28 months without complete remission until the first visit to our department. The symptoms of arthralgia were partially relieved by NSAIDs, however active inflammation with elevation of CRP and ESR values had persisted.

Although PAO is essentially benign,[9] osteoarthritis gradually advances despite NSAIDs and steroid therapy.[10] Moreover, a report described that chronic inflammation attributable to PAO caused secondary amyloidosis.[11]

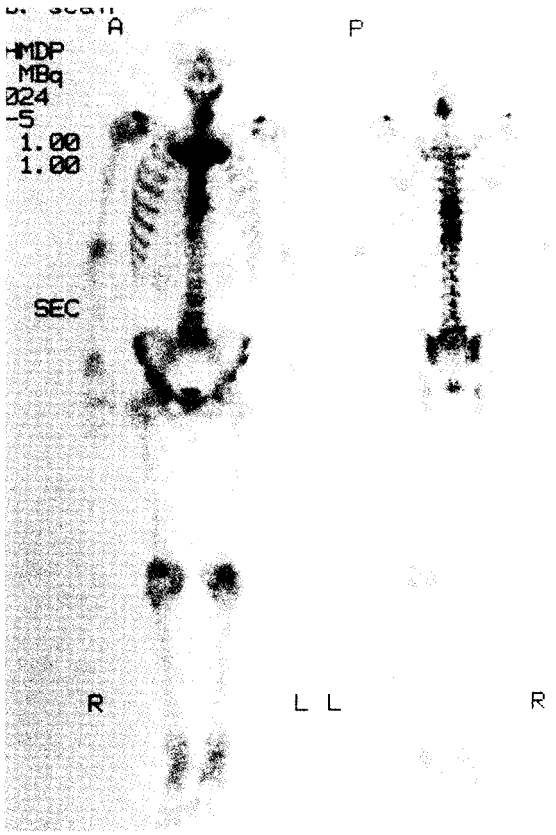

Figure 4 Bone scintigraphy after Keishi-ni-eppi-itto-ka-ryojutsubu therapy. Increased uptakes remains at costoclavicular area, knee joints and C3-7, Th9-11 and L3-5 in the spine.

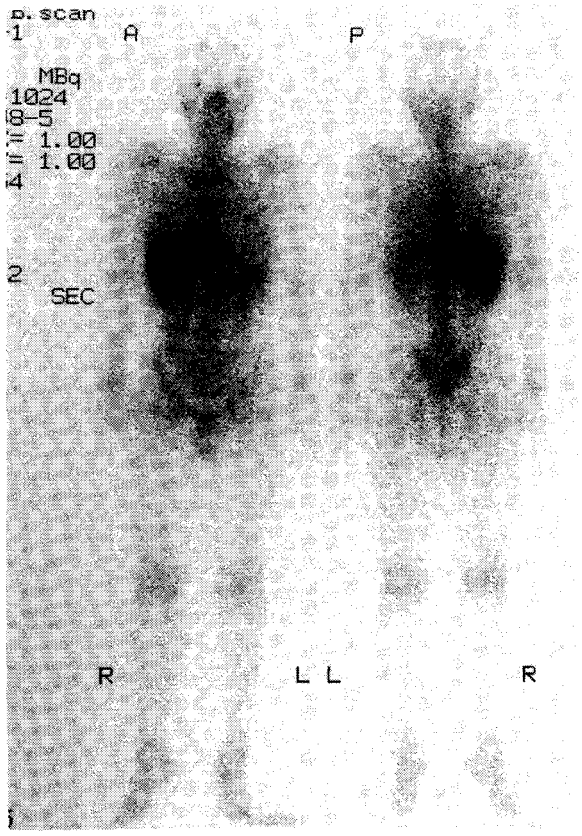

Figure 5 Gallium scintigraphy after Keishi-ni-eppi-itto-ka-ryojutsubu therapy, showing no increased uptake in the joints throughout the whole body.

Secondary amyloidosis, a potentially life-threatening disorder, is caused by deposit of AA fibrils which are catabolite derived from the acute phase reactant, serum amyloid A (SAA).[12,13] Thus, besides analgesic therapy, anti-inflammatory therapy which decreases the disease activity reflected in CRP and ESR values is preferable in patients with PAO. Many reports demonstrated resolution of secondary amyloidosis after withdrawal of the inflammatory stimulus.[14,15,16,17]

Gallium scintigraphy performed after improvement of CRP and ESR values did not demonstrate any accumulation in the joints throughout the whole body. Kobayashi reported that gallium scintigraphy as well as bone scintigraphy reveals accumulation at the joints with osteoarthritis in PAO patients.[18] The accumulation on bone scintigraphy persists long for years,[19] therefore, the improvement of disease activity in the patient may be reflected on the gallium scintigraphic findings. In this patient, the Kampo medicines were used in combination with NSAID which do not decrease either CRP or ESR values. The decrease in CRP and ESR values as well as alleviation of pain shown in this patient may be attributable to the Kampo medicines.

Kogure *et al.*[7] reported that Keishi-ni-eppi-itto-ka-ryojutsubu successfully treated patients with rheumatoid arthritis. This formula contains Ephedrae herba and Paeoniae radix, both of which have anti-inflammatory effects.[20,21] In the present patient, PAO was successfully treated with Keishi-ni-eppi-itto-ka-ryojutsubu, suggesting that this formula may have a palliative effect on various kinds of arthritis.

From ancient times, Unkei-to has been used for patients with hand eczema,[22] and a previous case report described improvement of polyarthralgia after Unkei-to therapy.[23] We applied Unkei-to to treatment of the patients in expectation of improving both PPP and PAO. In the patient, Unkei-to promoted an improvement of PPP, and recurrence became not so serious thereafter. The sole use of Unkei-to was not effective against PAO.

This case report showed the potential usefulness of Kampo medicines in a patient with PPP. We are not aware of any reports that described the useful effect of Kampo medicines on patients with PAO. Keishi-ni-eppi-itto-ka-ryojutsubu and Unkei-to may be a useful additional and alternative agent for the treatment of PPP and PAO. We encourage further accumulation of such case reports.

和文抄録

温経湯と桂枝二越婢一湯加苓朮附が奏効した掌蹠膿疱症性骨関節炎の1例を経験した。患者は38才男性で，1998年に掌蹠膿疱症性骨関節炎を発症し，増悪と寛解を繰り返していた。2000年8月，漢方治療を求めて当科を受診した。温経湯により，掌蹠膿疱症の手掌の皮疹はピークの10～20%にまで改善した。温経湯に加えて桂枝二越婢一湯加苓朮附を開始したところ，多関節痛は半減し安静時自発痛は消失した。CRPや赤沈値も減少し、現在までの5か月間，低値が持続している。疾患活動性が低まった後に施行されたガリウムシンチでは，全身のどの関節にも集積をみとめなかった。温経湯および桂枝二越婢一湯加苓朮附は，掌蹠膿疱症性骨関節炎に対して有用な追加療法あるいは代替療法となりうる可能性が示唆された。

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