CASE REPORT

Experience of Vinca Alkaloid-Induced Neuropathic Pain Alleviated by Shakuyakukanzoto

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ABSTRACT

Introduction: **Shakuyakukanzoto (SKT), a Kampo medicine, has been shown to alleviate paclitaxel-induced neuropathic pain in several studies. This report presents a case in which SKT was successfully used to treat vincristine/vinblastine-induced neuropathic pain.**

Case presentation: **A patient received anticancer drugs for almost 3 years to treat a low-grade recurrent cerebellar glioma. Two cycles of combination therapy with carboplatin and vinblastine and 12 cycles of carboplatin and vincristine were administered, followed by vinblastine monotherapy. The patient began to experience tingling oral pain on the second day after first injection of carboplatin and vinblastine. Three months after the initiation of chemotherapy, vinblastine was replaced with vincristine. The patient suffered severe hiccups. SKT was administered thrice daily to prevent hiccups. Thereafter, hiccups disappeared, and the oral pain was also relieved. SKT markedly improved the patient's quality of life during chemotherapy.**

Discussion: **The findings of previous studies showing an analgesic effect of SKT for chemotherapy-induced neuropathic pain by paclitaxel were consistent with the present result using vincristine/vinblastine. Vinca alkaloids inhibit spindle function by targeting microtubules to arrest cellular mitosis, similar to paclitaxel.**

Conclusion: **SKT had analgesic effects on oral neuropathic pain induced by vinca alkaloids, which have a similar mechanism of action as paclitaxel.**

KEY WORDS

chemotherapy, neuropathic pain, shakuyakukanzoto, vinblastine, vincristine

INTRODUCTION

Shakuyakukanzoto (SKT), a Kampo medicine, is reported to alleviate paclitaxel-induced neuropathic pain in humans and mice[1,2]. This paper presents a human case in which SKT was successfully used as a palliative medicine for neuropathic pain, an adverse effect of vinca alkaloids, with a similar mechanism of action as paclitaxel.

CASE PRESENTATION

Approximately 15 years ago, the author of this report (Pa.) received anticancer drugs for almost 3 years to treat a low-grade recurrent cerebellar glioma adjacent to the medulla oblongata. When Pa. was 33 years old, two cycles of combination therapy with carboplatin and vinblastine and 12 cycles of carboplatin and vincristine were administered[3]. Each cycle consisted of weekly therapy for four consecutive weeks, followed by a 2-week rest period. A magnetic resonance imaging performed after cycle 8 revealed shrinkage of the tumor, roughly equivalent to the size of the tumor before recurrence. Subsequently, monotherapy with vinblastine (biweekly for 9 months) was administered[4]. The chemotherapy terminated because the tumor remained the same size[5].

Pa. began to experience tingling oral pain on the second day after first injection of carboplatin and vinblastine. This pain occurred on both sides of the posterior part of the tongue, especially during saliva production, e.g., when commencing mealtimes, but did not persist while eating. Sometimes, pain was felt outside of eating, but it seemed to be related to saliva production and swallowing. The pain peaked by day 3-4 and largely subsided by day 5-6. During the third week of anticancer therapy, due to a low white blood cell count, Pa. received only carboplatin without vinblastine, which is highly hemotoxic. Then the oral pain did not occur at all. Three months after the start of chemotherapy, vinblastine was replaced with vincristine in combination with carboplatin. Pa. suffered severe hiccups for three days after administration. His primary physician asked the pharmacy to administer a drug to prevent hiccups, and SKT extract (2.5 g, Tsumura Co., Tokyo, Japan) was given three times daily[6]. Thereafter, the hiccups disappeared. More surprisingly, the oral pain was also relieved, and pain frequency was reduced. After switching to monotherapy with vinblastine, the oral pain symptoms remained mild. Another neurological symptom that occurred during chemotherapy, mild numbness at limb tips, remained during SKT treatment. Overall, SKT treatment markedly improved Pa.'s quality of life during chemotherapy, alleviating the pain and hiccups.

DISCUSSION

Oral pain during combination therapy with carboplatin and vincristine/vinblastine seems to be caused by vinca alkaloids treatment because it was absent during monotherapy with carboplatin but present during vinblastine monotherapy. Oral pain decreased dramatically following SKT treatment.

Approximately half of patients in one study experienced orofacial

Received on March 27, 2023 and accepted on April 7, 2023
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pain induced by vincristine[7], with a similar time course of pain as observed in the present case. Pain perception by Pa. fits the symptoms of first-bite syndrome, which has been reported during vincristine administration[8]. In first-bite syndrome, the first bite of meals induces severe pain caused by the loss of sympathetic innervation to the parotid gland, with pain gradually diminishing during subsequent bites[8]. The author speculates that glossopharyngeal nerve dysfunction was largely involved in oral pain experienced in this case[7].

The results observing an analgesic effect following SKT treatment for chemotherapy-induced neuropathic pain (CINP) by paclitaxel[1,2], were consistent with the present result using vincristine/vinblastine. Vinca alkaloids inhibit spindle function by targeting microtubules to arrest cellular mitosis, similar to paclitaxel[2,9].

To my knowledge, analgesic effects of SKT on vincristine/vinblastine-induced pain have not been previously reported in English literature, nor has specific SKT suppression of CINP except for paclitaxel-induced pain[1]. Additionally, goshajinkigan seems to be more used than SKT in alleviating CINP[1]. However, no studies have investigated its use in alleviating vincristine/vinblastine-induced pain.

When SKT is used as an adjunct to long-term chemotherapy, caution should be exercised given that glycyrrhizin included in kanzo may cause pseudohyperaldosteronism. Consequently, blood tests should be performed to check for hypokalemia[10]. Unfortunately, due to this adverse effect, SKT is contraindicated in some cancer patients. An analgesic effect was observed with only one ingredient, shakuyaku, with minimal adverse effects, and this option, combined with a convenient gel formulation could expand the potential use of SKT-derived analgesics[2].

CONCLUSION

Inspired by the results reported that SKT ameliorated neuropathic pain caused by paclitaxel, this paper presented one patient's experience in which SKT had analgesic effects on oral neuropathic pain induced by vinca alkaloids, which have a similar mechanism of action as paclitaxel.

CONFLICT OF INTEREST

The author declares that there is no conflict of interest.

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