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Contents

Thrice Monthly Volume 11 Number 15 May 26, 2023

REVIEW

MINIREVIEWS

ORIGINAL ARTICLE

Clinical and Translational Research

Retrospective Study

World Journal of Clinical Cases

Thrice Monthly Volume 11 Number 15 May 26, 2023

Contents

World Journal of Clinical Cases

Thrice Monthly Volume 11 Number 15 May 26, 2023

Contents

Contents

Thrice Monthly Volume 11 Number 15 May 26, 2023

ABOUT COVER

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CASE REPORT

Treatment of postherpetic neuralgia by bone marrow aspirate injection: A case report

Takahiro Honda Pazili

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Abstract

BACKGROUND

Postherpetic neuralgia (PHN) is the most frequent and a difficult-to-treat complication of herpes zoster (HZ). Its symptoms include allodynia, hyperalgesia, burning, and an electric shock-like sensation stemming from the hyperexcitability of damaged neurons and varicella-zoster virus-mediated inflammatory tissue damage. HZ-related PHN has an incidence of 5%–30%, and in some patients, the pain is intolerable and can lead to insomnia or depression. In many cases, the pain is resistant to pain-relieving drugs, necessitating radical therapy.

CASE SUMMARY

We present the case of a patient with PHN whose pain was not cured by conventional treatments, such as analgesics, block injections, or Chinese medicines, but by bone marrow aspirate concentrate (BMAC) injection containing bone marrow mesenchymal stem cells. BMAC has already been used for joint pains. However, this is the first report on its use for PHN treatment.

CONCLUSION

This report reveals that bone marrow extract can be a radical therapy for PHN.

Key Words: Bone marrow aspirate concentrate; Postherpetic neuralgia; Herpes zoster; Bone marrow mesenchymal stem cells; Pain syndrome; Case report

Core Tip: To our knowledge, this is the first report of bone marrow aspirate concentrates (BMAC) curing post-herpetic neuralgia (PHN). BMAC contains bone marrow mesenchymal stem cells and other important cytokines and has favorable results in treating joint pain. PHN is difficult to cure, and conventional medicines do not work well in most cases. BMAC may serve as a radical treatment. The fact that BMAC was useful for the treatment of PHN indicates that BMAC can be applied for other pain-related conditions.

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INTRODUCTION

Postherpetic neuralgia (PHN) is a pain syndrome that develops after herpes zoster (HZ) outbreak. Its symptoms include allodynia, hyperalgesia, burning, and an electric shock-like sensation owing to the hyperexcitability of neurons[1]. PHN is the most frequent complication of HZ; 5%–30% of the patients affected with HZ have PHN. Moreover, the symptoms last for years and deteriorate the patient's quality of life[2].

In some patients, the pain is intolerable and can lead to insomnia or depression[3]. PHN is difficult to treat, and no widely accepted treatment guidelines exist[4]. Additionally, the pain is drug-resistant, and the long-term use of pain medications is associated with adverse effects, including dizziness and dependence[5-7]. Although some interventional therapies, including Botox, nerve blockage, and transcutaneous nerve stimulation are available, more than 50% of patients do not respond to these treatments[3]. Therefore, radical therapy is needed.

We herein present the case of a patient whose PHN, which did not respond to conventional treatment, was completely cured using bone marrow aspiration injection. Mesenchymal stem cells in the bone marrow aspirate are known to secrete neurotrophic factors and anti-neuroinflammatory cytokines, which have anti-inflammatory, neuroprotective, and regenerative effects[8-10]; our favorable results for PHN are in line with these findings.

This study validates mesenchymal stem cells that secrete anti-inflammatory cytokines and implies that they can be used for anemia, myelodysplastic syndromes/acute myeloid leukemia (AML), chronic obstructive pulmonary disease (COPD), cardiovascular disease, diabetes mellitus (DM), and even aging itself because chronic inflammation in the bone marrow is related to these conditions.

CASE PRESENTATION

Chief complaints

A 65-year-old female patient had severe PHN in her left upper body.

History of present illness

The patient had an HZ infection 20 years ago. Although she received intensive antiviral therapy, she had severe PHN in her left upper body. She previously tried several pain medications, including Lyrica and nerve block injection, which were ineffective. Alternative treatments, including acupuncture or Chinese medicine, were also ineffective (Table 1). Her quality of life deteriorated due to the pain and because she constantly touched the painful area to stabilize her symptoms. The bones around the lesion were checked a few weeks before she received our therapy; an orthopedic surgeon at another medical facility confirmed that there were no bone fractures and other orthopedic-related problems. Although fibromyalgia can be a differential diagnosis, it was unlikely because the patient felt pain in only one area, which was along the HZ eruption area (Table 2).

History of past illness

The patient had no history of past illness.

Personal and family history

The patient had no personal and family history.

Physical examination

On physical examination, the patient was found to have pain in the upper left body.

Table 1 Treatment history

Patient age (yr)	Treatment history	Outcome
60 (onset of herpes zoster) to 70	Antipain medicine, including Lyrica	Not effective
61	Block injection a few times	Not effective
70–80	Chinese medicine for more than one year	Not effective
70–80	Acupuncture for 3 yr	Not effective
80	BMAC	Effective

BMAC: Bone marrow aspirate concentrate.

Table 2 Differential diagnosis

Differential diagnosis	Reason behind ruling out
Fibromyalgia	Pain was localized in only one area
Bone fracture	Denied by an orthopedic surgeon with X-ray images

Laboratory examinations
Not checked.

Imaging examinations
None.

FINAL DIAGNOSIS
The final diagnosis was PHN.

TREATMENT
Bone marrow aspirate extract was injected subdermally into the entire painful area. After obtaining informed consent, 100 mL of bone marrow was extracted from the ilium, and the extract was divided into 10 sterile spits. Subsequently, the bone marrow extract was centrifuged for 15 min at 1500 rpm to eliminate erythrocytes and plasma. After centrifugation, erythrocytes and upper plasma were discarded, and 1 mL of the concentrated bone marrow extract was obtained in each spit. Finally, 10 mL of concentrated bone marrow extract was injected.

OUTCOME AND FOLLOW-UP
During the first follow-up examination, at 1 mo after the procedure, the patient stated that her pain completely disappeared. The pain was measured using the Neuropathic Pain Symptom Inventory Scale, a questionnaire assessing five aspects of neuropathic pain: Superficial spontaneous pain, deep spontaneous pain, paroxysmal pain, evoked pain, and paresthesia/dysesthesia. Each of these items was quantified on a 0–10-point numerical scale. Before treatment, the scores were 6, 10, 5, 5, and 0 points for each item, respectively. At both 3 and 6 months after treatment, she reported scores of 0 points for all items. Moreover, she noticed that she did not need to touch her skin because she felt no pain and said that the treatment dramatically improved her quality of life. Notably, the number of times she touched the lesion area dramatically decreased from more than 20 times a day on average to 0. Overall, she was satisfied with the treatment.

DISCUSSION
It is suggested that bone marrow extract concentrate injection is a potential treatment for PHN. The

cause of PHN is the hyperexcitability of varicella-zoster virus-induced damaged neurons[1]. In our patient, the pain disappeared, suggesting that the bone marrow aspirate concentrate (BMAC) repaired the damaged neurons. BMAC is already used for joint pain, and its effectiveness has been reported[11]. A fresh autologous BMAC containing mesenchymal stem cells is a potential regenerative and proliferative element because of the synergistic coordination between cellular elements and the pool of extracellular matrix, growth factors, and cytokines[12]. Particularly, mesenchymal stem cells are considered effective for treating pain-related conditions[13]. This is because mesenchymal stem cells secrete neurotrophic factors and anti-neuroinflammatory cytokines, which have an anti-inflammatory, neuroprotective, and regenerative effect[8-10]. Stem cells secrete many nerve-protecting factors, including glial-derived neurotrophic factor (GDNF), brain-derived neurotrophic factor, insulin-like growth factor-I, nerve growth factor, and angiopoietin 1[14]. For example, GDNF accelerates myelination and functional recovery after nerve injury[15]. Additionally, stem cells can improve the function of spinal cord injury by these neurotrophic factors[16]. Therefore, the usefulness of BMAC containing mesenchymal stem cells for PNH is theoretically consistent with previous knowledge on stem cells. Furthermore, our findings are in consistency with those of a previous study, which concluded that fat grafting was effective for treating this disease PNH as fat and bone marrow aspirate contain mesenchymal stem cells[17]. Regarding the procedure's safety, although bone marrow puncture is considered invasive, no major adverse effects pertaining to BMAC therapy were reported, except for donor site pain[18]. However, in our experience, donor site pain in cases of BMAC is less frequent compared to that in cases of fat harvesting.

This study can be applied for other diseases. For example, if mesenchymal stem cells have the ability to secrete a sufficient amount of anti-inflammatory factors to ease chronic neuropathy, they may be helpful for anemia, MDS/AML, COPD, cardiovascular disease, DM, and even aging itself by increasing stem cell activity and capacity or the number of stem cells in the bone marrow. This is because these diseases are related to chronic inflammation in the bone marrow[19]. At least, mesenchymal stem cells can be a therapeutic target for these conditions. In fact, 5-Aza-2'-deoxycytidine, also known as decitabine, an FDA-approved MDS drug, is effective in delaying bone marrow mesenchymal stem cell aging[20].

This study had some limitations. First, we explained the therapeutic theory of BMAC based on stem cells. However, other unknown cells, cytokines, or substances in BMAC may have played a major role in the therapeutic effects observed. Additionally, areas healed through BMAC may have damaged tissues, including the skin rather than the nerves, contributing to the greatest effect of BMAC in this case.

Although the underlying mechanism remains controversial, using BMAC for treating PHN can be effective in patients whose main symptom is chronic pain. This implies that BMAC can also be applied to other nerve- or pain-related conditions.

CONCLUSION

We believe that BMAC is a treatment option for PHN, although large numbered randomized studies are required to ensure that its effectiveness is statistically significant.

Therefore, it is important that clinicians learn this procedure as BMAC requires no special equipment other than a centrifuge and can be manufactured in a sterile spitz and syringe. We consider this a "closed" system where there is a very little chance of contamination. Additionally, cell culture is not required and can be performed in an outpatient setting. Furthermore, BMAC is useful in clinical settings as a source of stem cells. Notably, evidence on the effectiveness of stem cell against various diseases, including cardiac, neurological, pulmonary, gastrointestinal, renal, genitourinary, metabolic, hematological, musculoskeletal, ocular, auditory, skin, and infectious diseases, is currently emerging[21]. This report of the effectiveness of BMAC for treating PHN in our patient indicates that it has a huge therapeutic potential for other diseases.

FOOTNOTES

Author contributions: Honda Pazili T did all the work for this paper.

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