CONCISE COMMUNICATION

Guselkumab improves joint pain in patients with pustulotic arthro-osteitis: A retrospective pilot study

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ABSTRACT

Pustulotic arthro-osteitis (PAO) is an osteoarticular complication of palmoplantar pustulosis (PPP). Although guselkumab, an anti-interleukin-23p19 antibody, has been shown to be effective for PPP, its efficacy for PAO is still not well understood. We conducted a retrospective observational study to evaluate the effectiveness of 28-week guselkumab treatment for five PAO patients in daily clinical practice. Four patients had sternoclavicular arthritis, and one had only sacroiliitis. Guselkumab improved pain visual assessment scale scores in all five patients by 54.2% (11.1–87.5%) on average at week 28 compared with baseline, and discontinuation or dose reduction of analgesics was possible in four of them. Three patients showed clinically significant improvement in Bath Ankylosing Spondylitis Disease Activity Index of 2 or more. On the other hand, beneficial change in Ankylosing Spondylitis Disease Activity Score of 1.1 or more was observed in only one patient. Bone scintigraphy demonstrated decreased uptake in sternoclavicular joints after guselkumab treatment in all four patients with sternoclavicular arthritis. Improvement of Palmoplantar Pustulosis Area and Severity Index was also confirmed. Guselkumab can be a treatment option for intractable PAO.

Key words: guselkumab, imaging, joint pain, palmoplantar pustulosis, pustulotic arthro-osteitis.

INTRODUCTION

Pustulotic arthro-osteitis (PAO) is an intractable complication of palmoplantar pustulosis (PPP), which is characterized by chronic inflammation affecting bones and joints. It commonly affects the clavicle, sternum, and sternoclavicular and sternocostal joints.1 PAO is treated by removal of focal infection,2,3 non-steroidal anti-inflammatory drugs (NSAIDs),4 cyclosporin,5,6 apremilast,7,8 methotrexate, sulfasalazine and/or biologics.9,10 In Japan, guselkumab (GUS), an anti-interleukin-23p19 antibody, was approved for PPP in 2018. Although the efficacy of GUS for PPP has been demonstrated in a placebo-controlled randomized trial,11 data on its efficacy for PAO is still limited. Thus, we conducted an observational study to evaluate the effectiveness and safety of GUS for PAO in a daily clinical setting.

METHODS

We retrospectively analyzed patients who had previously been diagnosed with PPP based on skin symptoms complicated with PAO and were treated with GUS at the Department of Dermatology, Nihon University Itabashi Hospital, between November 2018 and October 2019. The diagnosis of PAO was made by a board-certified rheumatologist (N. I.). This study was approved by the institutional review board of the hospital (RK-2003107). GUS (100 mg) was administrated at week 0, week 4 and every 8 weeks thereafter. The assessment period was from the initiation of GUS therapy (baseline) to the visit at week 28. Data on disease duration, smoking history, presence or absence of focal infection, and drugs used before and during GUS therapy were collected from medical charts. Disease activity was assessed with the following scales: Palmoplantar Pustulosis Area and Severity Index (PPPASI), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Ankylosing Spondylitis Disease Activity Score (ASDAS) and serum C-reactive protein (CRP). Scores on pain visual assessment scale (VAS) and patient’s global assessment (PGA) of disease activity in PPP and PAO were also collected. Technetium-99m bone scintigraphy or magnetic resonance imaging (MRI) were performed at baseline and week 28 or later for comparison. To evaluate safety, data were collected on the presence or absence of adverse events including abnormal laboratory values, infection, exacerbation of PPP and development of non-palmoplantar rash.

RESULTS

Five patients with PAO (one male and four females, 55.0 ± 12.1 years) received GUS during the survey period. Detailed patients’ backgrounds are summarized in Table S1. All five patients used some type of analgesic (NSAIDs in two patients and opioids in three). Of the five patients, four had sternoclavicular arthritis and one had only sacroiliitis. There
were three patients with sternoclavicular arthritis accompanied by arthritis affecting other joints. Further profiles of each patient are described in Table 1.

Reduction of pain VAS scores was observed in four of the five patients at week 12 by 51.5% on average (Fig. 1a). At week 28, all patients showed decreased pain VAS scores by 54.2% (11.1–87.5%) on average. PGA scores of disease activity improved from baseline in three patients at week 28, but were unchanged or worsened in the other two patients (Fig. 1b). The analgesics taken at baseline were completely discontinued in three of the five patients, and the dose of the analgesic was reduced in another patient (data not shown). Thus, GUS treatment resulted in substantial improvement of joint pain in the majority of patients.

At baseline, BASDAI was more than 4 in four of the five patients. After 28 weeks of treatment, two patients showed BASDAI of less than 4 (Fig. 1c). In addition, BASDAI improved by 2 or more in three patients. ASDAS indicated high disease activity (>2.1) in four of the five patients at baseline (Fig. 1d). At week 28, two patients achieved low disease activity (<1.3). ASDAS improved by 1.1 or more from baseline to week 28 in only one patient.

Bone scintigraphy and MRI were performed in four and one patient, respectively. In all four patients who underwent bone scintigraphy, uptake in the sternoclavicular joints decreased after GUS treatment. However, increased uptake was observed in some other regions in two patients (Fig. 2), in whom the possibility of exacerbation of inflammation in those sites could not be ruled out, even though there were no clinical symptoms. In the patient with only sacroiliitis, improvement of MRI findings was not observed at week 28 (Fig. S1).

Serum CRP levels were within the normal range throughout the follow-up period in all patients except for case 5 with a baseline level of 3 mg/L. Therefore, serum CRP was not useful in our patients.

Two of the five patients treated with GUS were free from skin manifestations of PPP throughout the assessment period (Fig. S2). In the remaining three patients, the baseline PPPASI ranged 3–21.4. At week 28, PPPASI decreased to between 0.3 and 2.6 (improvement rate, 13.3–94.4%).

In the five patients treated with GUS, no adverse events, such as abnormal laboratory values, infection or injection site reaction, were observed during the assessment period. No patients experienced exacerbation of PPP during the 28-week observation period in comparison with baseline conditions.

DISCUSSION

One of the major challenges in PAO treatment is assessment of disease activity using appropriate measures. There are still no established methods to evaluate disease activity of PAO. Yamamoto et al. conducted a subanalysis of patients with PAO in a PPP clinical trial and reported an improvement of EQ-5D pain/discomfort dimension scores in GUS-treated patients. However, the EQ-5D is a scale for the assessment of quality of life, which is not suitable for the evaluation of joint-specific symptoms. In this study, we used BASDAI, ASDAS, pain VAS and PGA for assessment. Pain VAS scores decreased in all five patients at week 28. Importantly, discontinuation or dose reduction of analgesics was possible in four patients. BASDAI and ASDAS were originally developed for ankyllosing spondylitis, and neither BASDAI nor ASDAS were used to assess disease activity of PAO. Therefore, this is the first study in which disease activity of PAO was assessed with these scales. While BASDAI is completely derived from subjective assessments, ASDAS, which incorporates CRP levels or erythrocyte sedimentation rate, allows for objective assessment of improvement or exacerbation of disease activity with numerical values. Three of five patients showed clinically significant improvement in BASDAI of 2 or more. Whereas improvement in ASDAS of 1.1 or more is considered clinically significant, such beneficial change was observed in only one of the five patients. GUS treatment may need to be longer than 28 weeks to yield improvements in BASDAI and ASDAS.
Figure 1. Time course of assessment scales for pustulotic arthro-osteitis. (a) Pain visual assessment scale (VAS). (b) Patient’s global assessment (PGA) of disease activity. (c) Bath Ankylosing Spondylitis Disease Activity Index (BASDAI). Scores of 4 or greater indicate suboptimal control of disease. (d) Ankylosing Spondylitis Disease Activity Score (ASDAS). ASDAS less than 1.3 indicates low disease activity.

Figure 2. Representative technetium-99m bone scintigraphy features before and after guselkumab treatment (case 4). While uptakes in the sternoclavicular joints decreased compared with baseline after guselkumab treatment, uptake in the lumbar spine was increased.
Although the usefulness of BASDAI and ASDAS for PAO should be examined in more detail through further studies, we have verified that GUS ameliorates joint pain in patients with PAO.

Imagings are alternative methods for the evaluation of severity of joint condition. In the clinical study on GUS, precordial lesions in PAO were mainly assessed by MRI, and severity scores based on MRI findings were improved by GUS treatment. However, MRI findings did not improve in our only patient with sacroilitis at week 28. Because osteitis also occurs in PAO, bone scintigraphy is often used to assess disease activity. In four patients who underwent bone scintigraphy in this study, uptake in the sternoclavicular joint area decreased after treatment, whereas the uptake in the spine and other sites increased at the same time in two patients. These results suggest that bone scintigraphy, which can simultaneously examine the activity of joint lesions in the whole body, may be more useful for PAO than MRI, in which only limited targeted areas are usually observable. On the other hand, MRI allows for distinction among inflammation of synchondrosis, bone marrow edema, soft tissue swelling and bone proliferation, and separate assessment of these conditions, but this cannot be done with bone scintigraphy. In addition, recently proposed MRI scoring enables quantification of severity. MRI can be used in consideration of affected joints. Thus, assessment of disease activity by imagings is also important for the evaluation of treatment responses.

In this observational study, GUS therapy alleviated joint pain and resulted in dose reduction of analgesics in PAO patients with good safety profiles. GUS can be an important treatment option for intractable PAO. Development of PAO-specific assessment scales is required in the future.

CONFLICT OF INTEREST: H. F. has received honoraria for speaking and consultancy from AbbVie, Eisai, Novartis, Janssen Pharmaceutical, Maruhou, Taiho, Eli Lilly and Mitsubishi Tanabe Pharma. T. T. has received honoraria for speaking and consultancy from AbbVie, Eisai, Novartis, Janssen Pharmaceutical, Maruhou, Taiho, Eli Lilly, Bristol-Myers Squibb and Mitsubishi Tanabe Pharma. N. I. has nothing to declare.

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Figure S1. Magnetic resonance imaging before and after guselkumab treatment in case 2. Bone marrow edema in the right ala of sacrum was unchanged at week 28 compared with baseline (short-T1 inversion recovery image).

Figure S2. Time course of Palmoplantar Pustulosis Area and Severity Index (PPPASI), Patients 2 and 3 were consistently free of skin symptoms (PPPASI, 0) throughout the observation period.

Table S1. Backgrounds of the patients treated with guselkumab.