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Case report

Efficacy of peficitinib in two patients with rheumatoid arthritis on maintenance hemodialysis

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Abstract

Objective: Treatment options for patients with rheumatoid arthritis on maintenance hemodialysis with an inadequate response to biologic agents have not been reported. In this report, we describe two patients who achieved remission after treatment with peficitinib.

Methods: Two 69- and 85-year-old patients with rheumatoid arthritis on maintenance hemodialysis were previously treated with biologics and started on peficitinib 100 mg/day after the secondary failure of biologics.

Discussion: In the two cases presented here, rheumatoid arthritis was almost in remission and there were no adverse events, although the patients were switched to peficitinib after secondary failure of the biologic agents. Among Janus kinase inhibitors, peficitinib has the lowest renal excretion; therefore, its administration in patients on dialysis is not contraindicated according to the package insert in Japan. The use of biologic agents in patients on hemodialysis has been reported to be associated with a high incidence of infections; therefore, care should be taken to avoid infections when administering Janus kinase inhibitors.

Conclusion: Janus kinase inhibitors with low renal excretion, such as peficitinib, may be effective in patients with rheumatoid arthritis on maintenance hemodialysis who have an inadequate response to biologic agents.

Key words: rheumatoid arthritis, maintenance hemodialysis, peficitinib, Janus kinase inhibitors

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Introduction

Janus kinase inhibitors have been reported to be effective in the treatment of patients with rheumatoid arthritis[1–4]. However, little is known about their efficacy in patients with renal failure or those on dialysis. This is because many Janus kinase inhibitors are renally excreted. The use of Janus kinase inhibitors in patients with rheumatoid arthritis and renal insufficiency is not recommended in view of safety concerns. However, because of its low renal excretion, peficitinib is not contraindicated in patients on dialysis in Japan according to the package insert. In this report, we describe two cases of patients with rheumatoid arthritis on maintenance hemodialysis who were administered peficitinib 100 mg/day and showed a favorable course of treatment.

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Case 1

A 69-year-old woman, who started maintenance hemodialysis at age 57 due to chronic renal failure, was diagnosed with rheumatoid arthritis at age 61, and started monotherapy with etanercept at age 63, achieving remission. However, the efficacy gradually decreased, and the patient was switched to tocilizumab. However, the DAS28-CRP (3.67) and SDAI (20.03) showed that the drug efficacy was insufficient, and peficitinib 100 mg/day was started as monotherapy in view of economic and safety considerations. If the efficacy was inadequate, the dose was increased to 150 mg/day, and peficitinib monotherapy was administered without any other drug therapy. After 100 mg/day of peficitinib, the disease activity gradually decreased and remission was achieved after 24 weeks. No adverse events were observed during peficitinib treatment (Figure 1).

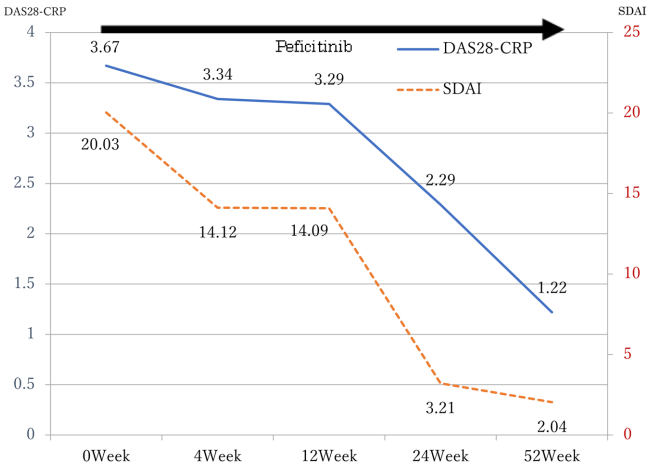

Figure 1 The clinical markers of case 1 during treatment.

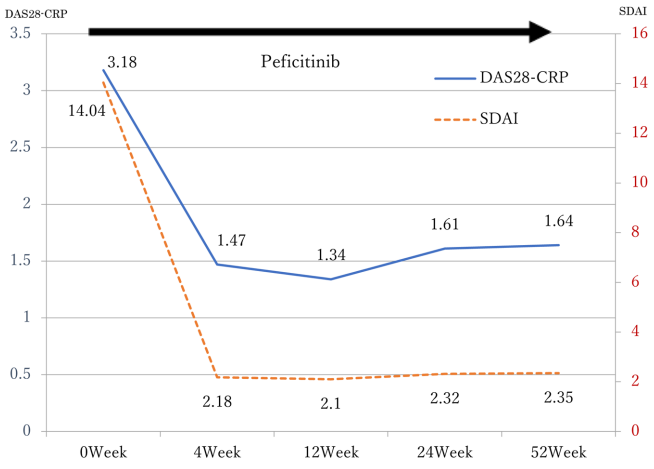

Figure 2 The clinical markers of case 2 during treatment.

Case 2

An 85-year-old woman, developed rheumatoid arthritis at the age of 73 and started hemodialysis at the age of 82. After the induction of dialysis, rheumatoid arthritis treatment was started initiated with etanercept, which was effective for 3 years. However, the effect of etanercept gradually diminished and she became secondarily ineffective on etanercept. Treatment with tofacitinib was initiated, but was discontinued due to the development of a hepatic disorder. Etanercept was then resumed, but was ineffective with DAS28-CRP (3.18) and SDAI (14.04); therefore, peficitinib 100 mg/day was started due to economic and safety considerations. After 4 weeks of treatment, the DAS28-CRP (1.64) and SDAI (2.35) remained low, and remission was achieved. No adverse events were observed during treatment with peficitinib (Figure 2).

Discussion

Methotrexate is a central drug used in the treatment of rheumatoid arthritis. However, methotrexate is difficult to use in patients on dialysis because of renal failure. Previous reports have shown that biologics are effective in patients with high disease activity rheumatoid arthritis on maintenance dialysis, and there have been reports on the use of TNF-α antibody agents, such as certolizumab pegol and etanercept, and non-TNF-α antibody agents, such as tocilizumab, in patients on dialysis[5–8]. However, no reports have been found on the response to the secondary ineffectiveness of these biologics.

Janus kinase inhibitors inhibit Janus kinase, which is required for intracellular transmission of stimuli by inflammatory cytokines. The efficacy of Janus kinase inhibitors in rheumatoid arthritis has been reported to be as good as or better than that of biologics[2]. However, adverse events such as herpes zoster, upper respiratory tract infection, pneumonia, tuberculosis, and sepsis have been identified, and caution is required[1–4]. The relationship between selectivity and safety of Janus kinase inhibitors has not yet been clearly established, but there are reports that the selectivity of Janus kinase does not affect its safety in clinical practice[9]. When using a Janus kinase inhibitor in patients with rheumatoid arthritis, it is important to consider patient comorbidities rather than Janus kinase selectivity and to select drugs based on differences in drug pharmacokinetics.

Peficitinib is considered to have the least impact on renal function of all the available Janus kinase inhibitors. Peficitinib is primarily metabolized in the liver by sulfotransferase (SULT) 2A1. Peficitinib is primarily excreted in the feces, with urinary excretion rates ranging from 12.5% to 16.8%[10]. When peficitinib was administered to patients with severe renal dysfunction (eGFR <30 mL/min/1.73 m^2), Cmax was 21.7% lower and AUCinf was 8.7% higher than in patients with normal renal function[11]. These values were not significantly different from those observed in the patients with normal renal function[12]. However, although this drug has the lowest urinary excretion rate of all Janus kinase inhibitors, some reports have raised concerns regarding the increased AUC in patients with severely impaired renal function[11, 13]. Unlike in patients with impaired renal function, there are no reports on the pharmacokinetics of peficitinib in patients on maintenance dialysis, and it is possible that the pharmacokinetics of peficitinib may not be similar to those in patients with impaired renal function. Although there have been previous reports of peficitinib in patients on maintenance hemodialysis, the package insert of peficitinib in Japan does not contraindicate the use of peficitinib in such patients. Based on previous reports of peficitinib hemodynamics, peficitinib could be administered to patients on maintenance hemodialysis[11]. In the present two patients, a lower dose of peficitinib of 100 mg/day was administered

for economic and safety reasons. The use of biologics in patients on hemodialysis has been reported to result in a high incidence of infections[14], and even with Janus kinase inhibitors, care should be taken to avoid infections. However, given the current treatment for rheumatoid arthritis, peficitinib may be useful in patients on hemodialysis who have had an inadequate response to biologics and for whom other treatment options are scarce.

Ethical considerations and patient consent: We give full consideration to the protection of personal information when presenting our research, and we explain in writing to the subject of the research and obtain his/her consent.

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