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Case Report

Two Cases of Abatacept Treatment for Patients with Rheumatoid Arthritis on Hemodialysis

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Abstract

Introduction: We report our experience with 2 RA patients on hemodialysis who were treated with ABT monotherapy.

Subjects and Methods: Two hemolysis patients (75-year-old and 42-year-old women with RA) were administrated with ABT monotherapy without concomitant use of methotrexate.

Results and Discussion: Case 1: remission from disease activity (DAS 28 under 3.1) has been continued even when the administration interval was prolonged to 4 weeks, and Case 2: remission has been maintained interval was to 2 weeks. No serious complications have occurred.

Conclusion: ABT monotherapy should be considered as a candidate for the treatment of RA patients complicated with CKD and/or heart failure.

Keywords: *Rheumatoid Arthritis; Hemodialysis; Abatacept; Monotherapy*

Abbreviations

CKD: Chronic Kidney Disease; RA: Rheumatoid Arthritis; MTX: Methotrexate; eGFR: Estimated Glomerular Filtration Rate; NSAIDs: Non-Steroidal Anti-Inflammation Drugs; ABT: Abatacept; BMI: Body Mass Index; ESRD: End-Stage Renal Disease; TNF: Tumor Necrosis Factor; ETN: Etanercept; RANKL: Receptor Activator of Nuclear Factor Kappa-B Ligand; TCZ: Tocilizumab; DAS: Disease Activity Score, HAQ: Health Assessment Questionnaire

Introduction

Japan has a very high life expectancy and its healthy life expectancy is the highest in the world. However, there are 13,300,000 people (12.5% of the population) with chronic kidney disease (CKD) in Japan [1]. There are 800,000 patients with rheumatoid arthritis (RA), and the number of RA patients who also have CKD is increasing due to complications of the disease, drug-induced (e.g., methotrexate [MTX]-induced) renal impairment, and aging [2]. A review of the estimated glomerular filtration rate (eGFR) in 6058 patients who visited our hospital during the period from 2012 to 2016 found that 414 (41.6%) of 995 patients aged 70 years or older and 158 (27.0%) of 585

patients with RA had an eGFR of < 60; thus, these patients were suspected of having CKD [3]. In addition, 49 patients (7.0%) with RA and 125 patients (10.5%) aged 70 years or older also had nephrogenic anemia [3]. Because MTX and non-steroidal anti-inflammation drugs (NSAIDs) are difficult to use in RA patients with CKD, only biologic monotherapy is possible. Abatacept (ABT) is suitable for Japanese patients who are relatively small, and is effective at even half of the regular dose [4,5]. We report our experience with 2 RA patients on hemodialysis who were treated with ABT monotherapy.

Case 1

The patient was a 75-year-old woman with a 5-year history of RA (stage 1, class 2). She had a height of 152 cm, weight of 43.2 kg, and body mass index (BMI) of 18.7 kg/m^2. She was diagnosed with a pancreatic tumor at the age of 52 years. At the age of 61 years, her chronic nephritis developed into renal failure, and hemodialysis was introduced. At the age of 69 years, she underwent pancreatic body and spleen resection. At the age of 70 years, she developed RA and visited our department of orthopedics. Heart failure and renal failure were found at her first presentation (Table 1). After consultation with the patient, we started monotherapy with ABT (Bristol-Myers Squibb, Orencia, 125 mg subcutaneous, once a week), a cytotoxic T-lymphocyte antigen 4 inhibitor. Medically, she was being treated with hemodialysis thrice weekly and with the administration of anti-hypertensives, proteinase inhibitors, thyroid gland powder, vitamin D, a calcium preparation, an anti-potassium preparation, an anticoagulant, and an anti-migraine drug. Adverse reactions were evaluated 1 week after the first administration of ABT, and subsequently the interval of ABT administration was prolonged to 2 weeks. When the disease activity subsided, the administration interval was prolonged to 3 weeks. Since the age of 73 years, her remission from disease activity (DAS 28 under 3.1) has been continued even when the administration interval was prolonged to 4 weeks, and now she is well 4 years after the start of treatment (Figure 1). No serious complications have occurred during the course of treatment, and her quality of daily life (score of health assessment questionnaire: HAQ under 0.5) has been well maintained.

Total protein	7.4 g/dL
Albumin	3.7 g/dL
Alkaline Phosphatase	357 U/L ↑
Amylase	142 U/L ↑
Creatinine	5.3 mg/dL ↑
eGFR	7mL/min/1.73m^2 ↓
Calcium	8.6 mg/dL ↓
Phosphorus	4.5 mg/dL
25-OH vitamin D	10 ng/mL
White blood cells	7800 (Lymphocytes : 2348)
Hemoglobin	12.9 g/dL
Platelets	31.8×10^4
C reactive protein	1.6 mg/dL ↑
Blood sedimentation test	29 mm/h ↑
Brain natriuretic peptide	248 pg/mL ↑
Anti-cyclic citrullinated peptide antibody (ACPA)	498 U/mL ↑
Anti-galactose-deficient immunoglobulin G antigen (CA-RF)	13.3 AU/mL ↑
Matrix metalloprotease -3(MMP-3)	145 ng/mL ↑
Sialylated carbohydrate antigen (KL-6)	743 U/ml ↑

Table 1: *Case 1: Clinical data on admission.*

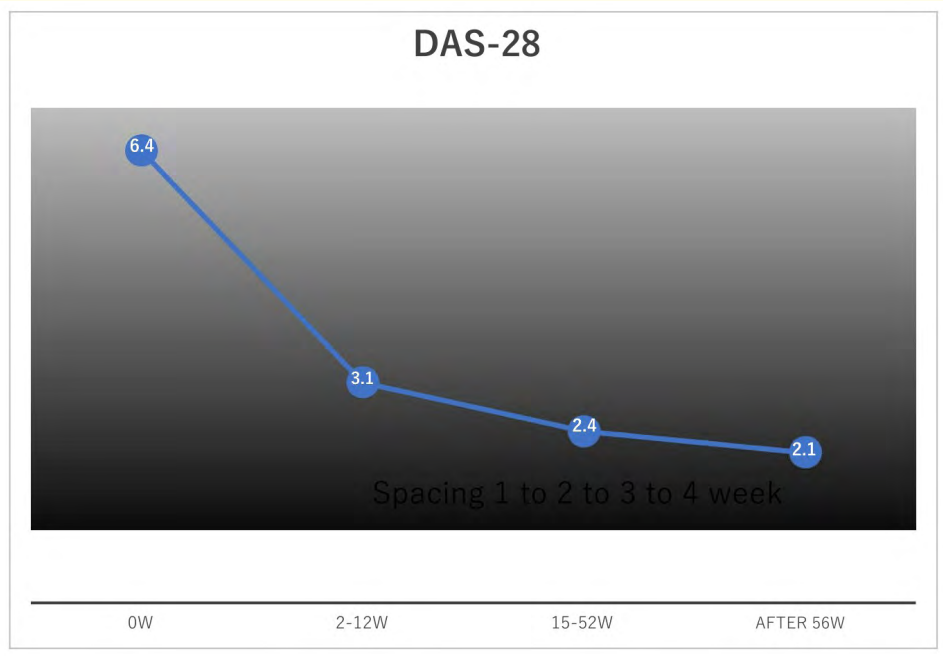

Figure 1: *Changes of disease activity score during ABT mono-therapy.*

Case 2

The patient was a 42-year-old woman with a 10-year history of RA (stage 4, class 2). She had a height of 156 cm, weight of 42.8 kg, and BMI of 17.6 kg/m2. At the age of 3 years, she developed nephritis. At the age of 24 years, her condition developed into end-stage renal disease (ESRD); therefore, hemodialysis was introduced. Her disease is familial, and both her mother and brother are on hemodialysis. She developed RA at the age of 32 years and had been treated with mizoribine (Japanese immunosuppressive disease-modified anti-rheumatic drug), an immunosuppressant, at 50 mg/day. At the age of 34 years, she visited our department of orthopedics. After having consulted with the patient about the result of the tests at her first presentation (Table 2), we started her on once-weekly monotherapy with etanercept (ETN; Pfizer, Enbrel 25 mg subcutaneous; recommended dose twice weekly), an anti-tumor necrosis factor (TNF) -α receptor antibody. Medically, she had been treated with hemodialysis 3 times weekly and by the administration of anti-hypertensives, vitamin D, a calcium preparation, an anti-potassium preparation, and an anticoagulant. Although her disease activity subsided after ETN monotherapy, her arthritis relapsed at the age of 40 years, and acetaminophen and a steroid were added. Subsequently, we switched ETN to ABT (125 mg subcutaneous, once every 2 weeks). Her disease activity decreased rapidly without any adverse reactions, and a remission has been maintained without any effects on renal or cardiopulmonary functions for a year since the start of ABT administration (Figure 2). No serious complications have occurred during the course of treatment, and the quality of her daily life (score of HAQ nearly 1.0 but she was satisfied) has been well maintained.

Total protein	7.0 g/dL
Albumin	4.4 g/dL
Alkaline Phosphatase	155 U/L
Amylase	117 U/L
Creatinine	7.5 mg/dL ↑
eGFR	5 mL/min/1.73m^2 ↓
Calcium	9.6 mg/dL
Phosphorus	4.9 mg/dL ↑
25-OH vitamin D	14 ng/mL
White blood cells	5300 (Lymphocytes : 1325)
Hemoglobin	12.3 g/dL
Platelets	18.4×10^4
C reactive protein	2.6 mg/dL ↑
Blood sedimentation test	27 mm/h ↑
Anti-cyclic citrullinated peptide antibody (ACPA)	99.7 U/mL ↑
Anti-galactose-deficient immunoglobulin G antigen (CA-RF)	19.6 AU/mL ↑
Matrix metalloprotease -3(MMP-3)	294 ng/mL ↑
Sialylated carbohydrate antigen (KL-6)	330 U/ml

Table 2: *Case 2: Clinical data on admission.*

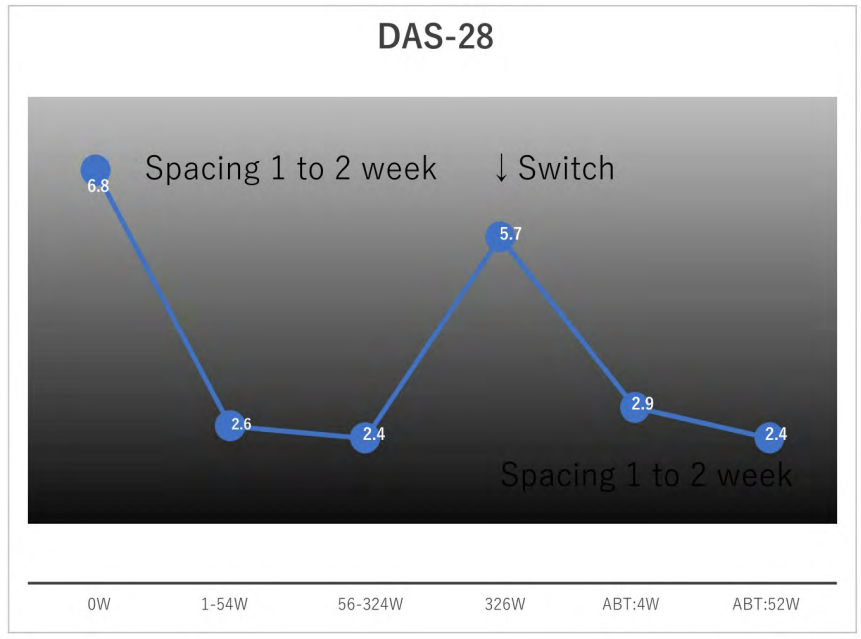

Figure 2: *Changes of disease activity score secondline ABT monotherapy.*

Discussion

For the treatment of RA complicated with other conditions, the use of biologic products that must be used concomitantly with MTX, not to mention NSAIDs or disease-modifying RA drugs, is difficult. Sometime opioids and acetaminophen selected for pain control in CKD and RA instead of NSAIDs. Japan is most progressing into aging society in the world. In case of aged but no CKD RA patients, commonly use of bisphosphonate and/or parathyroid hormone treatments selected for vertebral and femoral bone mineral density increase. In renal failure patients, anti-receptor activator of nuclear factor Kappa-B ligand (RANKL) antibody [6] can be used for bone destruction; however, this antibody does not have anti-inflammatory effects for RA.

Among available biologic products, ETN, ABT, and tocilizumab (TCZ: anti-interleukin-6 inhibitor) can be used as monotherapy without concomitant use of MTX, and among these 3 mono-therapeutic biologic products [7], ABT is the only drug that can be used in RA patients with renal failure and heart failure; in addition, its dose adjustment is reimbursable by health insurance in Japan [8]. Thus far, we have found that ABT is useful for Japanese patients [4] aged 65 years or older weighing 65 kg or less [5]. In both two patients with a low BMI, prolongation of the duration of ABT monotherapy allowed inhibition of RA DAS 28 and HAQ score without progression of complications.

Conclusion

In conclusion, ABT monotherapy without MTX and NSAIDs should be considered as a candidate for the treatment of RA patients complicated with CKD and/or heart failure.

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