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ORIGINAL ARTICLE

Impact of the COVID-19 pandemic on biologic treatment in psoriasis patients: A single-center retrospective study in Japan

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Abstract

The impact of the COVID-19 pandemic on biologic treatment for psoriasis in Japan remains to be elucidated. This study aimed to investigate changes in biologic treatment and patients' behavior of visiting our department, especially in psoriasis patients treated with biologics before and during the pandemic. Data were collected from medical records retrospectively. The numbers of new psoriasis patients before (2019) and during (2020) the pandemic were compared. Patients' behavior of visiting our department was evaluated. The number of new psoriasis patients who visited our department in 2020 decreased by 35.7% compared with that in 2019. The reduction rate of new patients with psoriasis vulgaris was 49.3%, whereas the numbers of new patients with psoriatic arthritis (PsA) and generalized pustular psoriasis (GPP) were almost the same in 2019 and 2020. The number of patients who newly initiated biologics did not decrease in 2020 compared with that in 2019. As of January 1, 2020, 215 psoriasis patients were treated with biologics. Six patients (2.8%) discontinued biologics treatment possibly due to COVID-19 in 2020. Among 212 patients with good adherence to visiting our department in the previous year, 24 patients (11.3%) refrained from their visits for at least 1 month. In most cases, refrainment was observed in April and May when the first state of emergency was in effect in Japan. In conclusion, the COVID-19 pandemic hindered patients from visiting our department. However, its impact on patients who needed intensive care, such as patients with PsA and GPP, and psoriasis patients treated with biologics, was limited.

KEYWORDS

biologics, coronavirus, COVID-19, Japan, pandemic, psoriasis, SARS-CoV-2, state of emergency

1 | INTRODUCTION

The outbreak of coronavirus SARS-CoV-2 disease (COVID-19) which was firstly identified in Wuhan, China, began in December 2019. The virus then spread all over the world, resulting in the declaration of a global pandemic by the World Health Organization on March 11, 2020.^{1,2} In Japan, the first patient infected with the coronavirus was identified on January 15, 2020. A state of emergency was declared in seven prefectures in Japan 3 months later on April 7, and then

the state of emergency was expanded across the nation on April 16. Although lockdown laws were not in force in Japan, people were asked to stay at home unless it was necessary to go out. Almost all commercial facilities and schools were closed until the state of emergency was completely lifted nationwide on May 21.

The fear of the risk of infection with the coronavirus and the recommendation that people reduce coming into contact with other people issued by the government could have hindered some patients from visiting a hospital or clinic. Tanacan et al. conducted a retrospective cohort study in Turkey and reported a significant decrease in hospital admissions during the pandemic period compared with the pre-pandemic period.³ A cross-sectional observational study performed in Iraq revealed that the pandemic's psychologic impact, the fear of attending hospitals, and the shortage of medications have led to an increase in the relapse rate of common chronic skin diseases, including psoriasis.⁴ Although there were no strict restrictions on going to a hospital or clinic in Japan, certain patients refrained from visiting a hospital or clinic. Focusing on psoriasis patients, since data on whether taking biologics for psoriasis had an effect on COVID-19 transmission were limited at the beginning of the pandemic, some patients were worried about continuing the biologic treatment. However, the impact of the pandemic on biologic treatment in psoriasis patients remains to be elucidated.

The pandemic popularized telemedicine, namely, remote consultation over the phone or on the internet⁵ in many countries, including Japan. Our hospital began to offer telemedicine to patients with chronic diseases who were in a stable condition in April 2020.

In this study, we investigated changes in the behavior of patients visiting our department before and during the pandemic, especially psoriasis patients. In addition, the impact of the pandemic on biologic treatment in psoriasis patients was examined by comparing the use of biologics before and during the pandemic. We also investigated patients' refrainment from visiting our department and utilization of telemedicine in psoriasis patients treated with biologics.

2 | PATIENTS AND METHODS

Data on patients visiting our department from January 2016 to December 2020 were collected retrospectively from their charts. To examine the impact of the pandemic on the visiting behavior of patients, the numbers of new patients who visited our department and patients referred to our department each year were investigated from 2016 to 2020. To assess the impact of the first declaration of a state of emergency, the ratio of the mean number of patients who visited our department per day in each month of 2020 to that in the same month of 2019 was calculated.

Next, we focused on psoriasis patients. The number of patients who were newly diagnosed with psoriasis vulgaris (PsV), psoriatic arthritis (PsA), or generalized pustular psoriasis (GPP) and the number of patients who newly initiated biologic treatment each year were examined from 2018 to 2020. Patients who switched biologics were excluded. In addition, we assessed the impact of the pandemic on patients who had already been treated with biologics for psoriasis in 2020. First, we counted the total number of patients who were being treated with biologics as of January 1, 2020, and then assessed the number of patients who discontinued biologics possibly due to the COVID-19 pandemic and the number of patients who refrained from visiting our department during 2020. Discontinuation of biologics was defined as ceasing biologic treatment and never receiving any biologic treatment at least until July 2021, when the data were collected. Patients who discontinued biologics due to having a THE JOURNAL C

good response or adverse events were excluded. A patient with refrainment from visiting our department was defined as a patient who had good adherence to visiting our department in the previous year (2019) and who canceled their appointment in 2020, refrained from their visit for at least 1 month, and made another appointment thereafter in 2020. The utilization of telemedicine was also evaluated.

An unpaired t-test was used to compare the means of two independent groups. Fisher's exact probability test was conducted to determine whether there were associations between two categorical variables. Statistical significance was set at P < 0.05. GraphPad Prism 8.4.3 (GraphPad Software, San Diego, CA, USA) was utilized for statistical analysis.

This study was approved by the ethics committee of Teikyo University (21-062) and was carried out under the principles of the Declaration of Helsinki. We obtained consent for this study by an opt-out method on the university website.

3 | RESULTS

3.1 | Number of new patients visiting our department each year

The number of new patients who visited our department each year is shown in Figure 1a. It had risen gradually from 2016 until 2019, but it decreased by 21.5% in 2020 compared with 2019. The number of patients referred to our department each year demonstrated the same trend (Figure 1b). The ratio of the mean number of patients who visited our department per day in each month of 2020 to that in







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the same month of 2019 is shown in Figure 1c, which revealed that some patients refrained from visiting our department from March 2020, when COVID-19 began to spread in Japan. The reduction rate was high especially in April and May, during the first state of emergency.

3.2 | Number of new psoriasis patients and those initiating biologic treatment each year

The number of patients who were newly diagnosed with PsV, PsA, or GPP at our department each year is shown in Figure 2a. It decreased by 35.7% in 2020 compared with that in 2019 (from 182 in 2019 to 117 in 2020). In particular, the number of newly diagnosed patients with PsV decreased by 47.2% (from 144 to 76, P = 0.0004), whereas the number of those with PsA or GPP did not decrease (PsA 34 in 2019 and 34 in 2020, GPP 4 and 7, respectively). The number of psoriasis patients who newly initiated biologic treatment did not decrease in 2020 compared with that in 2019 (53 in 2019 and 57 in 2020; Figure 2b). In 2019, biologics were newly introduced



FIGURE 2 (a) Number of patients who were newly diagnosed with psoriasis vulgaris (PsV), psoriatic arthritis (PsA), or generalized pustular psoriasis (GPP) each year from 2018 to 2020. (b) Number of psoriasis patients who newly initiated biologic treatment each year from 2018 to 2020. (c) Total number of cases of refrainment from visiting our department in each month of 2020 in patients treated with biologics

in 34/53 (64.2%) male patients and 19/53 (35.8%) female patients. The mean age of the patients was 52.5 \pm 16.3 years old. In 2020, biologics were newly introduced in 40/56 (71.4%) male patients and 16/56 (28.6%) female patients. The mean age of the patients was 48.2 \pm 14.8 years old. There were no significant differences in age or gender for the newly introduced cases of biologics (age, *P* = 0.1519; gender *P* = 0.5385). No significant difference was observed in the types of biologics for the newly introduced cases between 2019 and 2020 (*P* = 0.6280).

3.3 | Discontinuation of biologic treatment for psoriasis possibly due to the COVID-19 pandemic in 2020

Next, we assessed the impact of the pandemic on patients who had already started treatment with biologics for psoriasis. Two hundred and sixteen patients with psoriasis (PsV 132, PsA 65, GPP 18) were being treated with biologics as of January 1, 2020 (Table 1). Their mean age was 53.1 \pm 15.3 (standard deviation) years. Forty-four patients received an antitumor necrosis factor (TNF)-α antibody (infliximab, adalimumab), six received an anti-IL-12/23 antibody (ustekinumab), 111 received an interleukin (IL)-17 inhibitor (secukinumab, ixekizumab, brodalumab), and 54 received an anti-IL-23 antibody (guselkumab, risankizumab) as shown in Table 1. Among the 145 patients treated with biologics that can be self-injected at home (adalimumab, secukinumab, ixekizumab, or brodalumab), 125 patients (86.2%) were treated under self-injection at home and 20 (13.8%) received the injection by nurses or doctors at our department instead of self-injection. The mean age of patients treated under selfinjection at home was siginificantly younger than that of patients without self-injection (52.4 \pm 14.9 years old and 62.6 \pm 11.8 years old, respectively; P = 0.0041).

Among the 215 patients treated with biologics as of January 1, 2020, six patients (2.8%) discontinued biologic treatment in 2020 for reasons other than having a good response or adverse events, namely, possibly due to the COVID-19 pandemic (Table 2). One patient (case 1 in Table 2) lived in China and could not visit our department due to restrictions in overseas travel. In the other patients, although the reasons for discontinuation of biologic treatment were unknown, the COVID-19 pandemic was possibly a factor, considering the data that 165 patients with psoriasis were being treated with biologics as of January 1, 2019, among whom only one patient (0.6%)

Biologics	Anti-TNF-α ab	Anti- IL-12/23 ab	IL-17 inhibitors	Anti-IL-23 ab	All
PsV	21	6	55	50	132 (61.4%)
PsA	21	0	42	2	65 (30.2%)
GPP	2	0	14	2	18 (8.4%)
All	44 (20.5%)	6 (2.8%)	111 (51.6%)	54 (25.1%)	215 (100%)

TABLE 1 Types of psoriasis and typesof biologics in psoriasis patients receivingbiologics in our department as of January1, 2020

Abbreviations: Ab, antibody; GPP, generalized pustular psoriasis; IL, interleukin; PsA, psoriasis arthritis; PsV, psoriasis vulgaris; TNF, tumor necrosis factor.

discontinued biologic treatment in 2019 for reasons other than having a good response, adverse event, or death.

3.4 | Refrainment from visiting our department due to the COVID-19 pandemic in 2020

As for the visiting behavior of patients treated with biologics for psoriasis, among the 212 patients with good adherence to visiting our department in the previous year, namely, those who had never canceled their appointment in 2019, 24 patients (11.3%) refrained from their visits for at least 1 month in 2020. Most of these patients (18/24, 75%) were treated with biologics under self-injection at home. Seventeen patients refrained from visiting once, five patients refrained twice, and two patients refrained three times in 2020. The total number of cases of refrainment from visiting was 33. The greatest number of cases of refrainment from visiting was observed in April and May, during the first state of emergency in Japan (Figure 2c). Eight (18.6%) of 43 patients treated with anti-TNF- α antibodies, one (16.7%) of six patients with an IL-12/23 antibody, 11 (10.1%) of 109 patients with IL-17 inhibitors, and 4 (7.4%) of 54 patients with anti-IL-23 antibodies refrained from visiting. Eighteen (14.4%) of 125 patients treated with biologics under self-injection at home refrained from visiting.

In contrast, only nine patients (5.7%) refrained from their visits for at least 1 month in 2019 among the 159 patients with good

TABLE 2 Psoriasis patients who discontinued biologic treatmentin 2020 for reasons other than having a good response or adverseevents

Case	Age (year)	Sex	Type of psoriasis	Biologic	Month at discontinuation
1	37	М	PsV	IFX	February
2	57	F	PsA	ADA	February
3	60	М	PsV	GUS	April
4	28	М	PsA	ADA	October
5	53	М	PsV	ADA	October
6	25	М	PsV	GUS	December

Abbreviations: ADA, adalimumab; GUS, guselkumab; F, female; IFX, infliximab; M, male; PsA, psoriasis arthritis; PsV, psoriasis vulgaris.

INDEL O I Soliasis patients treated
with biologics who utilized telemedicine
in 2020

TABLE 3 Depringing notion to treated

adherence to visiting our department in the previous year, namely 2018. This underscores the impact of the pandemic on refrainment from visiting our department.

3.5 | Utilization of telemedicine in 2020

Six (4.8%) of the 125 patients who were treated with biologics under self-injection at home utilized telemedicine in 2020 (Table 3). Most of the patients first utilized telemedicine in April or May, namely, during the first state of emergency. Patients who needed to be injected at the hospital did not utilize telemedicine.

4 | DISCUSSION

The numbers of new patients, new psoriasis patients, and referred patients in 2020 apparently decreased compared with the respective numbers in the previous year. The number of new patients with PsV was considerably lower in 2020 than in 2019, whereas the numbers of new patients with PsA and GPP did not decrease in 2020 compared with those in 2019. These data indicate that the COVID-19 pandemic imposed an enormous impact on the visiting behavior of patients with PsA and GPP was limited, which could be accounted for by the fact that patients with PsA and GPP need intensive treatment since PsA patients suffer from pain and joint destruction due to arthritis and GPP patients present with systemic inflammation including malaise, fever, edema, and arthritis during the acute phase.

The number of patients who newly initiated biologics in 2020 was almost the same as that in 2019. The number of patients who discontinued biologics possibly due to the pandemic was six (2.8%) out of 215 patients. This indicates the limited impact of the pandemic on psoriasis patients whose eruption and/or arthritis was so severe or their quality of life due to psoriasis was so impaired as to need biologics.

The first state of emergency was in effect from April to May 2020, during which many patients refrained from visiting our department (Figures 1c and 2c). Furthermore, six patients who were being treated with biologics began to utilize telemedicine. Thus, the pandemic affected patients' behavior of visiting our department

Case	Age (year)	Sex	Type of psoriasis	Biologic	Month of first use of telemedicine
1	42	М	PsA	ADA	April
2	40	М	PsV	SEC	May
3	49	М	GPP	IXE	April
4	70	М	GPP	IXE	May
5	38	F	PsA	IXE	May
6	32	М	PsA	IXE	August

Abbreviations: ADA, adalimumab; GPP, generalized pustular psoriasis; F, female; IXE, ixekizumab; M, male; PsA, psoriasis arthritis; PsV, psoriasis vulgaris; SEC, secukinumab.

enormously, especially during the first state of emergency. Among psoriasis patients who were being treated with biologics and refrained from visiting, most (75%) of the patients were undergoing self-injection at home, which indicates that self-injection of biologics at home resulted in flexibility in visiting behavior.

As for the study limitations, the data were collected at a single center in Japan. The trends could be different in individual hospitals and clinics. In addition, our hospital is located in the urban area in Tokyo. Accessibility to a hospital or clinic and the extent of the pandemic differed according to location, and could affect the results in other locations. The state of emergency in Japan did not restrict patients' behavior under the law. Under the state of emergency, people were merely asked to stay at home without any punishment, although almost all people and commercial facilities obeyed the request during the first state of emergency. The situation was quite different in Japan from that in some other countries where a strict lockdown was instituted. The results in other countries could be different from our results.

In conclusion, the COVID-19 pandemic hindered patients from visiting our department, especially during the first state of emergency in Japan. However, its impact on patients who needed intensive care, such as those with PsA and GPP, and those treated with biologics, was limited.

CONFLICT OF INTEREST

M.K. received grants for research from Torii Pharmaceutical, Eisai, Maruho, and Novartis Pharma, and honoraria for lectures from Maruho, LEO Pharma, Eisai, AbbVie, Kyowa Kirin, Eli Lilly, Taiho Pharmaceutical, Mitsubishi Tanabe Pharma, and Janssen Pharmaceutical. Y.T. received grants for research from Maruho, LEO Pharma, Eisai, AbbVie, Kyowa Hakko Kirin, Taiho Pharmaceutical, Celgene, and Eli Lilly, and honoraria for lectures from Maruho, LEO Pharma, Eisai, AbbVie, Kyowa Kirin, Eli Lilly, Taiho Pharmaceutical, Mitsubishi Tanabe Pharma, and Janssen Pharmaceutical.

ETHICAL APPROVAL

This study was approved by the ethics committee of Teikyo University (21–062) and was carried out under the principles of the Declaration of Helsinki.

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