

Short Communication

An Awareness Survey on COVID-19 among Japanese Patients with Fabry Disease

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ABSTRACT

The purpose of this study was to clarify the effects of the coronavirus disease 2019 (COVID-19) pandemic on the lives and medical care of Japanese patients with Fabry disease and how healthcare providers can support the continued treatment of these patients in the future. A questionnaire survey was conducted with members of the Japan Fabry Disease Patients and Family Association. The questionnaire was mailed to 156 patients and was returned by 87 (response rate, 56%) ; 83 questionnaires were considered valid and were analyzed. The study found that most of patients with Fabry disease had already received or wanted to receive a vaccine and were “very worried” about COVID-19. In addition, the COVID-19 pandemic had changed the patients’ lives and affected their physical and mental health. Although the percentage of patients who were able to continue treatment was higher than we expected and the percentage who wanted home infusion therapy was lower than we expected, some patients were anxious about coming to the hospital or had switched to oral pharmacological chaperone therapy. Therefore, to be prepared for pandemics, such as COVID-19, a system of care at home for patients with Fabry disease should be developed.

(Jikeikai Med J 2022 ; 69 : 29-34)

Key words : Fabry disease, COVID-19, enzyme replacement therapy, home infusion therapy, vaccination

INTRODUCTION

Fabry disease (FD) is a lysosomal storage disease, characterized by a genetic deficiency of the lysosomal enzyme α -galactosidase A, which results in the accumulation in various organs of glycolipids, such as globotriaosylceramide¹. This accumulation causes corneal opacities, angiokeratoma, neuropathic pain, and gastrointestinal symptoms in childhood and eventually causes renal, cardiac, and cerebrovascular complications in adulthood. Although FD is an X-linked recessive disease, its clinical symptoms develop in males and, to a milder extent, in females². Treatments of

FD approved in Japan are enzyme replacement therapy (ERT), which is the intravenous infusion of purified α -galactosidase A, and pharmacological chaperone therapy, which is the oral administration of a medicine that stabilizes the mutant enzyme. Most patients undergo ERT while visiting a hospital because home infusion therapy is approved only if a patient cannot visit owing to severe symptoms.

The coronavirus disease 2019 (COVID-19), which was reported as a pneumonia of unknown cause in Wuhan, China, in December 2019, quickly spread worldwide and was declared a pandemic by the World Health Organization in March 2020. In Japan, per statistics of the Ministry of

Received : June 13, 2022 / Accepted : June 28, 2022

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Health, Labour and Welfare, as of February 27, 2022, approximately 4.9 million people had been infected with COVID-19, and 23,000 people had died³. Therefore, the pandemic's effect on the treatment of FD is assumed to have become more difficult, because patients might avoid coming to the hospital owing to the fear of COVID-19 infection. Continuing treatment of FD is important, but if treatment is discontinued, symptoms do not immediately worsen. Therefore, we have wondered whether COVID-19 has prevented patients from visiting hospitals and has affected their continuation of ERT. In addition, although vaccination against COVID-19 is strongly recommended for patients with FD, their willingness to be vaccinated might differ from that of members of the general population without underlying diseases or of patients with other chronic illnesses. The effects of COVID-19 on the continuation of treatment and the willingness of patients with FD to receive home infusion therapy in Europe have been reported⁴⁻⁸ but the effects have not been reported regarding patients in Japan. Also not reported are the results of surveys on vaccine awareness among patients with FD. Because medical care systems differs between Japan and Europe, the effects of COVID-19 on FD medical care might also differ.

Therefore, the aim of the present study was to acquire basic data that can promote the continuation of ERT and vaccination in Japanese patients with FD during the COVID-19 pandemic. This study examined patients' willingness to be vaccinated, the effect of COVID-19 on their lives, the role of outpatient medical care, and the possibility of home infusion therapy, based on a questionnaire survey of Japanese patients with FD.

MATERIAL AND METHODS

Research design

This cross-sectional fact-finding study used the unsubscribed questionnaire method.

Study participants

The participants of this study were 156 patients with FD who were members of the Japan Fabry Disease Patients and Family Association (*Fukuro-no-kai*) and were 20 years or older.

Research methods

1. Method of distributing the questionnaire

The request letter, consent form, and questionnaire were sent by postal mail in July 2021 to the chairman of the Japanese Fabry Disease Patients and Family Association, who then sent consent forms and questionnaires to patients of the association. To confirm that consent to participate in the study had been obtained from the patients, the first section of the questionnaire had a check box that stated "I agree to the questionnaire."

2. Questionnaire

The questions were related to the following variables: (1) sex and age, (2) treatment method, (3) whether the patient was infected with COVID-19, (4) willingness to receive the COVID-19 vaccination, (5) source of information on COVID-19, (6) whether the pandemic had changed the patient's life, (7) whether the patient was continuing treatment, (8) whether the pandemic had affected hospital visits, (9) whether the patient wished to receive home infusion therapy, (10) the patient's degree of worry about COVID-19 infection, (11) household size, and (12) if any family member had FD, whether the patient wished to have them vaccinated.

Ethical considerations

This study was approved by the Ethical Committee of The Jikei University School of Medicine for Biomedical Research 33-109(10724)

RESULTS

Patients' background

The questionnaire was mailed to 156 patients and was returned by 87 (response rate, 56%); 83 questionnaires were considered to have valid responses and were analyzed (Table 1). Valid responses were received from 28 men and 55 women. The most common treatment was ERT, which was received by 23 men and 42 women; pharmacological chaperone therapy was received by 2 men and 8 women.

Two patients stated that COVID-19 made going to the hospital difficult and caused them to change from ERT to pharmacological chaperone therapy, an oral medication treatment requiring less frequent visits.

Table 1. Clinical and demographic data

	Men	Women
Number of patients	28 (33.7%)	55 (66.2%)
Average age, years	45.5	54.3
Age range, years	22–75	27–83
Treatment		
Enzyme replacement therapy	23 (82.1%)	42 (76.3%)
Pharmacological chaperone therapy	2 (7.1%)	8 (14.5%)
Clinical trial	1 (3.5%)	1 (1.8%)
None	2 (7.1%)	4 (7.2%)

Data received with questionnaires

Of the 83 patients with FD, only 1 had been infected with COVID-19 by August 2021 (Table 2). Vaccines had been given to 56 patients and had not been given to 27 patients. Of the 27 patients who had not been vaccinated, 15 wanted to be vaccinated in the future, 4 did not, and 8 were unsure. Many of the patients who did not wish to receive the vaccine cited doubts about its safety. One patient said that her physician had prevented her from receiving the vaccine because she was allergic to a medication.

The source of information about COVID-19 for the largest number of patients was television. The next most common source was the internet. A less common source of information for patients was physicians. Sources of information did not differ significantly between patients who wanted to be vaccinated and those who did not (data not shown).

When asked if COVID-19 had affected their lives, 49 patients answered “yes” and 34 answered “no.” Specifically, the patients reported fewer opportunities to meet with others and go outside their homes, effects on their work, and physical and mental health effects. They said that they could not receive vaccines (owing to FD) and, as a result, were unable to meet others; had lost their jobs; did not go out, except to the hospital, for fear of infection; and, thus, became depressed.

When asked if the pandemic had affected their hospital visits, 17 patients answered “yes,” 65 answered “no,” and 1 did not answer. When asked if they were continuing treatment, 76 answered “yes” and 7, including 6 patients who did not receive treatment, did not answer the question. The most common reason for the effect of the pandemic on hospital visits was the means of transportation, such as driving to the hospital by car instead of taking public transport. Some patients were temporarily unable to receive treat-

ment because of COVID-19 outbreaks at the hospital they were visiting.

Regarding whether they were willing to receive home infusion therapy among the 65 patients receiving ERT, 22 answered “yes,” 18 answered “no,” 24 answered “either way” (meaning home infusion therapy or hospital visit), and 1 did not answer. Most of the patients who answered “yes” cited the reason as being a reduction in the burden of hospital visits. For patients who answered “no,” the reason cited was the safety of hospital treatment.

Regarding worry about COVID-19 infection among patients with FD, 40 patients were “very worried,” 27 were “somewhat worried,” 15 were “a little worried,” and 1 was “not worried at all.”

No significant correlation was found between the desire for vaccination and household situation (data not shown).

DISCUSSION

The present study of patients with FD found that the level of willingness to receive vaccines was high for 71 (85.5%; 56 had already received and 15 were willing to receive the vaccine) of 83 patients. This percentage was higher than the 70% among patients with chronic diseases who wanted to receive the vaccine in a survey conducted by Leading Tech in April 2021⁹.

The present survey of patients with FD revealed that their most common sources of information about COVID-19 were television, followed by the internet, family and friends, their physician, and newspapers, indicating that only 30% (25 of 83 patients) received information from physicians (Table 2). Similar results have been found by a study of patients with lysosomal storage diseases⁶, indicating that patients do not have access to their healthcare providers for seeking advice. If patients obtain information about vaccines from television or the internet, only side effects might be emphasized and efficacy might be left behind. Having patients refrain from vaccination as a result of such information is not desirable. If members of the medical staff were to ask patients directly if they had any questions rather than only waiting for patients to ask questions, they can be seen by patients as consulting partners who can provide appropriate information.

Having their lives changed as a result of the COVID-19

Table 2. Answers to questions

Have you been infected with COVID-19? (n=83)	
Yes	1 (1.2%)
No	82 (98.7%)
Have you received the vaccine against COVID-19? (n=83)	
Yes	56 (67.4%)
No	27 (32.5%)
Would you like to receive a vaccine against COVID-19? (Unvaccinated patients, n=27)	
Yes	15 (55.5%)
No	4 (14.8%)
Not determined	8 (29.6%)
What is your source of information about COVID-19? (multiple answers possible) (n=83)	
Television	71
Internet	44
Family/Friends	31
Newspaper	25
Physician	25
Social media	22
Radio	7
Other	4
Has your daily life been affected? (n=83)	
Yes	49 (59.0%)
No	34 (40.9%)
Have hospital visits been affected? (n=83)	
Yes	17 (20.4%)
No	65 (78.3%)
No answer	1 (1.2%)
Have you continued to receive treatment? (n=83)	
Yes	76 (91.5%)
No	0 (0.0%)
No answer including no treatment	7 (8.4%)
Would you like to receive home infusion therapy? (Patients receiving enzyme replacement therapy, n=65)	
Yes	22 (33.8%)
No	18 (27.6%)
Either way (hospital visit or home therapy)	24 (36.9%)
No answer	1 (1.5%)
How worried are you about COVID-19 infection? (n=83)	
Very worried	40 (48.1%)
Somewhat worried	27 (32.5%)
A little worried	15 (18.0%)
Not worried at all	1 (1.2%)

pandemic was reported in the present study by a percentage of patients (59%, 49 of 83 patients) which was lower than we expected. However, amongst the changes, “less chance to see people,” “less chance to go out,” and “effect on work” were not limited to patients with FD, whereas “physical and mental effects,” were reported by these patients and by patients with other underlying diseases¹⁰. The COVID-19 pandemic has caused patients with FD to live with worries about infection and serious illnesses and to

lose opportunities to relax owing to fewer chances to meet with others and leave their homes. As a result, patients with FD are under considerable mental stress. In fact, in the present survey, 2 patients stated having developed depression and anxiety neurosis. Thus, because of COVID-19, patients with FD have experienced a change in their lives and physical and mental health effects.

To the question “Have you continued to receive treatment?”, the answer of “yes” was given in the present

study by 91.5% of patients. However, we asked this question because some patients might have been able to continue treatment despite interruptions. In Poland, as in Japan, ERT is generally provided in hospitals, but 25% of patients with FD who received ERT had difficulty going to the hospital^{4,5}. However, in Turkey⁶, Italy⁷, and Israel¹¹, many patients who had received ERT in hospitals have reported the treatment being discontinued. In Japan, patients appear able to continue treatment despite having difficulty visiting the hospital. In Italy and other countries in which home infusion therapy is provided, treatment was interrupted for only 8 of 129 (11%) patients with FD⁸, suggesting that many patients who receive home infusion therapy are able to continue treatment.

In February 2021, home infusion therapy was approved in Japan for patients who could not visit hospitals. In the present survey of patients with FD, treatment was requested at home by 25 of all 83 patients (30.1%) and by 22 of 65 patients (33.8%) who were receiving ERT. Over all rate was lower than that reported overseas⁴ and lower than we expected. Perhaps home infusion therapy remains a subject of concern. However, as in the case of the COVID-19 pandemic, the future reduction of medical care is a strong possibility, and establishing a system that allows physicians and nurses to provide home infusion therapy is important⁵⁻⁷.

In a survey similar to ours by Wolf et al. about the degree to which 630 patients with chronic illnesses in the United States were worried about COVID-19 infection¹², 24% of patients were “very worried,” 39% were “somewhat worried,” 23% were “a little worried,” and 13% were “not worried at all.” Because the patients in that survey had an average age of 62.1 years, they were older than the patients with FD in the present study, who had a average age of 45.5 years in male and 54.3 years in female. In the study by Wolf et al¹², the underlying illnesses were heart disease in 24% of patients, lung disease in 25%, diabetes in 54%, and hypertension in 75.2%, and organ transplantation had been performed for 20% of patients. Although surveys cannot be easily compared owing to differences in period, method, and patient age, a possible reason “very worried” (48% of patients) was the most common answer in the present study is that patients with FD are more strongly worried about COVID-19 than are patients with other chronic diseases.

Limitations of this study

Because the present study did not use a face-to-face interview, whether the patients accurately understood the purpose of the questions is unclear. In addition, because we did not maintain a list of correspondence, we were not able to correlate survey data with clinical data. In addition, because the answers to the survey were subjective rather than objective, a possibility was bias.

CONCLUSION

The present study revealed that COVID-19 causes patients with FD to make changes in their lives and affects their hospital visits, treatment methods, and physical and mental health. Most of the patients of this study had a willingness to receive a COVID-19 vaccine, but the finding that most of their information about COVID-19 had been obtained through television and the internet suggests that they had few opportunities to be directly informed by medical personnel, who were not fully available to them as consultants. Few patients requested home infusion therapy, but most patients were able to continue treatment at hospitals as outpatients. Home nursing for ERT has increased in Europe and the United States, and a system to enable home infusion therapy might need to be established in Japan.

Acknowledgments : We would like to express our sincere gratitude to the Japanese Fabry Disease Patients and Family Association and its representative, Mr. Hisao Harada, for their cooperation in this study. We would also like to thank Editage (www.editage.com) for English language editing.

Conflict of Interest : Toya Ohashi is clinical advisor of JCR Pharmaceuticals. These activities have been fully disclosed and are managed under a Memorandum of Understanding with the Conflict-of-Interest Resolution Board of The Jikei University School of Medicine.

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