

Case Report

Onset of Oral Lichen Planus Led to Direct-Acting Antiviral Therapy in a Patient with Long-Term Hepatitis C: The Role of a Dentist as Gatekeeper

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Keywords

Oral lichen planus · Chronic hepatitis C · Hepatitis C virus · Direct-acting antivirals · Interferon

Abstract

Oral lichen planus (OLP), a chronic inflammatory mucocutaneous disease, is an extrahepatic manifestation of a hepatitis C virus infection. In recent years, direct-acting antivirals (DAAs) have made great strides in the treatment of hepatitis C. However, there might be a lack of information about the treatment strategies available among those with this condition. Herein, we report a case of an 85-year-old female patient who was diagnosed with hepatitis C at the age of 55 but had not received antiviral treatment over the past 30 years. She underwent DAA treatment following a recommendation from her oral surgeon after the onset of OLP. The patient had declined interferon therapy in the past, owing to concerns about its side effects. She was unaware of the benefits of DAA treatment, probably due to communication difficulties caused by senile hearing loss. Consultation with an oral surgeon for an erosive form of OLP led her to receive antiviral therapy for hepatitis C. She achieved a sustained virologic response (SVR) following the DAA treatment, along with improvements in the signs and symptoms of OLP. Oral surgeons play an important role as gatekeepers in guiding untreated hepatitis patients toward appropriate treatment.

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Introduction

Approximately 56.8 million people worldwide are persistently infected with hepatitis C virus (HCV), which is a significant cause of liver disease-related death [1]. In addition to liver disease, HCV infection is associated with the appearance of many extrahepatic manifestations, such as cryoglobulinemia, lymphoproliferative disorders, diabetes mellitus, and lichen planus [2, 3]. In recent years, treatment with interferon (IFN)-free direct-acting antivirals (DAAs) has gained popularity and demonstrated efficiency in eliminating HCV [4, 5]. The long-term benefits of eliminating HCV with DAAs have been demonstrated [6]; moreover, DAAs are reported to reduce the risk of developing extrahepatic manifestations [7].

The identification of untreated HCV-infected patients in Japan is challenging. Herein, we report a case of an 85-year-old female who was aware of being infected with HCV but was not treated for the condition for the past 30 years. A consultation with a dental surgeon led to a diagnosis of oral lichen planus (OLP), and appropriate treatment was recommended for both HCV infection and OLP. This study demonstrates that dentists play an important role as gatekeepers of hepatitis C treatment.

Case Presentation

An 85-year-old Japanese woman visited the Tsuji Dental and Oral Surgery Clinic on September 17, 2021, complaining of pain in her buccal mucosa. She had received dental treatment at her family dentist's office in April 2021, when the dentist first indicated the presence of OLP in the buccal mucosa. Subsequently, she complained of pain in the area while eating and was referred to our clinic by her family dentist. White lesions were found on the buccal mucosae, on both sides, along with erosions on the left buccal mucosa (Fig. 1). The lesions were clinically diagnosed as OLP by an oral surgeon. Beclomethasone dipropionate 50 µg was sprayed daily on the oral mucosa twice daily for pain relief.

The patient was diagnosed with hepatitis C after receiving a blood transfusion during a hysterectomy for uterine cancer at age 55. Consequently, she regularly visited a hospital with a full-time hepatologist for 30 years (from age 55 to 85) but did not receive antiviral therapy for the HCV infection. She was taking ursodeoxycholic acid once daily as anti-inflammatory therapy for several years. The patient was diagnosed with hypothyroidism at around 65 years of age and was taking levothyroxine sodium hydrate daily. Additionally, she was diagnosed with cholelithiasis and age-related hearing loss. She did not use a hearing aid and was able to communicate. No signs of dementia were observed.

IFN therapy was recommended to the patient by her hepatologist in the past. However, she refused the treatment due to concerns about the side effects; the reason for refusal of treatment was determined using a questionnaire, owing to the age-related hearing loss (Table 1).

DAA treatment for hepatitis C was introduced in Japan in 2014. The hepatologist had recommended this treatment to the patient several times in the past, but she did not accept antiviral therapy because she could not understand the physician's explanation due to hearing loss. The patient confided that she was aware that her hearing loss was interfering with her communication abilities; yet she pretended to be able to hear for years because she did not want to interrupt the flow of conversation in the doctor's office. She said that she "could not be bothered to ask the doctor to repeat" and "did not understand the technical terms used by the doctor."

During her first visit to our hospital, the patient and her family were informed that OLP is an oral potentially malignant disorder most likely caused by HCV infection and can be cured if

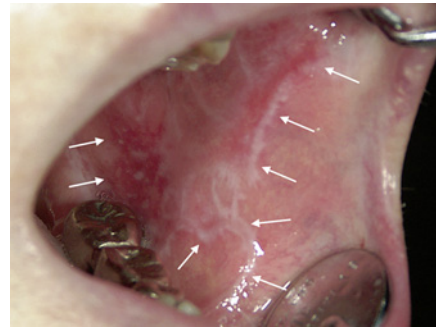


Fig. 1. Image showing lacy white striated lesions and erosions on the left buccal mucosa during the initial visit (September 17, 2021) (white arrows).

the virus is eliminated by antiviral therapy. She had little knowledge about the latest treatments for hepatitis C; hence, the benefits of IFN-free DAAs were explained, and treatment at a specialized facility was recommended. Consequently, DAA treatment (glecaprevir/pibrentasvir for 8 weeks) was started at a specialized medical facility on February 4, 2022, based on Japanese guidelines for the management of HCV infection, and the HCV RNA was undetectable within 4 weeks of treatment. Table 2 shows the results of the biochemical blood tests. The Japanese medical insurance system does not allow blood tests in dental clinics; therefore, the tests were performed at other hospitals. Improvements in OLP followed by the absence of pain were observed after starting the DAA treatment (Fig. 2). The use of beclomethasone dipropionate became almost unnecessary.

Discussion

Approximately 1–1.5 million people are estimated to be infected with HCV in Japan. Antiviral therapy using DAAs has fewer side effects and is more effective than the conventional IFN and ribavirin combination therapy [4, 5]. DAAs with very high SVR rates have dramatically improved the treatment of HCV, but the identification of potentially untreated HCV-infected patients remains challenging.

OLP is a chronic inflammatory disease and an oral potentially malignant disorder with signs of dyskeratosis. The prevalence of this disease is estimated to be about 1% of the general population [8]. Numerous associations between OLP and HCV infection have been reported in several meta-analyses; OLP patients were reported to have a 2.8–6-fold higher risk of HCV infection [9–12]. Our previous population epidemiology cohort study in a highly HCV-infected area of Japan (X town: the average positive rate of anti-HCV antibody among residents was 24%) showed that the prevalence of OLP was significantly higher among infected residents than among the uninfected residents, and it appeared to increase over time [13–15]. DAA treatment in HCV-infected OLP patients effectively cured the oral disease by eliminating the virus [16].

The patient had refused antiviral therapy for 30 years, despite being aware that she was infected with HCV. The main reason for the refusal was her concern about the side effects. Additionally, she declined DAA therapy, which has almost no known side effects, due to communication issues resulting from hearing loss. The development of pain due to OLP 3 decades after the HCV infection triggered the decision to receive DAA treatment.

IFN therapy was the standard of care for hepatitis C before the advent of DAAs. However, not all patients accept IFN treatment, even if they are eligible. In our previous study on the barriers to IFN treatment uptake, we used surveys to collect information from 254 pairs of HCV-infected patients and doctors from eight medical institutions in town X [17]. The factors influencing treatment acceptance or refusal among patients indicated for IFN treatment were as follows: the attending medical institution, gender, and presence of complications (odds

Table 1. Reasons why the patient declined IFN therapy despite the physician's recommendation

No.	List of reasons	Please select all reasons that apply	Please select one reason that most applies to you
1	Worried about the side effects	Yes	Yes
2	High cost	No	No
3	Seemed to be unnecessary because of being asymptomatic	No	No
4	Was busy	Yes	No
5	Was anxious	Yes	No
6	Did not want others to know about my illness	No	No
7	Did not seem appropriate due to my age	No	No
8	Did not seem to be urgent	No	No
9	Was reluctant to go to other hospitals or clinics	No	No
10	Was satisfied with current treatment	No	No
11	Family objection	No	No
12	Did not seem appropriate due to the presence of other illnesses	No	No
13	Seemed to be bothersome to go to clinics more often	No	No
14	Seemed to be ineffective	No	No
15	Did not like injection	No	No
16	Explanation by physicians was insufficient	No	No
17	Could not understand the explanation by physicians	Yes	No

IFN, interferon.

ratios of 18.06, 3.65, and 3.63, respectively). Concern about the side effects of the treatment was the main factor, and it was more common among women than men [17].

Hearing loss is a common problem among the elderly. It can cause communication difficulties and contribute to social isolation, depression, and dementia [18, 19]. A recent study, which analyzed data from another population-based longitudinal cohort study, reported that using a hearing aid can reduce cognitive decline [20]. According to the National Institute for Longevity Sciences-Longitudinal Study of Aging (NILS-LSA) conducted in Japan, the prevalence of hearing loss – defined as a good hearing level of ≥ 25 dB – increased dramatically among those aged 65 and older; approximately 16,553,000 people aged 65 and older experienced hearing loss in Japan [21]. Japan has a super-aging population, and age-related hearing loss is a national issue.

Previously, we reported similar case scenarios wherein patients were diagnosed with OLP by their dentists and referred for HCV treatment; the patients were unaware that they had been infected with the virus and uninformed about the standard treatment for HCV [22, 23]. Thus, medical professionals must be conscious of the fact that many patients, particularly older individuals, do not have adequate medical knowledge, probably due to poor communication.

In conclusion, this report presents the case of a hepatitis C patient who did not receive antiviral therapy for 30 years but accepted the treatment only after the onset of OLP. Dentists are expected to play a role in directing patients to receive specialized treatments at medical

Table 2. Summary of the clinical condition of the oral lesion and the laboratory data

	Normal range	One week after the first visit	Before DAA treatment	2 weeks during DAA treatment	SVR12	SVR24
Clinical condition of OLP		Presence	Presence	Improvement	Unknown	Improvement
Total protein, g/dL	6.6–8.1	7.1	6.9	6.8	Unknown	7.2
Albumin, g/dL	4.1–5.1	4.1	3.8	3.8	Unknown	3.7
AST, U/L	13–30	34	43	26	23	21
ALT, U/L	7–23	24	32	17	14	10
LDH, U/L	124–222	181	182	184	161	160
ALP, U/L	38–113	88	94	112	123	86
Gamma GTP, U/L	9–32	13	14	15	11	10
Total cholesterol, mg/dL	142–248	179	208	Unknown	Unknown	Unknown
LDL, mg/dL	65–163	83	92	Unknown	Unknown	Unknown
Triglyceride, mg/dL	30–117	69	76	Unknown	Unknown	Unknown
Total bilirubin, mg/dL	0.4–1.5	0.5	0.4	0.4	0.5	0.5
Cholinesterase, U/L	201–421	322	305	Unknown	Unknown	255
BUN, mg/dL	8–20	15	20	20	12	12
Creatinine, mg/dL	0.46–0.79	0.62	0.61	0.52	0.57	0.51
Na, nmol/L	138–145	143	143	143	143	140
K, nmol/L	3.6–4.8	4.7	4.6	4.6	4.0	3.9
Cl, nmol/L	101–108	107	105	103	106	104
CRP, mg/dL	0.00–0.14	<0.02	Unknown	Unknown	Unknown	Unknown
HBsAg	Negative	Negative				
AFP, ng/mL	0.0–10.0	2.7	4.0	Unknown	Unknown	Unknown
White blood cell, 10 ³ /μL	3.3–8.6	3.5	3.7	3.6	4.4	5.1
Red blood cell, 10 ⁶ /μL	3.86–4.92	4.06	4.08	4.20	4.29	3.81
Hemoglobin, g/dL	11.6–14.8	12.8	13.0	13.3	13.4	11.6
Hematocrit, %	35.1–44.4	39.1	39.7	41.2	41.1	35.8
Platelet count, 10 ³ /μL	158–348	153	173	160	144	175
Prothrombin time, international normalized ratio		0.98	0.89	0.97	Unknown	Unknown
HCV viral load, logIU/mL	Not detected		5.7		Not detected	Not detected
HCV serogroup			Unable to decide			

(Continued on following page)

Table 2. (continued)

	Normal range	One week after the first visit	Before DAA treatment	2 weeks during DAA treatment	SVR12	SVR24
TSH, $\mu\text{IU/mL}$	0.500–5.000	Unknown	5.580	Unknown	0.942	Unknown
FT4, ng/dL	0.90–1.70	Unknown	1.57	Unknown	1.14	Unknown

DAA, direct acting antiviral; SVR, sustained virological response; OLP, oral lichen planus; AST, aspartate aminotransferase; ALT, alanine aminotransferase; LDH, lactic dehydrogenase; ALP, alanine aminotransferase; gamma GTP, gamma glutamyl transpeptidase; LDL, low-density lipoprotein; BUN, blood urea nitrogen; Na, sodium; K, potassium; Cl, chloride; HBsAg, hepatitis B surface antigen; AFP, alpha fetoprotein; HCV, hepatitis C virus; TSH, thyroid stimulating hormone; FT4, free thyroxine 4.



Fig. 2. The white lesions in the left buccal mucosa had reduced after DAA treatment (May 13, 2022) (white arrows).

institutions by utilizing their expertise. It should be emphasized that a multidisciplinary approach by dentists and hepatologists can helpfully treat untreated HCV-infected patients. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see www.karger.com/doi/10.1159/000528681).

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Statement of Ethics

Ethical approval for the publication of a case report exclusively for the prevention and diagnosis or treatment of an injury or disease is not required in accordance with national guidelines. Written informed consent was obtained from the patient for the publication of this case report and accompanying images. This research work complied with the guidelines for human studies and was conducted ethically in accordance with the World Medical Association Declaration of Helsinki.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Yumiko Nagao: follow-up of the patient's clinical course, conception, design, analysis and interpretation of data, drafting and revising the article, and final approval. Masahide Tsuji: concept, design, analysis and interpretation of data, drafting and revising the article, and final approval.

Data Availability Statement

All data generated or analyzed during this study are included in this published article and its online supplementary material.

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