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Case Report

Evolution of Necrotizing Periodontitis in a Patient with Multiple Sclerosis

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Abstract: Multiple sclerosis (MS) and necrotizing periodontitis (NP) are two diseases whose aetiology and pathophysiology do not seem to have a common link; however, the treatment of MS with monoclonal antibodies and the decrease in humoral immunity that this entails can be a trigger or an aggravation in patients who present NP. We present a clinical case of NP in which its clinical manifestations, treatment and evolution during therapy with ocrelizumab are reflected. During the evolution of the case, a rapid progression of NP was evidenced. During her evolution, the patient suffered bilateral pneumonia due to COVID requiring treatment with corticosteroids and antibiotics, which led to clinical relief of her NP. Given this important clinical finding, we consider of great interest the regulated dental monitoring of those patients with MS before, during and after the administration of monoclonal antibodies to prevent periodontal deterioration.

Keywords: periodontitis; periodontal disease; necrotizing periodontitis; periodontal treatment; multiple sclerosis; relapsing-remitting multiple sclerosis

1. Introduction

Multiple sclerosis (MS) is an inflammatory and neurodegenerative autoimmune disease of the central nervous system (CNS). Immunomodulators and immunosuppressants are used in its treatment. Ocrelizumab is a humanized monoclonal antibody against the CD20 antigen of B cells, and among its side effects, a significant increase in infections has been described [1]. Necrotizing periodontitis (NP) is a periodontal infection that causes necrosis and ulceration of the interdental papilla, gingival bleeding, pain, pseudomembrane formation, halitosis, loss of periodontal attachment and bone destruction [2]. It is an infectious condition with predisposing factors in which the immune response of the host plays a fundamental role [3].

2. Case Presentation

A 28-year-old woman (March 2021) was diagnosed with relapsing-remitting multiple sclerosis (RR-MS) in 2018 and began treatment with monoclonal antibodies (ocrelizumab) in November 2019. Among her medical history, it stands out that she smokes 10 cigarettes a day, is a social drinker on weekends, and is allergic to coconut. The patient is wearing an occlusal discharge splint.

During home confinement in Spain due to the COVID-19 pandemic (March-May 2020), the patient reported an acute outbreak of gingival pain with bleeding, as well as generalized discomfort, alleviated with the use of chlorhexidine digluconate mouthwash for two weeks. After confinement (May 2020), the patient returned to the dentist for her usual consultation and underwent a scale-out and a panoramic radiograph (Figure 1). In November 2020, she was administered a dose of ocrelizumab. A few weeks later, she reported a new outbreak accompanied by the loss of papillae and intense gingival pain.

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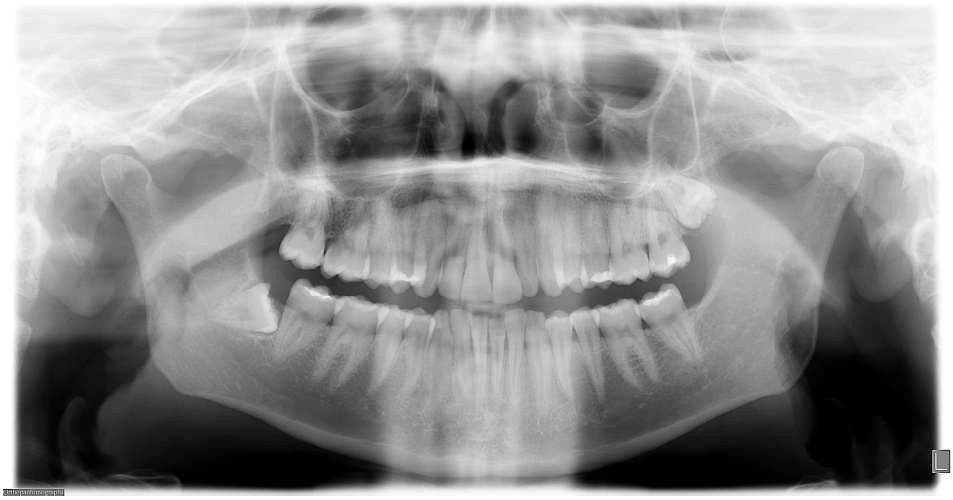

Figure 1. OPG May 2020.

In April 2021, after performing cytometry, the population of CD19/CD20+ B lymphocytes was 0%. This percentage reflects profound humoral immunosuppression, indicating on the one hand the effectiveness of the treatment administered and on the other hand the predisposition to bacterial infections.

In May 2021, the patient's medical records were sent to us for review. New records were made with an intraoral photographic study, a new panoramic radiograph (Figure 2) and a periodontogram format of Spanish Society of Periodontology and Osseointegration (SEPA) format, (Figure 3). The patient presented migration and fanning of the lower incisors due to thrust. The study of the occlusion did not show interferences or prematurity. The patient reported pain, and the exploration showed loss of insertion and recessions in the upper and lower incisors (Figures 4-9).

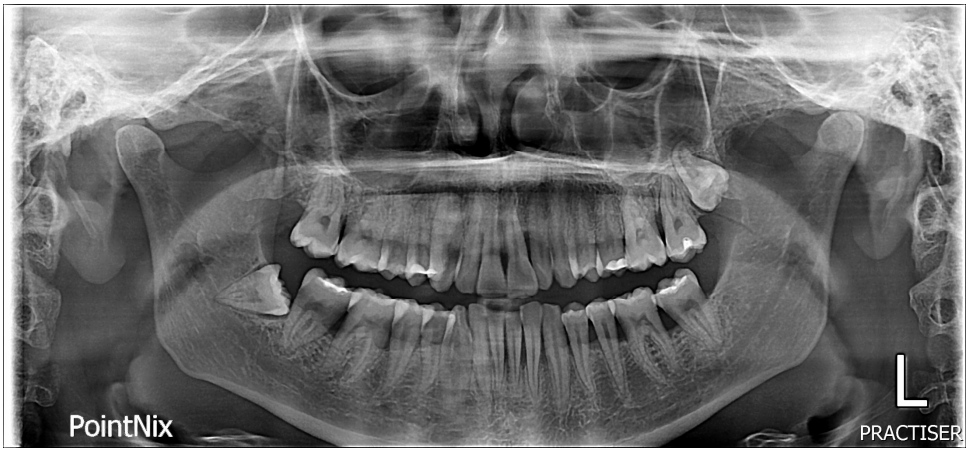

Figure 2. OPG May 2021.

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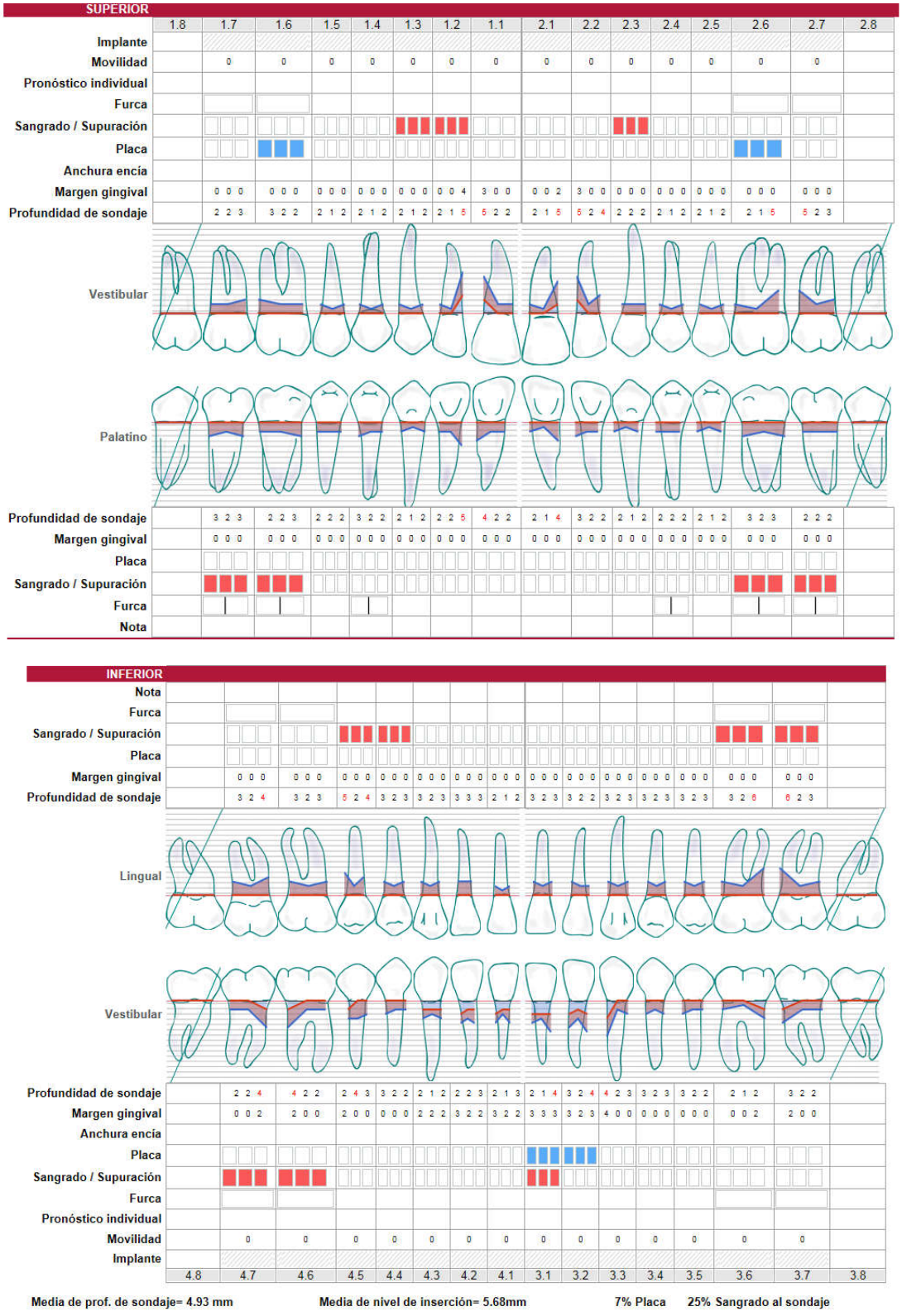

Figure 3. SEPA Periodontogram.

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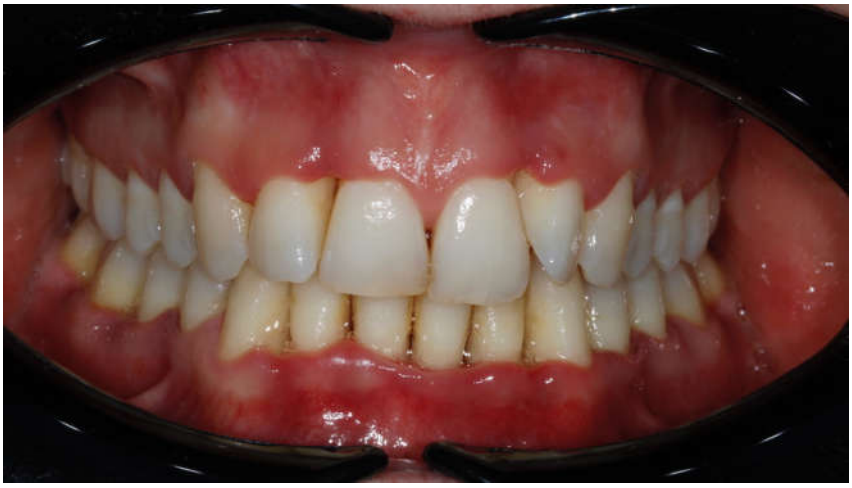

Figure 4. May 2021 intraoral photographic study (frontal view).

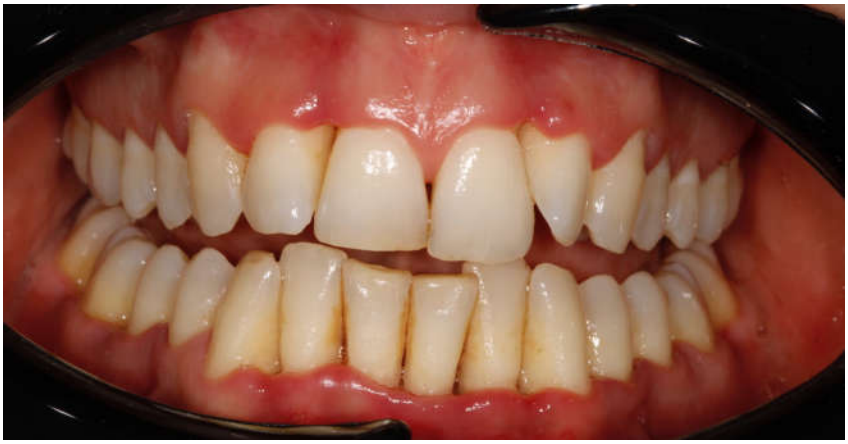

Figure 5. May 2021 intraoral photographic study (protrusive view).

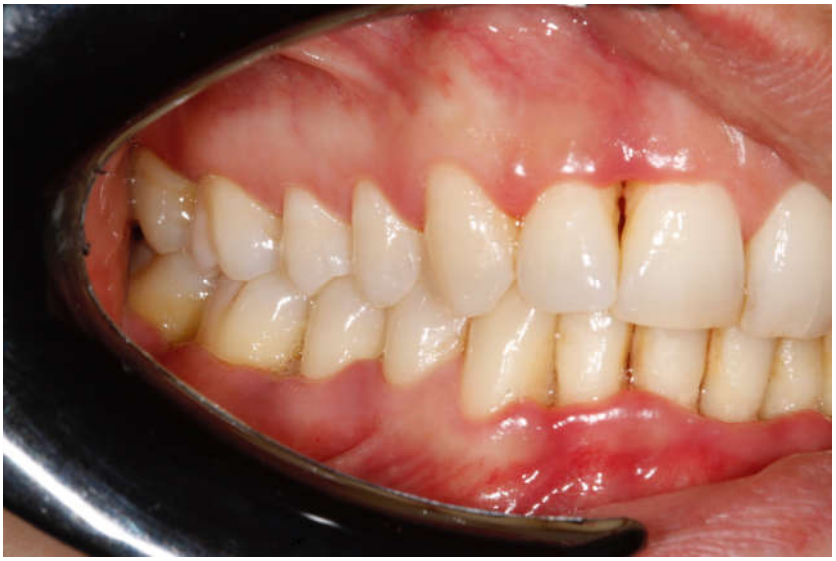

Figure 6. May 2021 intraoral photographic study (right side).

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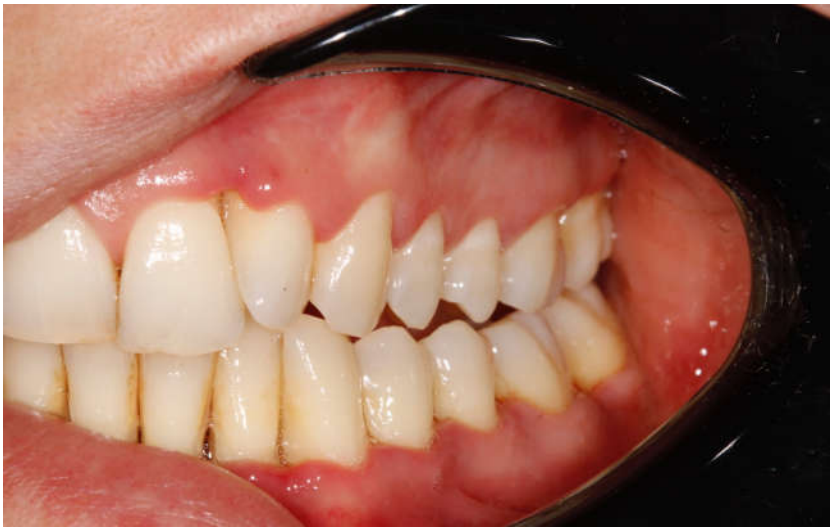

Figure 7. May 2021 intraoral photographic study (left lateral).

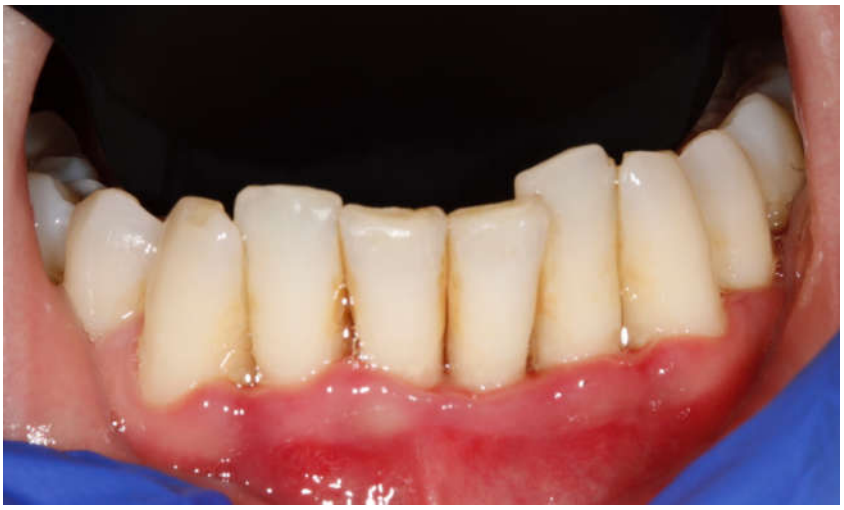

Figure 8. May 2021 intraoral photographic study (detail of the lower incisors with decapitation of the papillae).

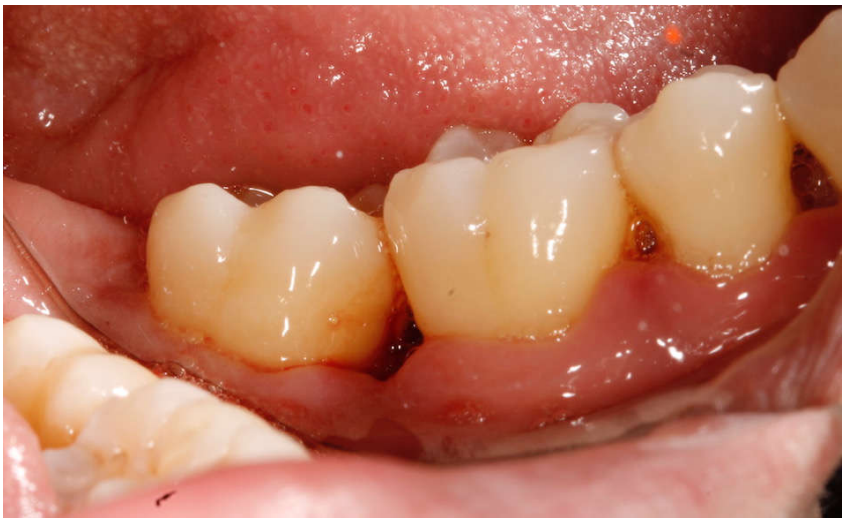

Figure 9. May 2021 intraoral photographic study (detail of lower left molars with decapitation of the papillae).

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The results of the microbiological study indicate the presence of Prevotella intermedia and Tannerella forsythia (Figures 10 and 11). Both are microbes frequently associated with periodontitis.

RESULTADO DEL ANÁLISIS CUANTITATIVO DE BACTERIAS POR qPCR-TIEMPO REAL

	Número de bacterias	Grado de patogeneicidad
Aggregatibacter actinomycetemcomitans (Aa)	0	Ausente
Tannerella forsythia (Tf)	538.954	Alto
Porphyromonas gingivalis (Pg)	0	Ausente
Treponema denticola (Td)	0	Ausente
Prevotella intermedia (Pi)	473.945.352	Alto
Campylobacter rectus (Cr)	0	Ausente

Figure 10. Microbiological examination results.

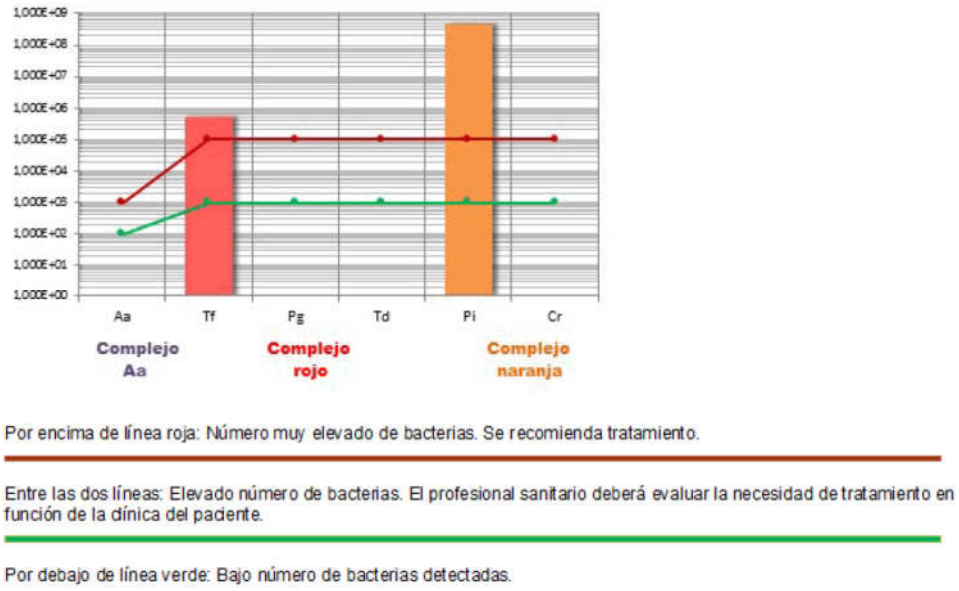

Figure 11. Graph showing the proportions of Tannerella forsythia and Prevotella intermedia present in periodontal pockets.

Table 1 shows the summary of the patient's clinical history.

Despite the cultures, because the patient was scheduled to receive a new dose of ocrelizumab (May 2021), it was advisable to allow 4-6 weeks before continuing with her periodontal treatment due to possible immunosuppression. Ten days after administration of ocrelizumab, a new outbreak with severe gingival pain was reported, presenting ulcerative lesions in 3.6 and 3.7 and lower incisors. At this time, the patient began treatment for smoking cessation. Rinses with 0.12% chlorhexidine digluconate, reinforcement of hygiene techniques and oral irrigators were prescribed.

In June 2021, periodontal treatment for hemiarchies was resumed, leaving a separation of one week between both appointments. The rinses were maintained with 0.12% chlorhexidine digluconate every 12 hours for 15 days followed by rinses with a mouthwash of panthenol, cetylpyridine chloride and zinc lactate. One month after the last session of subgingival instrumentation, a periodontogram of control was conducted in which

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an average probing depth of 3.74 mm, an average insertion level of 4.64 mm and 7% bleeding on probing was observed. The data are summarized in Table 2.

Table 1. Outline of key clinical events.

March-May 2020		COVID-19 pandemic confinement
May 2020		OPG Tartrectomy in your dental centre
November 2020		Ocrelizumab dose
December 2020		Gingival pain and perception of embrasures
March 2021		1st visit
April 2021		Analytical
May 2021	4	Periodontogram Microbiological study OPG
	14	Ocrelizumab dose
	25	Gingival pain Ulcerative periodontal lesions in 3.6-3.7 and in the anteroinferior front Tobacco cessation
June 2021	2 sessions of subgingival instrumentation Chlorhexidine digluconate 0.12% Oral irrigator	
July 2021	Periodontogram Analytical	
August 2021	COVID vaccine (Pfizer)	
September 2021	9	Gingival pain Periodontal lesions ulcerative
	21	Periodontogram OPG
October 2021	Periodontal maintenance	
November 2021		Third dose vaccine (Pfizer)
	19	Ocrelizumab dose
	28	COVID +
December 2021	14	Hospital admission, bilateral pneumonia, antibiotics, methylprednisolone, oxygen and NSAIDs
January 2022	5	Hospital discharge
	11	Periodontal review, OPG
	24	Periodontogram Periodontal maintenance
March 2022	10	COVID + treatment with Remdesivir
	22	Periodontal review

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Table 2. Summary of periodontal data.

	Mean probing depth	Mean insertion level	Plaque index	Bleeding index
May 2021	4.93 mm	5.68 mm	7%	25%
July 2021	3.74 mm	4.64 mm	2%	7%
September 2021	2.98 mm	4.72 mm	2%	3%
January 2022	2.95 mm	3.55 mm	8%	3%

In July 2021, a new analysis was performed (July 2021) where the lymphocyte populations were analysed and where the levels of CD3/CD4+ in the normal range were observed, which would indicate that the cellular immunity of the patient was preserved.

In September 2021, the patient presented a new outbreak of pain in the lower molar area. After the second dose of the COVID vaccine (Pfizer), she suffered a pseudo-outbreak of MS with loss of vision in the left eye and paresthesia in the left hand lasting less than 24 hours. The patient reported that during the summer, her daily habits were unstructured, with less oral hygiene and greater social activity. She presented with canker sores in the jugal mucosa and in the interproximal area of lower molars (Figure 12). Tooth polishing was performed with a brush and prophylaxis paste and rinsed with 0.12% chlorhexidine digluconate.

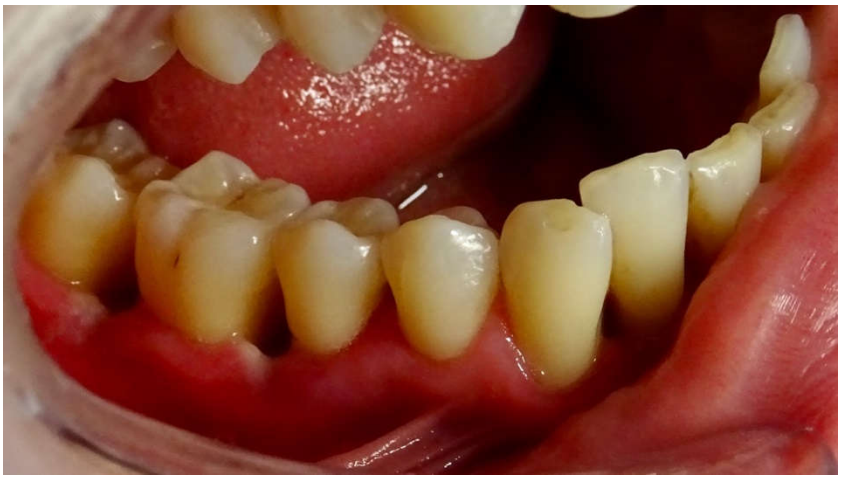

Figure 12. Decapitation of the interproximal papillae of the lower molars.

Fifteen days later (September 2021), a new periodontogram and panoramic radiograph were performed (Figure 13), which detected greater bone loss in the areas of 2.6-2.7, 3.6-3.7 and 4.6-4.7 compared to the one performed 5 months before.

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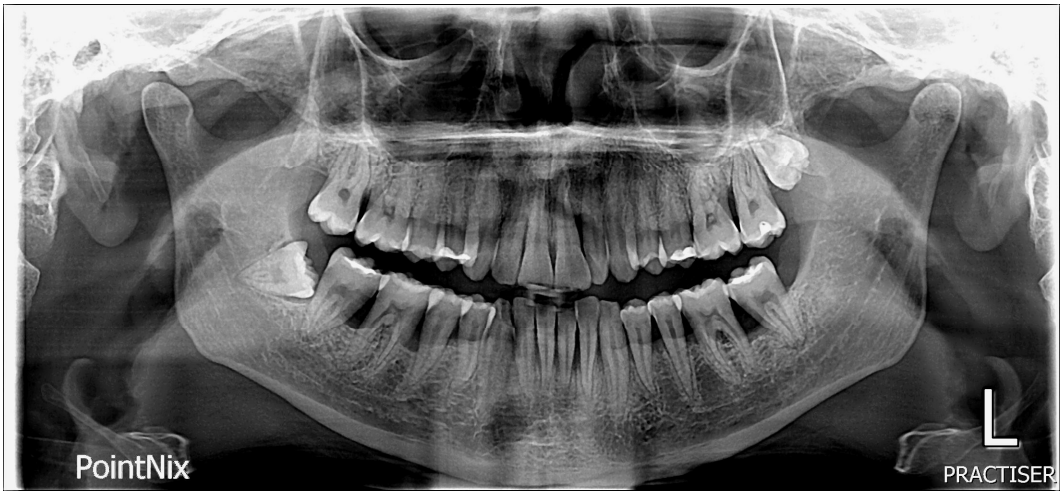

Figure 13. OPG September 2021.

One week later, the patient presented a new outbreak with gingival pain in the interproximal area of the lower molars. During this time, the patient commented that she had been under a lot of stress with irregular rest periods (Figures 14 and 15).

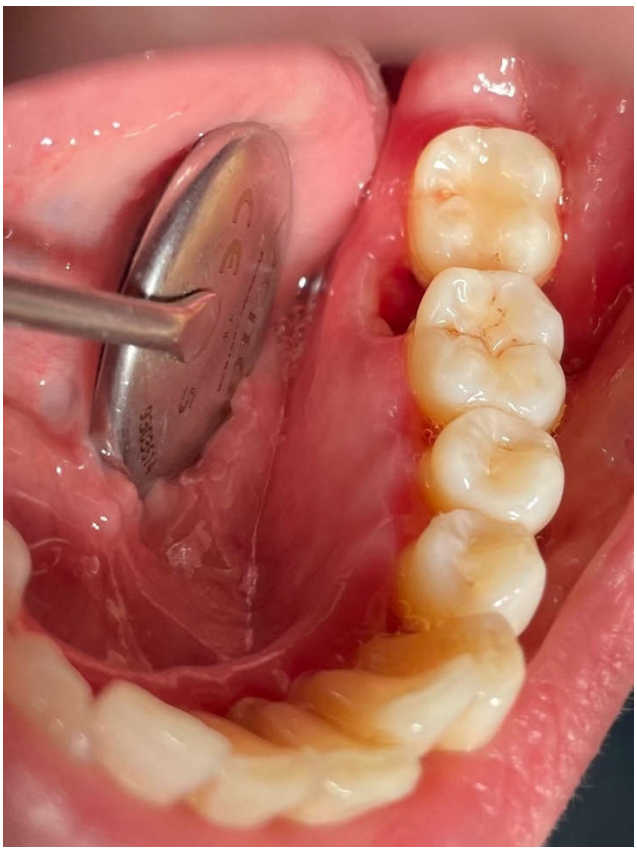

Figure 14. New outbreak affecting the interproximal area of the lower incisives.

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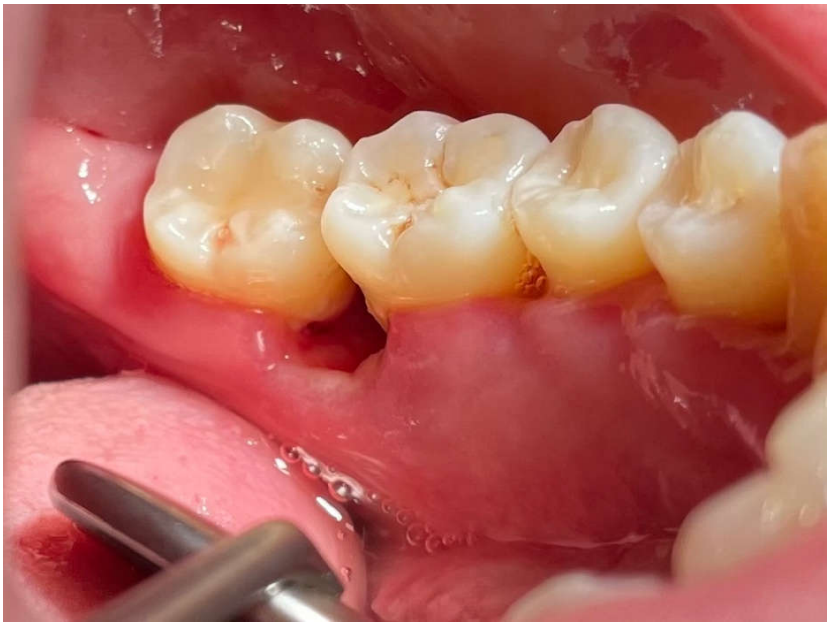

Figure 15. New outbreak affecting the interproximal area of the lower molars.

On November 19, she received a new dose of ocrelizumab. Although the patient had received a third dose of COVID-19 vaccine, she was exhibiting COVID-19 symptoms, and on day 24, a positive diagnosis of COVID-19 was confirmed. The patient reported general discomfort that improved over the course of a week. However, on December 7, there was a worsening associated with the onset of fever (38.5°), chills and dyspnoea. The patient was hospitalized following a diagnosis with bilateral pneumonia due to COVID-19 in an immunocompromised patient (Figure 16). She was treated with azithromycin 500 mg, methylprednisolone, oxygen and nonsteroidal anti-inflammatory drugs (NSAIDs) and was discharged on January 5, 2022.

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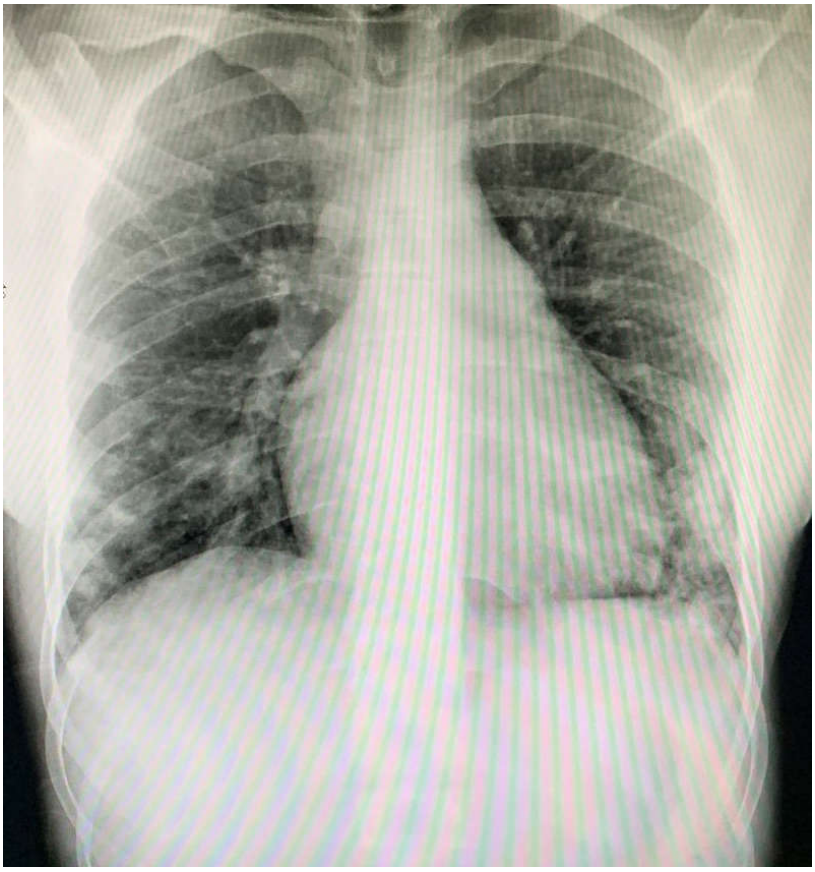

Figure 16. Chest X-ray showing bilateral pneumonia due to COVID-19.

On January 11, her gingiva had a coral pink colour with orange peel stippling due to the total absence of oedema and gingival ulcerative lesions, which were compatible with gingival health. New intraoral photographs were taken, a new periodontogram and panoramic radiograph were conducted, and a periodontal maintenance session was given (Figures 17-21).

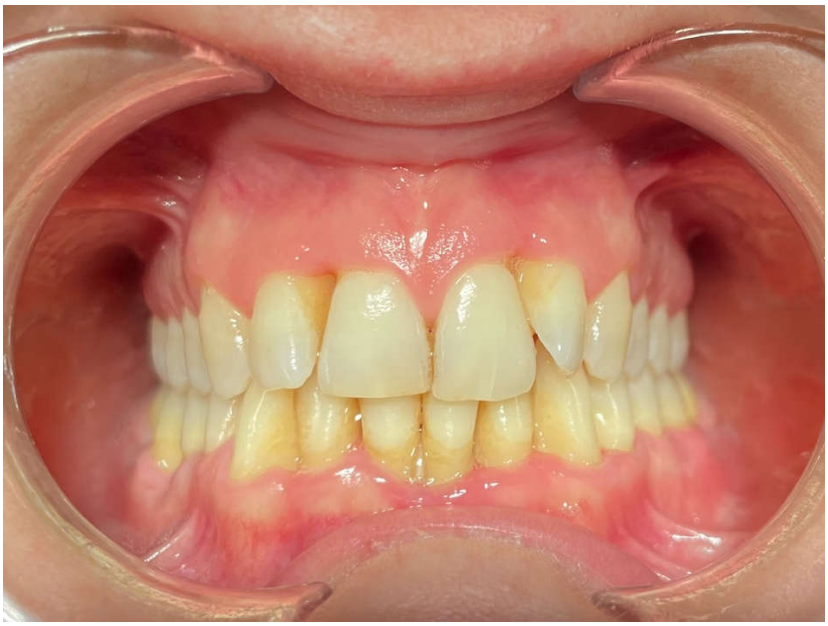

Figure 17. January 11 Intra-oral photographs (frontal view).

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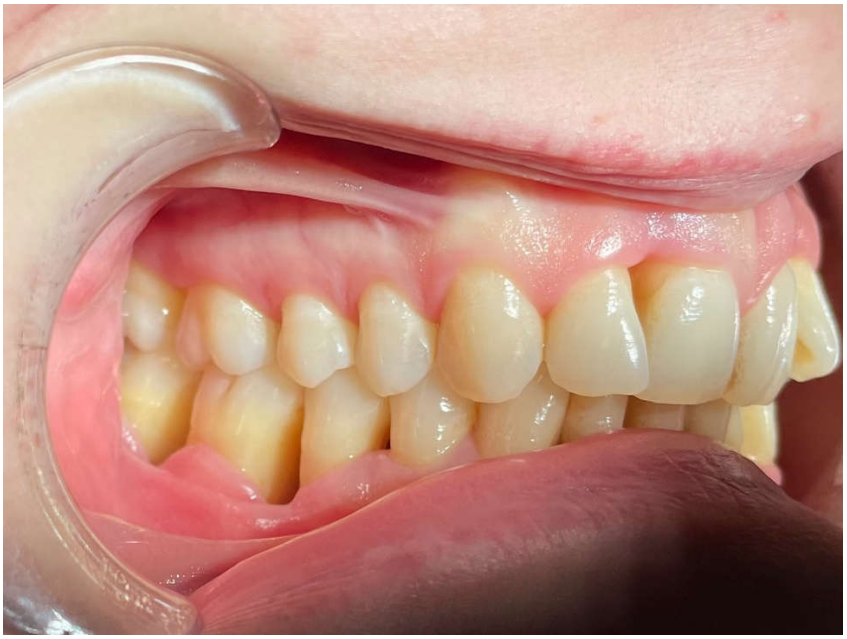

Figure 18. January 11 Intraoral photographs (right lateral view).

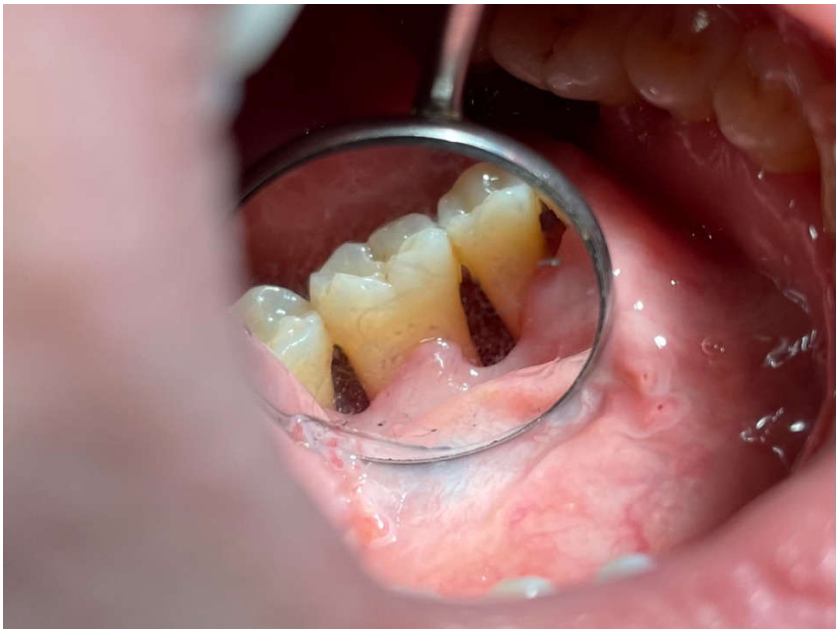

Figure 19. January 11 Intraoral photographs (right lateral lingual view).

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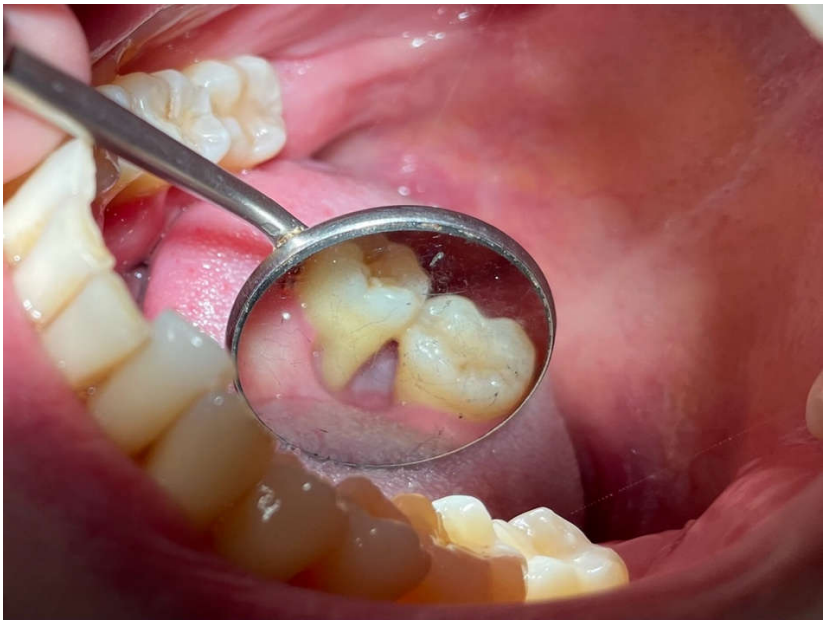

Figure 20. January 11 January 11 Intraoral photographs (left lateral lingual view).

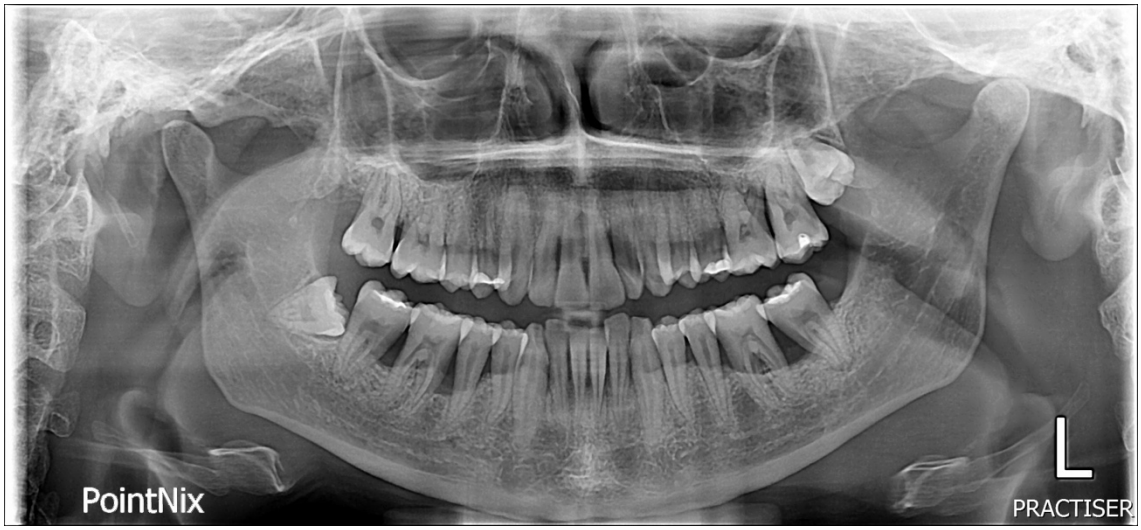

Figure 21. OPG January 2022.

The evolution of the periodontal parameters (periodontograms performed by the same explorer) is shown in Table 2.

In March, the patient was again diagnosed with COVID-19. She had mild symptoms and was treated with three doses of remdesivir. A few days after being discharged, a new periodontal review was performed, the results of which were similar to the previous exam.

3. Discussion

The physical sequelae and the progressive deterioration produced by MS may imply greater difficulty in performing proper oral hygiene or in accessing adequate oral care. The medication used for its treatment (immunomodulators) and to alleviate its symptoms (corticosteroids) can have effects on the oral mucosa (xerostomia, gingival hyperplasia, mucositis, thrush, dysgeusia, candidiasis or angular cheilitis), which potentially contributes to worse oral health [4]. Cockburn et al. [5] indicated that up to 18 oral problems related to the drugs used have been described. In addition to favouring the appearance of opportunistic infections.

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In the case of periodontitis, it has been suggested that because both MS and periodontitis have an inflammatory basis, there could be some association between both diseases [6]. However, Gustavsen et al. [7] indicated that they did not find a significant association between the two after adjusting for smoking habits in their study, while Sheu and Lin [8] found evidence of this association in women but not in men. Hatipoglu et al. [9] found higher values in the plaque index, probing depth and gingival index in patients with high physical disability than in patients with low disability.

In the case of monoclonal antibody therapy, and more specifically in the case of natalizumab (Tsyabri), Zhang and Meng [10] indicate that possible oral complications after its use include mucositis, thrush, headache and risk of opportunistic infections (fungal, viral orand bacterial).

Necrotizing periodontal diseases (NPD) are infectious conditions with predisposing factors in which the immune response of the host plays a fundamental role. Both periods of psychological stress and situations of immunosuppression are predisposing factors for the worsening of the disease [5]. The first analysis showed profound humoral immunosuppression (population of CD19/CD20+ B lymphocytes of 0%), while the second analysis showed CD3/CD4+ in the normal range, which would indicate that the cellular immunity of the patient was preserved.

In the course of anamnesis, the patient indicated how she began to perceive a worsening of her oral health during home confinement due to COVID-19. This situation produced an increase in the level of emotional stress, as she was unable to leave the house and could not carry out her daily activities. Psychological stress affects human immune function [11], which leads to an increased risk of infections or their progression. Burtscher et al. [12] found that the isolation of people in combination with the fear of contagion and quarantine, as well as a possible information overload, caused chronic stress and was associated with adverse effects on mental health. Thus, the patient's perception of a worsening of her periodontal state during home confinement could be related to the degree of stress she felt and could have contributed to worsening the degree of immunosuppression she already had due to the medication she was taking.

This is the first time that an NP has been described in the course of RR-MS treatment. We have found that this NP is linked to treatment with immunomodulators, which cause a significant decrease in humoral immunity. This case highlights the need for an oral care protocol in those patients who will receive immunomodulation.

To prevent patients with RR-MS from suffering an outbreak of NP, we recommend a periodontal study prior to the start of treatment, a risk assessment, and motivation and reinforcement of oral hygiene measures. Likewise, a maintenance periodontal therapy program should be established with reviews prior to immunomodulatory treatment.

4. Conclusion

Given the possible relationship between the immunomodulation of patients affected by RR-MS and the risk of presenting an NP, we recommend an evaluation and dental follow-up of patients with MS before, during and after the administration of monoclonal antibodies.

Author Contributions: Conceptualization, JMMC. and ASP; methodology, JMMC and ASP.; software, AJG.; validation, AJG and MJMV.; formal analysis, ASP and JMMC.; investigation, JMMC.; resources, JMMC; data curation, ASP and AJG.; writing—original draft preparation, JMMC and MJMV; writing—review and editing, ASP and AJG.; visualization, AJG., ASP., and MJMV.; supervision, ASP.; project administration, ASP. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki. As this is a clinical case description, approval by the ethics committee was not required. The patient agreed to have his clinical data presented.

Informed Consent Statement: Informed consent was obtained from subject involved in the study

Data Availability Statement: All data are available on request by mail to the author of the correspondence arturosa@um.es, after anonymisation of the identification data.

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Conflicts of Interest: The authors declare no conflict of interest.

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