

Treatment of a case of atrophic-erosive lichen planus refractory to topical corticosteroid with endoret-PRGF and rehabilitation with dental implants

Eduardo Anitua DDS, MD, PhD, Spain

Introduction

Oral lichen planus is a chronic inflammatory mucocutaneous disease that generally affects the skin and oral mucosa.^{1,2} It was first described by Erasmus Wilson in 1869 and is the most frequent non-infectious pathology of the oral cavity with a reported prevalence of 2% of the adult population.^{3,4} It is more frequent in adults and its etiology remains unknown, although its pathogenesis involves autoimmune phenomena mediated by CD8+ lymphocytes, mainly epithelial, which trigger a series of events that lead to necrosis of the basal keratinocytes, mainly through tumor necrosis factor (TNF-alpha).^{8,9} Finally, this condition of the basal keratinocytes generates hyperkeratosis (with orthokeratosis

or parakeratosis) and/or epithelial atrophy.³⁻¹² Several factors have been described that could contribute to the onset, perpetuation or worsening of lichen planus lesions, which classically occurs in outbreaks with periods of remission or latency. These factors can be grouped into local factors (mechanical, prosthetic, metals in contact with the oral mucosa), chemical factors (tobacco and alcohol), drugs (antimalarials, antihypertensives, nonsteroidal anti-inflammatory drugs, diuretics...), and systemic diseases (anxiety, diabetes, hypertension), as well as some connection with certain viruses such as hepatitis C and human papilloma virus.¹⁰⁻¹⁶

In the oral cavity, six clinical forms of LP have been classically described: white forms (reticular, papular and plaque) and red forms (erosive, atrophic-erythematous and bullous).¹⁷ The skin



Figs. 1–6: Clinical images of the patient upon arrival at the clinic, showing different areas with high involvement of the OLP with deep ulcerations that prevent the patient from maintaining conventional hygiene.

lesions usually appear as pruritic purple papules or purple plaques. They are usually located in the flexural areas of the arms and legs, as well as on the nails and scalp.^{19,20} About 30-50% of patients with oral lesions have associated skin disorders, with oral involvement being more frequent (90% of cases of lichen planus).^{20,21} The treatment of choice for OLP is topical corticosteroids due to their ability to modulate the inflammatory response and curb the immune response, in addition to their easy handling by the professionals who usually treat this pathology.^{8,22} Within this pharmacological group, there are different options in terms of the type of corticosteroid (mainly triamcinolone acetonide, fluamcinolone acetonide, clobetasol propionate and betamethasone), the formulation (orabase, aqueous solution and oily ointment), the daily regimen to be used and the period of maintenance of the corticosteroid.²³⁻²⁷ Studies comparing the efficacy of some corticosteroids with others have obtained very different results, and there is no clear recommendation as to which type of corticosteroid is more effective than another, nor are there any clinical practice guidelines that advise on treatment doses and drug maintenance time.²⁶⁻²⁸

Apart from corticosteroids, other immunomodulatory agents have been used for the topical treatment of OLP. The most used are cyclosporine, tacrolimus, pimecrolimus and retinoid.¹⁰ Cyclosporine is mainly used in oral solution (50–1,500 mg/day) or in orabase (26–48 mg/day), although it has not been shown to have a greater effect than corticoids, being its side effects greater than those of corticosteroids.^{10,29-31}

Finally, for cases refractory to conventional treatments, different options have been described, such as thalidomide, 308 nm UVB excimer laser, biological agents such as efalizumab or azathioprine, extracorporeal photochemotherapy, Dapsone, mycophenolate mofetil and hydrochloroquine.³²⁻⁴⁸

All treatments for the most refractory cases achieve some degree of remission, although the drugs used sometimes generate many side effects and there are no large case series demonstrating that one of the treatments achieves high efficacy. In this regard, our study group has published series of cases presenting erosive oral lichen planus, with a multitude of lesions, refractory to conventional treatment and to subsequent alternatives with greater side effects that have been treated with PRGF-Endoret infiltrations with good results.⁴⁹⁻⁵¹ This technology has also been tested in other autoimmune pathologies, in which ulcer-like lesions are produced in the oral cavity that are resistant to treatment, as in the case of pemphigoid, also with good results.⁵² Similarly, our study group has also described a surgical and prosthetic protocol to achieve successful long-term implant-supported rehabilitations in this type of patients, with minimally invasive techniques and prostheses that do not generate any type of tissue reaction upon contact with soft tissue.

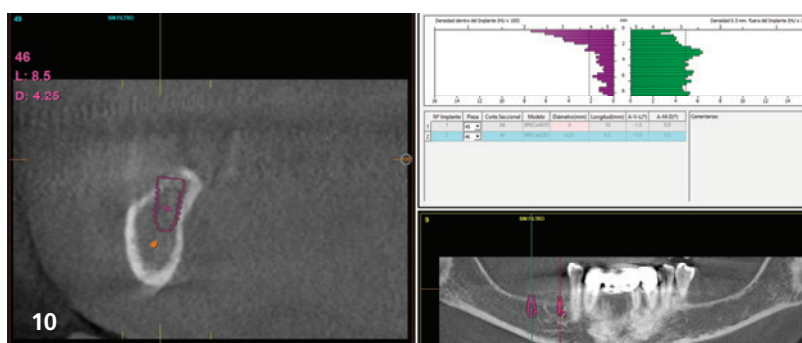
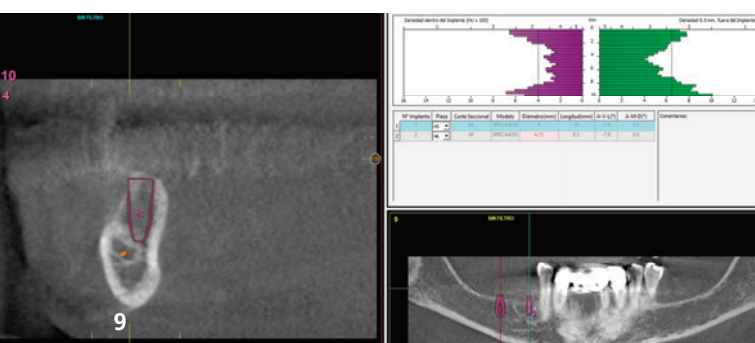
This case report shows a case treated with PRGF-Endoret to resolve recurrent oral lichen planus lesions refractory to conventional treatment, as well as the step-by-step rehabilitation process with dental implants.



Fig. 7: Images of the patient after the first course of topical corticosteroid, extraction of teeth with high mobility and periodontal maintenance. **Fig. 8:** Three months after the first OLP treatment and preparation of the anterior bridge. A remnant of gingival inflammation can be observed, which makes the patient unable to maintain proper plaque control.

Clinical case

A 65-year-old female patient came to our clinic requesting treatment for an atrophic-erosive oral lichen planus (OLP), diagnosed several months ago in another clinic, which causes intense oral lesions that do not allow proper hygiene and generate pain related problems. The patient also reported that several teeth are loose with abundant bleeding and a solution is being sought for these areas. In the initial examination, an erosive lichen planus with extensive gingival involvement was observed, which prevented the patient from performing proper hygiene with a high inflammatory component and several erosive lesions in the jugal mucosa and tongue (Figs. 1–6). The patient was first treated for oral lichen planus with the usual treatment of topical corticosteroids, using a rinse of triamcinolone acetonide 0.5% in aqueous oral solution together with nystatin 100,000 IU per milliliter. This rinse was performed for 10 minutes, with a dose of 10 milliliters, once a day (at night, before going to sleep) for one month at full dose and then lowered to half dose the following 15 days and another 15 days with half dose every other day. Subsequently, the product was discontinued, and a basic periodontal treatment was carried out with extraction of the teeth with high attachment loss, taking advantage of a decrease in



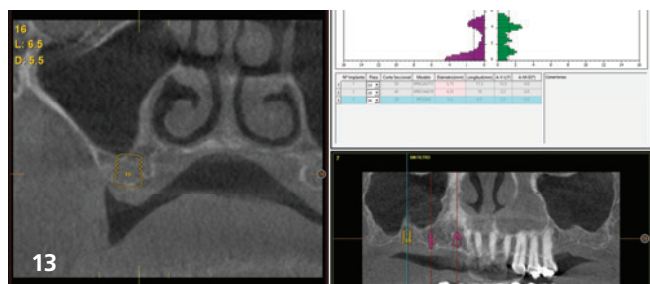
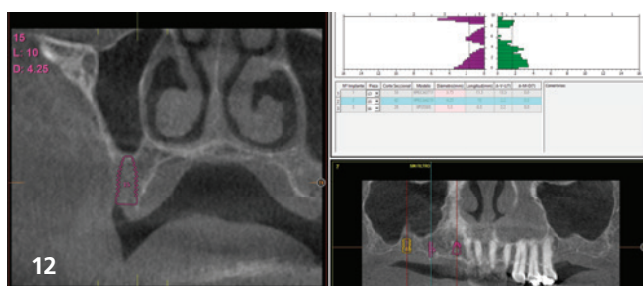
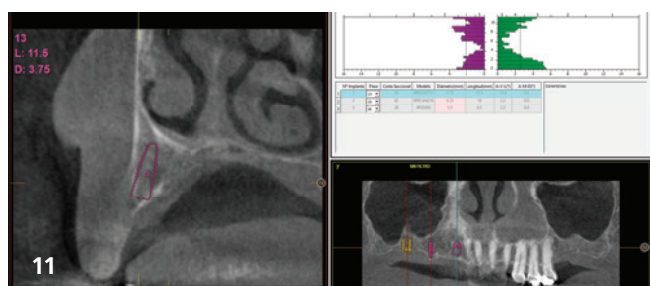
Figs. 9 & 10: Images of the planning of the fourth quadrant where the planned implants can be observed.

OLP symptoms (Fig. 7). At this stage the patient was able to maintain a low degree of inflammation and the restoration of the missing teeth was considered. The first phase involved making a conventional bridge on a natural tooth in the anterior-inferior area and continuing with the check-ups. Inflammation and erosive wounds were reduced in the first two months, but the patient continued to have gingival injuries that made it difficult for her to maintain proper oral hygiene (Fig. 8).

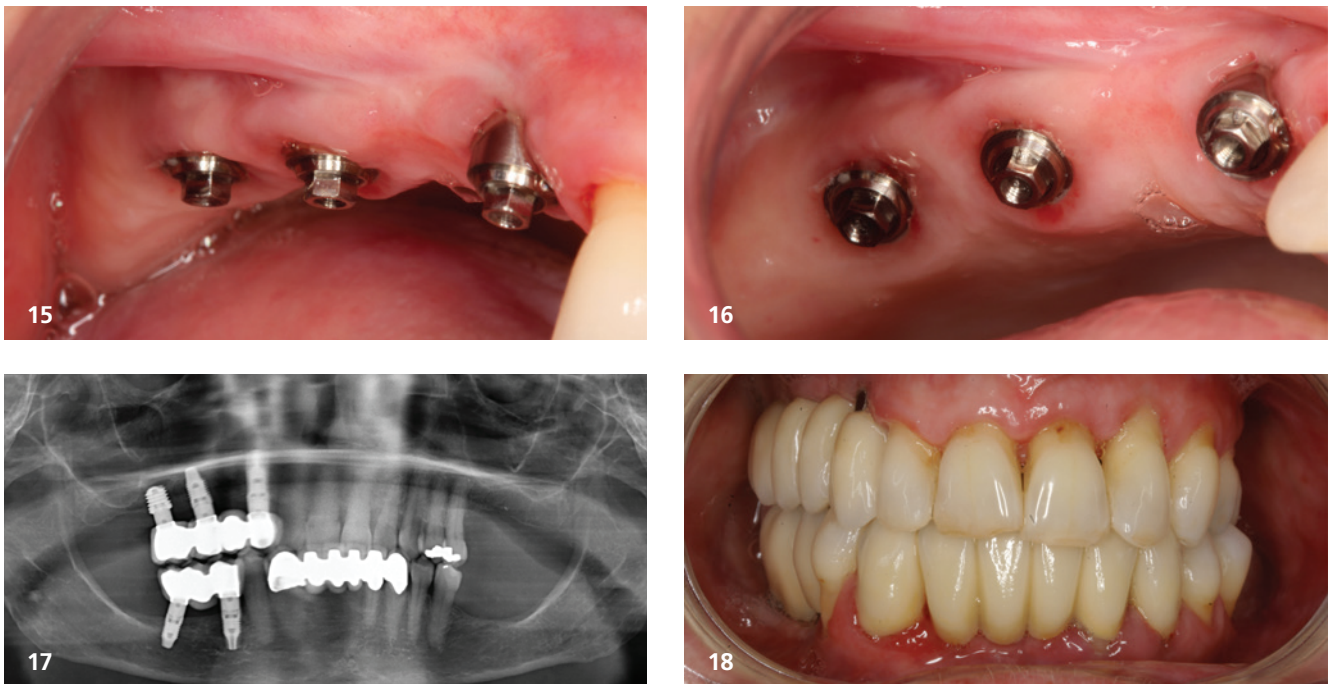
With the clinical picture of OLP under control, although not completely asymptomatic, the radiological diagnosis for the replacement of posterior teeth was performed. At the patient's request, the first and fourth quadrants were reconstructed, leaving the second and third quadrants as they were after periodontal treatment. The upper and lower sections were analysed, planning narrow platform implants in four of the five implants to be inserted, with the most distal implant in the first quadrant being a short implant of larger diameter (Figs. 9–13). In most patients in general, the lesser the surgical trauma, the lesser the consequences of our act, both at that moment and

in the long term, since, if in the future the reversibility of the treatment should be necessary, with a lesser occupation of the bone bed, this retreatment would be more predictable. In these cases, moreover, where the subject suffers a pathology that affects the oral mucosa, the less surgical trauma the patient receives, the better and faster the recovery will be, as has been described in studies we have published with dental implants in patients with OLP.⁵³

Four months after placement, the implants were loaded. For the preparation of the prosthesis a technique described by our study group was carried out, based on the use of inert materials that do not produce tissue reaction and could generate a worsening of the symptoms in patients with mucosal pathology such as OLP.^{53,54} The entire prosthesis was prepared using transepithelials (Multi-im), as this distances the critical point of the prosthesis–implant connection and maintains the gingival ridge area with less inflammation (Figs. 15 & 16). The metal framework of both bridges is drilled in grade IV titanium (Ti-6Al-4V), to avoid any type of reaction in the mucosa of these patients. The ce-



Figs. 11–13: Planning sections of the second quadrant where the narrow implants to be placed in the most mesial area and a distal implant of larger diameter and shorter length can be observed. **Fig. 14:** Panoramic X-ray after placement of dental implants.



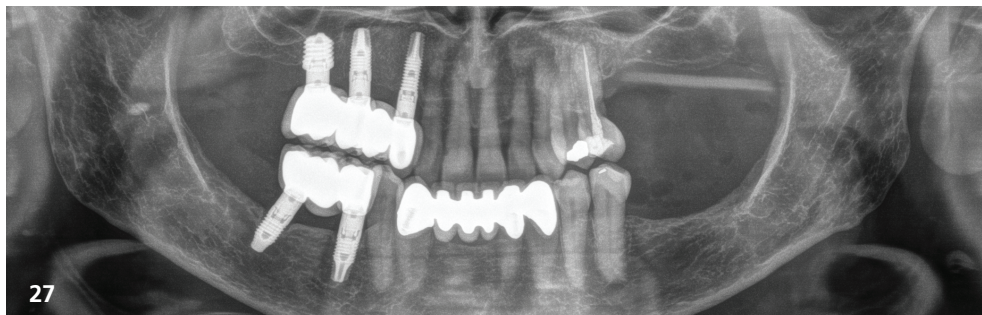
Figs. 15 & 16: Clinical images of transepithelials. The excellent behavior of the soft tissues around them can be observed. **Fig. 17:** Panoramic X-ray once the restoration has been completed and fitted. **Fig. 18:** Restoration once placed in the patient.

ramic was designed and injected at high pressure (lithium disilicate) and was cold cemented on the metal framework. Finally, the area in contact with the gingival ridge, which will be the most critical area in terms of tissue reaction, was finished in composite, without applying pressure on the soft tissue. This composite area also allowed us to be flexible in terms of changing its morphology and gingival settling as many times as necessary. The polishing of the area must be exquisite to avoid the

accumulation of bacterial plaque (Figs. 17 & 18).^{53,54} After one year of follow-up, the patient presented severe erosive lesions of her OLP and conventional treatment with topical corticosteroids was established. In this case, topical corticosteroids were used (triamcinolone acetonide 0.5% in aqueous solution for 30 days and the concentration was doubled for another month) and systemic corticosteroids (prednisolone 1 mg/kg/day for another month) and after failing to achieve healing of the ulce-



Figs. 19–21: Images after conventional treatment was completed unsuccessfully, with painful lesions in several areas. **Figs. 22–24:** Images after infiltration. The erosive lesions have resolved, and the patient's pain has decreased to the point of being able to perform activities of daily living without pain.



Figs. 25 & 26: Images after three years of follow-up. **Fig. 27:** Final X-ray at three years of follow-up.

rative lesions, infiltration with PRGF-Endoret was performed in the areas that remained erosive, according to the protocol published by our study group.^{49,50} With the infiltration, the painful condition was resolved, and the patient was able to resume her activities without pain.

Discussion

The treatment of choice for OLP is based on topical corticosteroids.¹⁻³ In some cases, these conventional treatments do not have the desired effect or there are patients in whom painful lesions continue to develop after treatment, preventing the patient from leading a normal pain-free life. Other treatments have been described for these more refractory cases. All treatments achieved some degree of remission, although the drugs used sometimes generate many side effects and there are no large case series that demonstrate that one of the treatments achieves a proven efficacy.³³⁻⁵¹

The use of plasma rich in growth factors has favoured in other types of ulcer pathology such as pemphigus the regeneration of affected tissue through growth factors such as platelet growth factor (PGF), transforming growth factor beta (TGF-beta), epithelial growth factor (ECGF), fibronectin and vascular endothelial growth factor (VEGF).⁵⁵

One of the main advantages of the use of PRGF-Endoret in the treatment of this type of lesions is the absence of side effects since in none of the cases of the study adverse effects have been found because of its application. The infiltration of PRGF-Endoret also manages to control pain as soon as the first infiltration is performed, considerably reducing it.⁵³⁻⁵⁵ Another important point is the design of the prosthesis. Our study group has described the protocol for designing prostheses on implants based

on the use of titanium, injected ceramic and completing the gingival area with composite resin, a fact that had not been documented until the publication of our first work.⁵⁴

Conclusions

Prosthesis preparation in patients with oral lichen planus following a careful protocol both during implant placement and prosthesis preparation is predictable and an alternative to consider, especially for those patients with a higher number of erosive outbreaks, where the placement of a conventional removable prosthesis would be more harmful. Thus, PRGF-Endoret infiltrations are used to reduce those flare-ups refractory to conventional treatment as shown in this clinical case.

Contact address

Eduardo Anitua DDS, MD, PhD^{1,2,3}

1 Private practice in oral implantology, Eduardo Anitua Institute, Vitoria, Spain.

2 Clinical researcher, Eduardo Anitua Foundation, Vitoria, Spain.

3 University Institute for Regenerative Medicine and Oral Implantology - UIRMI (UPV/EHU-Fundación Eduardo Anitua), Vitoria, Spain.

Jose Maria Cagigal 19

01007 Vitoria, Spain

+34 945 160653

eduardo@fundacioneduardoanitua.org

Literature

