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Case Report

COLLAGEN MATRIX FOR SOFT TISSUE REGENERATION: BASIC PRINCIPLES AND CASE REPORT

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ABSTRACT

Currently, the first-choice surgical technique for the regeneration of periodontal tissues is the execution of a free flap harvest from the palate. Starting from the 1990s, the use of collagen matrices of heterologous origin was introduced to replace the palatal graft with the main purpose of obtaining comparable results but reducing morbidity. In the following case study, a graft with a collagen matrix is reported. Resorbable matrix intended to provide support to soft tissue avoiding localized gingival recessions.

KEYWORDS: *collagen matrix, soft tissue regeneration, soft tissue augmentation, soft tissue defect*

INTRODUCTION

Currently, the first-choice surgical technique for regeneration of periodontal tissues is the execution of a free flap harvest from the palate and then repositioned at the receiving site. The graft can be composed of connective tissue or by both epithelium and connective tissue. This technique gives appreciable and stable results over time (1).

Starting from the 1990s, the use of collagen matrices of heterologous origin was introduced to replace the palatal graft with the main purpose of obtaining comparable results but reducing the risk of postoperative complications. In fact, the literature highlights the frequent and various complications related to collecting tissue from the palate: edema, bleeding, tissue necrosis, intense pain, patient discomfort, and greater operating times (2, 3).

The most recent literature shows that collagen matrices are useful in increasing the volume of soft tissues and can lead to similar qualitative clinical results compared to the surrounding tissues in terms of texture, volume, and color (4). This new technique, therefore, appears promising for the regeneration of periodontal and peri-implant soft tissues; it can be

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potentially the first-choice technique. To better investigate the procedure, a case grafted with collagen matrix is reported and pertinent literature is discussed.

Case report

A male patient came to the Dental Clinic of Borgo Roma Hospital (Verona) asking a rehabilitation for the upper left lateral incisor. He was in good health, and, at oral examination, had good periodontal health, not presenting inflammatory conditions. Radiographic exams were performed on tooth revealing caries and root fractures. The following surgical

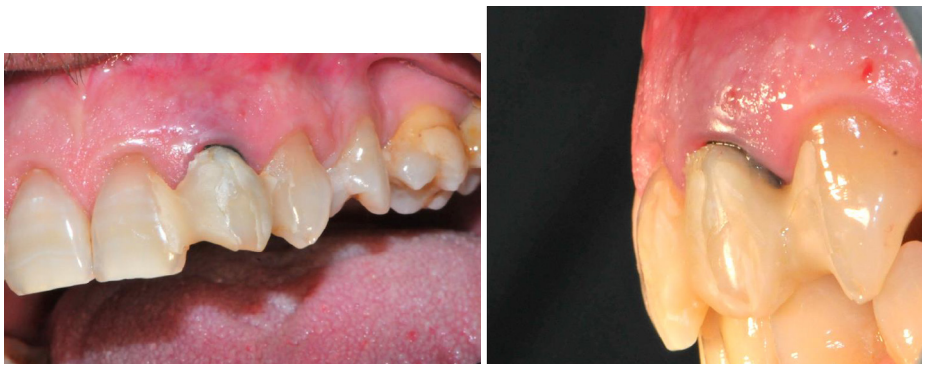

Fig.1 *Initial clinical situation: the anesthetically critical situation is evident on element upper left lateral incisor, with dark pigmentation on the root, compromising the smile of the patient.*

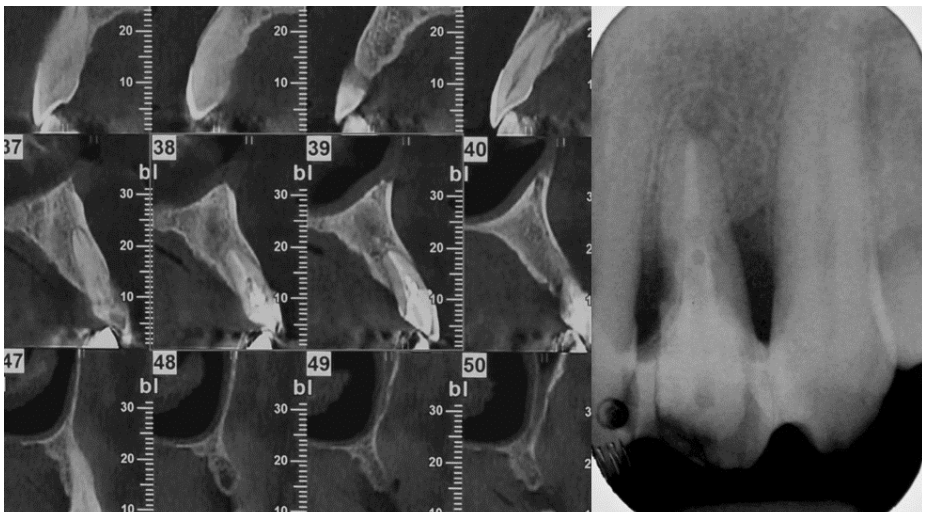

Fig. 2 *TC and Intraoral radiography: a periapical radiolucency is evident on the element upper left lateral incisor which presents root caries and root fracture. A moderate bone loss is also evident.*

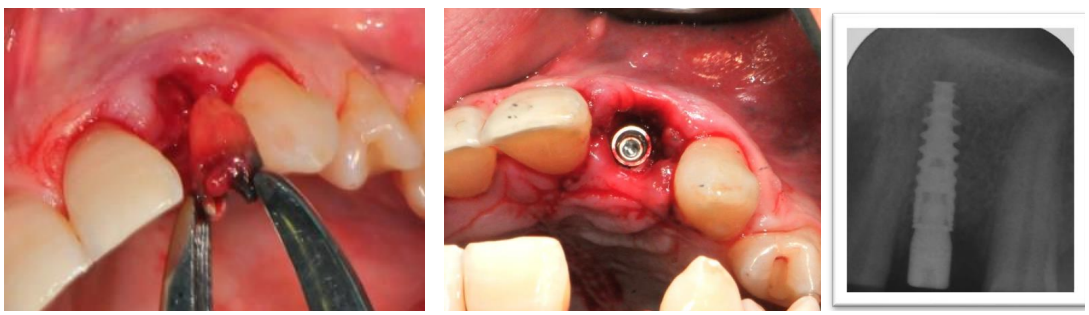

Fig. 3 *Atraumatic extraction of the tooth is performed, and then a post-extractive implant is inserted without immediate loading.*

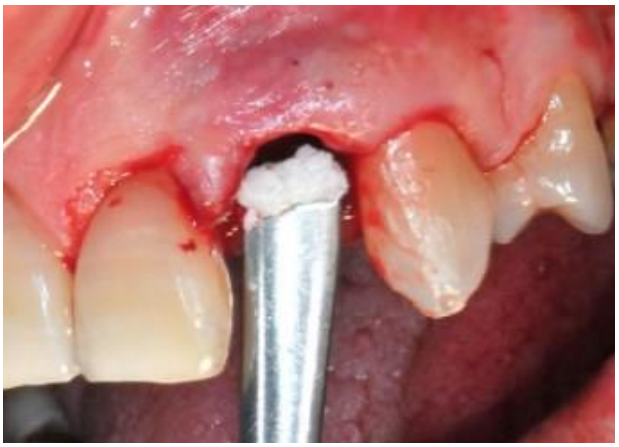

Fig.4. *Insertion of collagen matrix to fill the bone defect*

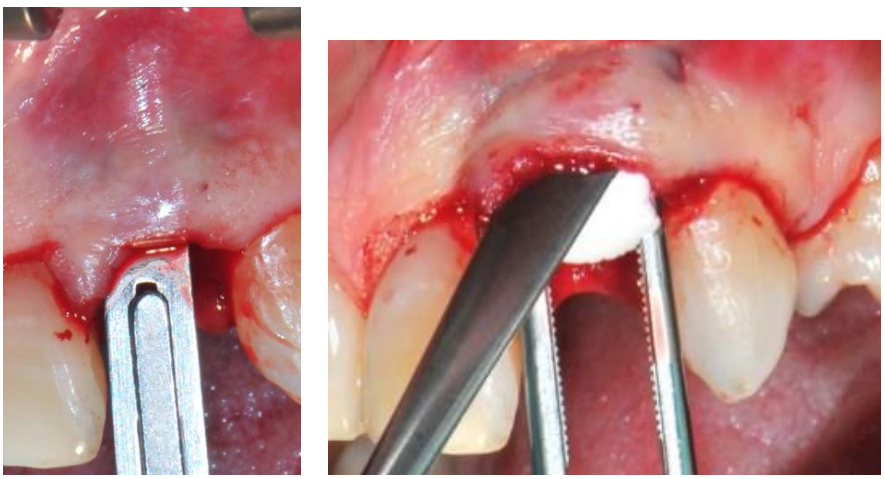

Fig.5 *Preparation of the envelope flap and insertion of collagen matrix inside the envelope*

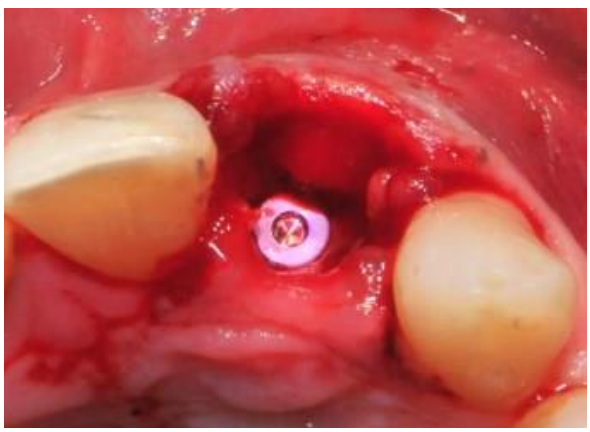

Fig. 6 *Collagen matrix inside the pocket formed by two folds of the gingiva.*

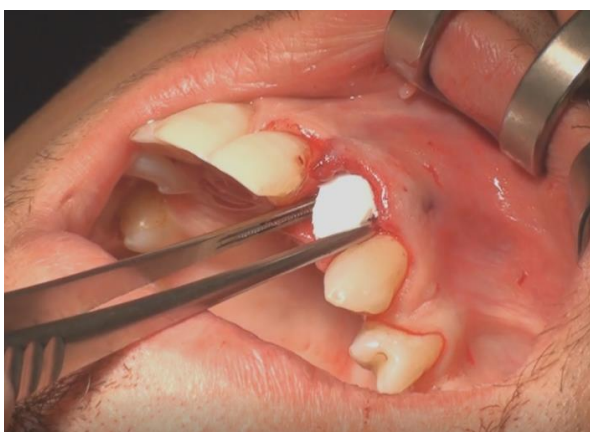

Fig.7. *Collagen matrix covering the post-extractive alveolus on the occlusal surface.*

approach was performed: extraction plus guided bone regeneration (GBR) insertion of collagen matrix (CM) to obtain soft tissue augmentation and coronally advanced flap (CAF). In this case, socket preservation and a post-extractive implant without immediate loading were performed. The surgery took place on May 2015, and a 4-year follow-up is reported (Fig. 1-7).

Envelope technique and box technique

The insertion of the collagen matrix (CreosTM mucogain, Nobelbiocare) inside an envelope flap requires a partial thickness flap on the buccal side, without therefore involving the periosteum. The flap must go beyond the mucogingival line to be able to create a tension-free envelope. At this point, the collagen matrix can be easily inserted into the created space and the flap is coronally advanced (CAF) (Fig. 8).

By carrying out an extension of the envelope technique, the box technique is introduced, which involves the use of two portions of collagen matrix: one, cut in a triangular shape (a), is placed in a vestibular envelope flap, and the other, rectangular (b), covers the post-extraction socket in the occlusal area. The box technique is therefore used when it is necessary to preserve the soft tissues at the same time as the alveolus volume (Fig. 9, 10).

After 4 years of follow-up, a good convexity of the buccal side of the alveolar ridge is obtained, which reproduces the curvature physiologically given by the presence of the root. This characteristic was maintained over time, with the tissues that undergo maturation and recession in a more evident way at the level of upper left central incisor. The color of the regenerated soft tissues is well camouflaged compared to that of the surrounding gums (Fig. 11, 12).

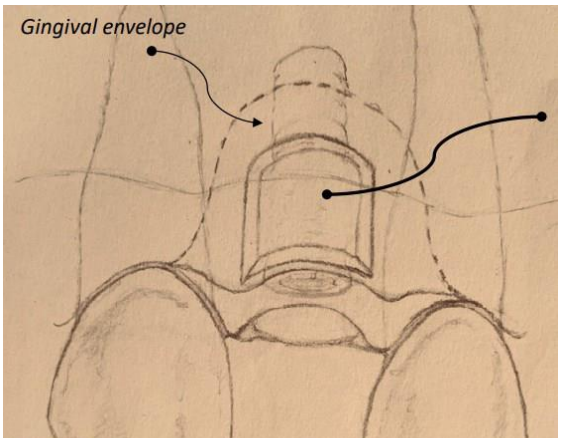

Fig. 8. *Explanatory drawing of the envelope technique.*

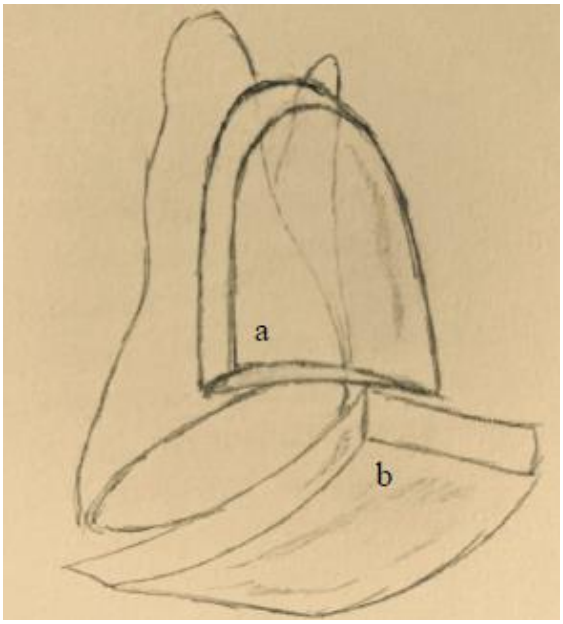

Fig. 9. *Explanatory drawing of the box technique: two portions of collagen matrix are placed (a and b).*

DISCUSSION

Periodontal soft tissue treatment is considered in relation to two types of needs:

- Aesthetic needs: promoting a natural appearance of soft tissues to obtain the integration of prosthetic elements with adjacent teeth, increasing the volume of soft tissues in patients

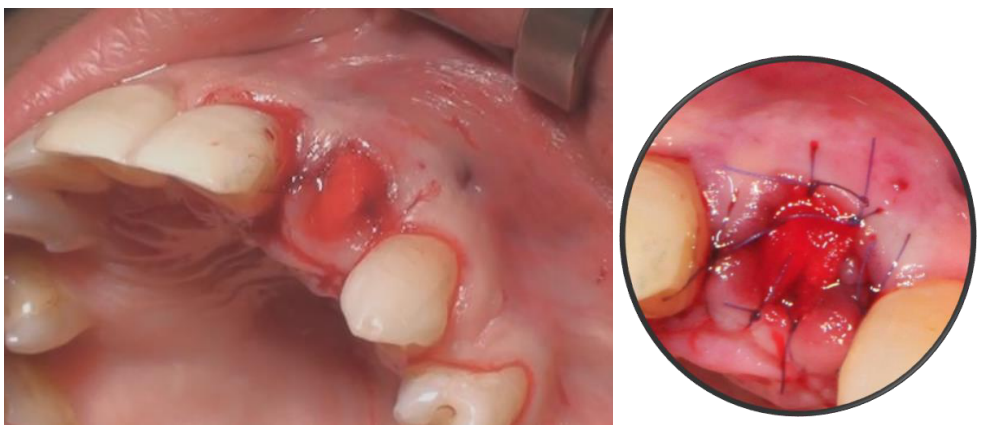

Fig. 10. *Suture of the wound*

with thin gingival biotype, correcting the mucogingival line when the smile line is high (5, 6).

- Functional needs: preventing soft tissue recession and volume loss is essential to reduce dental sensitivity and root caries, allow effective oral hygiene, protect post-extraction sites that have received grafts, and avoid exposure of the dental root or implant with consequent periodontitis and peri-implantitis. In case of the presence of subgingival restorative margins, modest plaque and inflammation control, specific orthodontic movements, and removable prosthesis hooks, a minimum thickness of 2 mm of keratinized tissue is required to maintain periodontal and peri-implant health (5).

The current approach to periodontal soft tissues is performed by using autologous palatal grafts in 75 - 80% of cases.

To preserve soft tissues, protect grafted sites, and increase the volume of soft tissues, connective tissue graft (CTG) is the first choice; for augmenting peri-implant soft tissues the most used methods are free gingiva grafting (FGG) and CTG; to augment connective tissue the most effective approach is a coronally advanced flap (CAF) associated with CTG / FGG (7); finally, to correct recessions around teeth and implants, the procedure of first choice is the association of a CAF plus CTG (8).

Autologous gingival grafts (FGG and CTG) are therefore now considered the "gold standard" procedures when an increase in soft tissues is necessary: in fact, they offer success rates and clinical results unmatched by other solutions, especially in long-term evaluation. However, heterologous grafting materials, such as collagen matrices, could represent a valid option for mucogingival surgery as they can provide an augmentation of keratinized tissue without the need for a palate harvest (5).

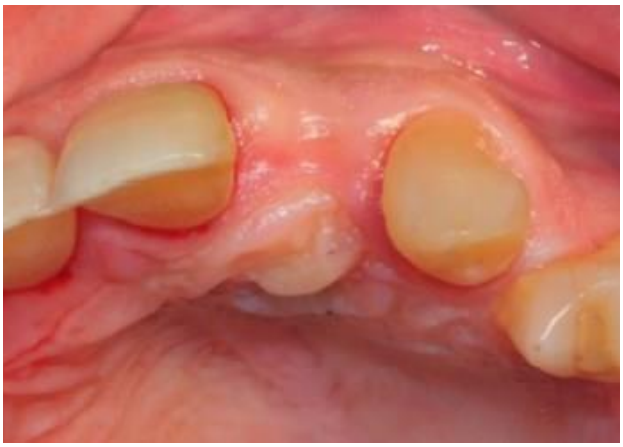

Fig. 11. *Clinical situation after 6 months of follow up*

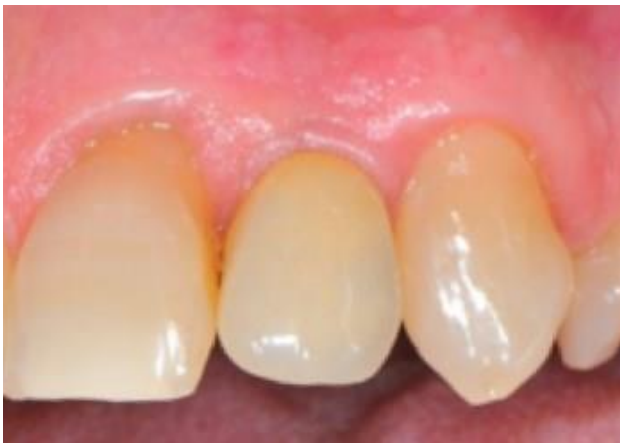

Fig. 12. *Clinical situation after 4 years of follow up*

Collagen is the main component of the matrix used in mucogingival surgery. It has numerous properties, including those offering support to cells, being resorbable, biocompatible, and easily manipulated. Collagen also has hemostatic activity and represents a chemotactic factor for the cells responsible for tissue regeneration (4).

Collagen material has the following advantages: biodegradable, bioabsorbable, non-toxic, and biocompatible; hemostatic, not antigenic, widely available and readily obtainable in pure form from living organisms (constitutes more than 30% of vertebrate tissues), synergic with other bioactive components, formulated in many different forms, plasticity due to high tensile strength, easily modifiable via functional groups to obtain desired materials (i.e., long-lasting depolymerization)

Collagen material has the following critical issues: hydrophilicity leading to too rapid degradation, high cost of purifying type I collagen, and possible trojan for infection.

In 1979, Green et al. (9) showed that it was possible to obtain growth of epithelial cells in vitro; in the same study, it was seen that fibroblasts also easily undergo proliferation. For a long time, therefore, the possibility of using epithelium and connective tissue obtained "in the laboratory" as grafts to resolve wounds or improve their healing has been under study.

Then, the Verona School published three studies, two in vivo and one in vitro, which demonstrate the favorable biological effects that these collagen membranes have on soft tissue healing (10, 11, 12).

The in vitro results demonstrated that a collagen matrix of porcine origin could have favorable biological effects on the proliferation and adhesion of gingival keratinocytes: an increase in the production of IL-6, a factor favoring cell proliferation, was observed if the collagen matrix was present. The keratinocytes adhered in a short time and in a fixed manner to the membrane and were able to interconnect with each other: they formed an epithelium with an architecture

that could be superimposed on the "in vivo" one (10).

Promising results for tissue regeneration with collagen membranes have also been obtained in vivo, both in patients (11) and animal cavies (12).

The study published by De Santis et al. in 2019 showed that the collagen matrix can integrate into connective and epithelial tissues within 10 days and be reabsorbed in 20 days. It is able to reduce the inflammatory infiltrate and stimulate the proliferation of fibroblasts and keratinocytes, as well as induce a process of neo-angiogenesis; acts as a scaffold for tissue regeneration, thus allowing a process called mucus - neo – genesis (11).

Tissue healing via allogeneic collagen matrix was also evaluated by Thoma et al. (13) in a randomized controlled clinical trial on twenty patients: each patient underwent two palatal biopsies, one group was then left to heal spontaneously, and the other group received the insertion of the collagen membrane. Biopsies of the treated sites were then performed at variable intervals to histologically evaluate the healing process. It was observed how, in the sites treated with the collagen membrane, keratinization was higher than in the control sites as early as the fourth and eighth-day post-surgery. So, the membrane, maintaining the space and causing less granulation tissue formation, was beneficial during the early stages of healing.

The formation of new connective tissue within the matrix develops with collagen degradation. The breakdown of the membrane into oligopeptides and amino acids is accomplished by collagenase, gelatinase and protease (14, 15).

CONCLUSIONS

Collagen matrix instead of the palatal graft is a promising device to be grafted in a proper periodontal bed; it has the potential to be the preferred in the future if more studies confirm a clinical good and stable results over time.

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Conflict of Interest

The authors declare no conflict of interest.

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Case report

OPEN BITE WITH SKELETAL CLASS III RELATIONSHIP TREATED USING OF CLEAR ALIGNER: A CASE REPORT

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ABSTRACT

This study reports the case of a female patient aged 32 affected by an open bite with skeletal class III. She had never been treated due to the fear of any surgical solution and multiple concerns about wearing fixed appliances that may negatively impact her life quality. A non-extraction treatment with clear aligner (CA) was done.

The aim of this case report was to describe this orthodontic treatment focusing on the diagnosis and the possibility of improving the biomechanics using CA.

KEYWORDS: *progenism, mandible, maxilla, treatment, orthodontic*

INTRODUCTION

In an adult with open bite and skeletal class III, the first choice is a surgical treatment. In the reported case, orthodontic-orthognathic treatment would have been successful and provided good stability. Since the patient refused the surgical option, a non-surgical treatment was considered. Literature supports this option because both surgical and non-surgical treatments can close open bites, and the stability is above 75% with both treatments (1–5). The patient also desired an aesthetic appliance not to compromise her social relationships. Therefore, there was just one option: treatment with a clear aligner (CA). CAs could offer a more aesthetic and invisible approach.

Moreover, it is conceivable that patients treated by CAs had less psychological discomfort than those treated by other fixed appliances in the upper and lower arches at different ages (6-16). In the literature, articles are published about open bite cases treated successfully using clear aligners (17, 18). This kind of treatment represents a valuable tool for correcting open bite and mild third class after a proper diagnosis (17).

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The aim of this case report was to describe the orthodontic treatment in an adult with open bite and skeletal class III, focusing on the possibility of biomechanics using CA and deciphering the advantages and disadvantages.

CASE REPORT

The patient, a 32-year-old woman, came to the Dental Clinic with the desire to improve her smiling aesthetic. She was in the permanent dentition status with dentoskeletal open bite and skeletal class III relationship. The intraoral examination showed an Angle class I on the left side and an Angle class II first molar relationship (1/2 unit) on the right side. The overbite was negative (Overbite: -1). Anterior and lateral overjet were reduced, and the upper midline was deviated by 1.5 mm on the left side. Lower and upper jaws have mild crowding with the dystopia of upper wisdom teeth. Extraoral examination showed a symmetrical face with an excess of the lower third of the face. The profile was straight. The examination showed a reverse smile arch, crowding, dental open bite, and midline deviation. There was a dental plaque and a thin gingival tissue biotype (Fig. 1).

The panoramic X-ray highlighted the presence of all permanent teeth except the lower wisdom teeth. The cephalometric analysis revealed a skeletal class III (AN/Pg: -2°) with a hypodivergent pattern (SN^GoGn: 38°) and upper incisors proclination (I-ANS-PNS: 126°) to compensate for the skeletal class III (Fig. 2).

Finally, the intraoral scans were performed, and both arches' digital casts were obtained. The patient did not receive any previous dental or orthodontic treatment. The medical history did not report any temporomandibular disorders or systemic pathologies, while she presented atypical swallowing and altered tongue position.

Fig. 1. *Initial records*

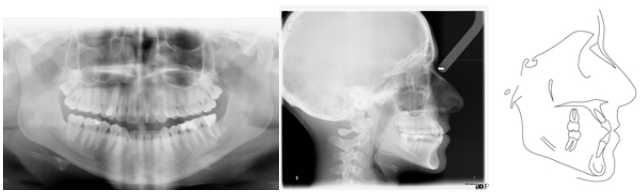

Fig. 2 *Initial X-rays*

Objectives

In agreement with the patient, the treatment objective was to close the open bite. In the literature, the open bite closure with CAs can be achieved thanks to a combination of maxillary and mandibular incisor extrusion and maxillary and mandibular molar intrusion, leading to mandibular rotation and reduction in anterior facial height. The closure of the open bite by performing an anterior incisors extrusion can affect the long-term results. Incisor extrusion and molar intrusion determine the mandibular counterclockwise rotation and higher stability; this is an advantage for CAs due to the thickness of the material covering the posterior teeth and the bite forces exerted by the patient. Otherwise, the fixed appliances do not obtain vertical control, or some appliances even extrude posterior teeth and determine a worsening of the facial aesthetic (19, 20).

Maxillary and mandibular incisors were significantly retracted during the treatment to achieve a good anterior intercuspation (21)the mechanism of anterior open bite closure using clear aligners (Invisalign, Align Technology, Santa Clara, CA, USA), and this movement was efficient because when CAs "push the teeth, they are not pulled simultaneously."

In order to improve the lateral overjet, an expansion was planned with CA, and it could be considered a slow maxillary expansion (22). We had an objective of 2 mm of upper lateral expansion on each side to improve the lateral overjet and obtain a change of arch form. Distalization to gain an Angle class I on both sides and to solve the crowding after the extraction of upper wisdom teeth was also planned. The movement of upper molars when a distalization movement of at least 1.5 mm bodily can realize by using CAs (23). Intermaxillary elastics were used to have a dentoalveolar compensation to the malocclusion of skeletal class II. During this research, all operators wore surgical masks to prevent the respiratory system virus (24) and maintain office hygiene (25).

RESULTS

All goals were achieved, and the occlusal, functional, and esthetic results were satisfactory. The outcome was rewarding for the clinicians and appreciated by the patient. A class I relationship on both sides was obtained with a correct overjet and overbite, centered midline, and a good alignment, with good coordination of the arches. Extraoral records showed nice esthetics with a full pleasant smile with a correct smile arch. The panoramic x-ray showed good root parallelism on both arches and no root resorption. The skeletal values were corrected, with an improvement of all the values: a skeletal class I was achieved with a good upper and lower incisor inclination; the overjet and the overbite showed average values, and the gingival tissue remained stable without any recessions. The patient's compliance with CAs and elastics was high and contributed to this outstanding achievement. Invisalign® CAs were used (Fig. 3-4).

Fig. 3. *Initial records*

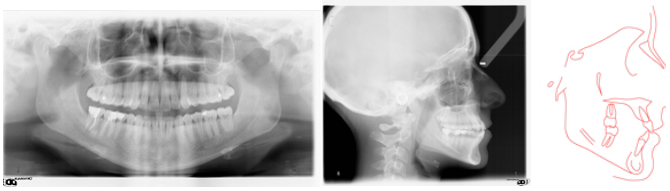

Fig. 4 *Initial X-rays*

DISCUSSION

Cephalometric superimposition on the cranial base showed excellent final results. Specifically, the following dental movements were obtained: distal movements of posterior teeth without extrusion, extrusion and retraction of upper and lower incisors, and dentoalveolar compensation with an improvement of skeletal class III to skeletal class I. No change in vertical values was reported, as expected in adult patients (26).

Regarding the literature, several issues are controversial. The evaluation of oral and general health is recommended for potential medical problems before and during the orthodontic treatment (27-30). Methodological problems have always to be considered: small sample size, bias and confounding variables, lack of method error analysis, blinding in measurements, and deficient or missing statistical methods (1).

CONCLUSIONS

Treatment of an adult with open bite and skeletal class III using CAS needs a good diagnosis to evaluate the severity of malocclusion properly, plan the treatment using all orthodontic tools, and discuss them with the patient to improve his/her compliance during the whole treatment.

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Case Report

PATHOLOGIC TOOTH MIGRATION AND ATYPICAL SWALLOWING IN PERIODONTAL PATIENTS: A NEW APPROACH WITH ELASTODONTIC THERAPY - CLINICAL SERIES.

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ABSTRACT

Several publications describe the possibility and limits of orthodontic treatment in periodontal patients to achieve good occlusion. Pathologic tooth migration (PTM) is a change in tooth position that occurs when a disruption of forces maintains teeth in a normal relationship. PTM can result in severe dental disfiguration and compromise a patient's self-esteem. In order to correct this pathologic and unaesthetic condition, different orthodontic appliances are described in the literature. Among them, elastodontic devices have been recently proposed with good results in terms of patient compliance and treatment efficacy. The aim of this work is to evaluate the use of elastodontic devices for PTM correction in a series of periodontally compromised patients. The reported cases demonstrated that elastodontic treatment could support and complete periodontal therapy with an occlusal stabilization activity, especially in cases characterized by occlusal trauma. This additional therapy stabilized teeth movement recovery a harmonic occlusion, recovery an acceptable aesthetics, and corrected altered muscle functions such as atypical swallowing. Further studies are needed to investigate these innovative therapeutic procedures better.

KEYWORDS: *periodontitis, malocclusion, tooth, migration, device*

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INTRODUCTION

Periodontitis is an infectious and inflammatory disease that progressively destroys tooth-supporting structures, is one of the most widespread diseases, and is the leading cause of tooth loss in adults (1). Periodontitis is a bacterially induced inflammatory disease linked to the individual's oral microbiota and immune system (2). However, the microbial insult is not enough *per se* to induce the onset of the disease (3, 4).

The development of periodontitis is also due to an individual susceptibility linked to a genetic basis (5) and/or to lifestyles (especially smoking and poor oral hygiene) and/or trauma from occlusion (6), which allows bacteria to express their pathogenic potential (7).

In every patient affected by periodontitis, it is necessary to define and follow a treatment strategy that eliminates the opportunistic infection and prefigures the clinical outcome parameters. The periodontal treatment plan provides for an initial phase of infection and risk factors control, including patient motivation, instrumental (scaling and root planing), and, in selected cases, pharmacological (local or systemic) therapy (named etiologic or causal therapy). This therapy, in most cases, can bring the clinical indices of periodontitis, such as full-mouth bleeding score (FMBS), full-mouth plaque score (FMPS), probing depth (PD), and clinical attachment level (CAL), within physiological limits (8). However, these results may not be achieved in all sites, particularly those with high initial PD and intrabony defects. For these reasons, it is necessary a re-evaluation; when it is positive, the patient will be introduced to a supportive periodontal therapy; otherwise, it will be possible to opt for an additional non-surgical or surgical therapy to eliminate the irritative factors not removed by the etiologic therapy and modify the anatomy of pathologically altered hard and soft tissues. It is also very important to eliminate or to take under control the risk factors for periodontal disease like smoking, stress, anatomic, and trauma of occlusion.

Some authors found that occlusal therapy can reduce the long-term progression of periodontal disease and could be considered an important adjunctive therapy in the treatment of periodontal disease (9, 10).

In order to control trauma of occlusion in periodontal patients, there are more therapeutic options; the best is orthodontic therapy.

The goals of the treatment of occlusal traumatism may be summarized as follows:

elimination or reduction of tooth mobility;

establishment or maintenance of a stable and reproducible maximal intercuspal habitual position;

provision of efficient masticatory function and a comfortable occlusion with acceptable phonation and aesthetics;

elimination of parafunctional habits and pathologic tooth migration (PTM).

PTM is defined as a change in tooth position that occurs when there is disruption of forces that maintain teeth in a normal relationship (11). A recent study demonstrated that most patients with moderate-to-severe periodontitis need or could take advantage of orthodontic therapy because of esthetical and functional changes caused by PTM (12). Another recent retrospective study evaluated the long-term response of periodontal tissues and survival rate of teeth with advanced attachment loss and PTM in 21 periodontitis patients treated with combined periodontal and orthodontic treatment. All anterior migrated teeth functioned at the end of 10 to 15 years of maintenance. Residual probing depths and clinical attachment levels improved after treatment and remained stable through the follow-up. In highly compliant patients, all migrated teeth with an initial unfavourable prognosis showed long-term clinical stability (13). Pathologic tooth migration can result in severe dental disfiguration and devastate a patient's self-esteem. A prevalence in periodontal patients of 55.8% was recently reported (14).

Tooth migration is often the motivation for patients to seek periodontal therapy. According to Brunsvold M.A. (15):

1. most cases of moderate to severe PTM require a team approach to achieve treatment success. Periodontal therapy is followed by orthodontic therapy, which usually involves fixed appliances. Prosthodontic treatment is often required following orthodontic therapy;
2. when PTM is in the early stages, periodontal therapy alone is sometimes effective in producing spontaneous migration correction. This correction has been reported after non-surgical and surgical treatment;
3. light intrusive orthodontic forces are effective in treating extrusion and flaring if inflammation is controlled during all phases of treatment;
4. most patients with PTM have moderate to severe periodontitis. Several studies describe successful orthodontic treatment in these patients if inflammation is controlled.

Many factors influence tooth position; therefore, there are many possible etiologic factors for PTM. The multiple causes of incisor flaring emphasize the complexity of differential diagnosis (6).

The main factors known to influence tooth position are:

tissues of the periodontium;

occlusal factors;

soft tissue pressures of the cheek, tongue, and lips;
a variety of oral habits.

Periodontal inflammation (9) and eruptive forces also influence tooth position (Fig. 1). In order to correct PTM, there are a lot of different techniques described in the literature (16-20). However, some studies (19-20) indicated that conventional orthodontic treatment with light intrusion forces could be a reliable treatment method for PTM if gingival inflammation is controlled before, during, and after orthodontic therapy.

All these studies agree that inflammation associated with periodontitis must be carefully controlled before, during, and after orthodontic therapy. The authors also agree with this therapeutic approach but underline that conventional orthodontic treatment is an option that receives poor compliance from periodontic patients. It is no coincidence that, despite mechanical protocols specifically calibrated on periodontal disease elements and proposed and validated for over 20 years, it is generally not well accepted by the patient. It is one of the therapies considered useful and necessary but not practiced in everyday clinical reality. On the other hand, traditional orthodontics has some important disadvantages in managing adult and periodontal patients, the main of which is that it could have a negative impact on daily hygienic procedures (21-23). Furthermore, recent literature has shown that the maintenance of the activity indices of periodontal disease can be kept under control more predictably through the use of removable rather than traditional fixed orthodontic devices (24). Among the removable devices used for treating PTM, the elastodontic device (and therapy - ET) could be the most useful.

ET is nowadays increasingly used in orthodontic interceptive treatment. It uses removable elastomeric functional appliances that produce neuromuscular, orthopedic, and dental effects. Thus, these devices are useful in the developmental age, when skeletal structures are characterized by important plasticity and adaptation capacity, allowing for removing factors responsible for malocclusions (25). Elastodontic appliances improve orthodontic parameters such as Overjet (OVJ) and Overbite (OVB) and eliminate functional disorders of the stomatognathic system and act in a three-dimensional way within the oral cavity, improving breathing, swallowing, and postural problems, especially if associated with targeted functional exercises. Furthermore, these devices act as rehabilitative therapy for altered muscular functions. The presence of a lingual ramp and a button for the tongue, in addition, allows the restoration of a correct posture and lingual function. Furthermore, elastomeric devices are generally well tolerated by patients requiring simple collaboration and management, and they are both simple to use and comfortable.

The aim of the study is to propose the use of ET in periodontal patients affected by PTM. Four cases of ET in PTM patients with moderate and severe periodontitis are reported.

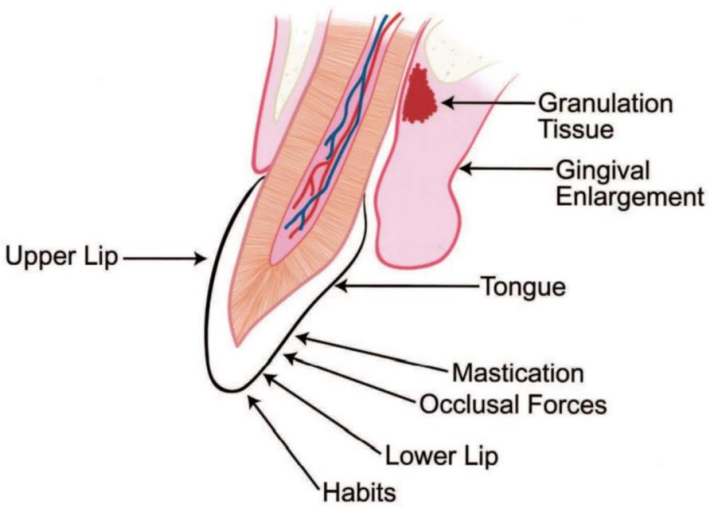

Fig. 1. *Main factors influencing tooth position.*

CASE REPORT

Clinical Case 1

A 40-year-old woman presented to our private practice with the complaint of "poor aesthetics due to periodontitis, pathologic tooth migration, and diastema". The anamnesis resulted in the absence of systemic pathologies, no allergy, no trauma in the orofacial area, no smoking, and familiarity with periodontitis. On enquiring further, she was generally unhappy with the appearance of his front teeth and smile because of her PTM and diastema. Intermittent pain and tooth sensibility episodes would occur, and the patient also complained about bleeding gums associated with periodontitis.

Intraoral examination revealed adequate oral hygiene, moderate periodontitis, with more severe localization on the lower and upper frontal sectors; during clinical exams dentists wear masks to prevent the spread of the virus that causes COVID-19 (26).

Diastema was seen between #12 #11; anterior splaying of the upper and lower incisors; these lower incisors were already splinted previously due to progressive pathological mobility. The presence of anterior splaying and grade 2 mobility on the upper central incisors, associated with widening the periodontal spaces highlights primary occlusal trauma. The examination of swallowing showed the presence of "atypical swallowing" with a low tongue posture and oral breathing. Based on data collection, the problem list is summarised as follows:

periodontitis;
hopeless teeth #42,41,31,32;
PTM #12 ,11,21,22;
diastema #12,11;
reduced overjet and overbite;
trauma of occlusion;
atypical swallowing and mouth breathing.

On the basis of the problem list, the treatment goals for this patient were, at first, to eliminate periodontitis by etiologic periodontal therapy, followed by maintenance therapy by reinforcing meticulous oral hygiene.

Immediately after, it was necessary to face the "extra periodontal" problems already listed: hopeless teeth #42, 41, 31, 32; PTM #12, 11, 21, 22; diastema #12, 11; the trauma of occlusion, and para functions; the latter was responsible for part of the patient's symptoms and represented dangerous "mechanical" risk factors for periodontal tissues already reduced by the disease. To address the extra-periodontal problems, the Authors first acted on the mandible by extracting the irrecoverable incisors and replacing them with a traditional non-removable prosthesis anchored on the two canines # 43 # 33. This has the dual purpose of resolving edentulousness but also of regularizing the (altered) overjet and overbite by acting on the length and inclination of the lower incisors. At the same time, they used an innovative myofunctional trainer; it is a non-traditional nocturnal device, a "three-dimensional byte". Thanks to this particular device, it was first of all intended to reposition the jaw possibly dislocated as a result of the dental migrations resulting from the disease itself; these migrations are, in fact, the cause of and pre-contacts that are very harmful to the residual periodontium and capable of altering the correct mandibular posture.

In the specific case, the jaw was dislocated forward, potentially traumatizing for the periodontium of the upper frontal teeth where the diastema and the PTM were found. The aim was also to obtain a more correct static and dynamic occlusal pattern, in the absence of which a bad work of the periodontium of the most overloaded elements is inevitable, which would consequently be more exposed to the risk of progression or recurrence.

Above all, the para-functions present were addressed: atypical swallowing and oral breathing; in fact, they develop excessive and harmful forces on a periodontium already reduced (although healed) by the disease. Therefore, it was decided to use an innovative myofunctional trainer to solve extra-periodontal problems. This appliance is not a common nocturnal occlusal splint, but it is a "three-dimensional byte" made in elastic medical silicone. The myofunctional trainer consists of a double-track, one for the upper arch and the other for the lower arch, and it is a one-piece device wrapping both arches. A horizontal plane, more rigid, on which the arches lay down, is made to level the dental arches according to a predetermined anatomical plan. Two softer vertical flanges, one internal and one external, can wrap the arches to neutralize abnormal centripetal and/or centrifugal muscle forces that may insist on the arches to obtain more harmonious shaping. The used appliance is shown in Fig. 2.

The device generally follows the shape and diameter of the arches, the anteroposterior relationship of the arches themselves (1, 2, 3 class), and the vertical relationship. This last and very important parameter, managed by providing along the occlusal horizontal plane with differentiated thicknesses, has allowed in this specific case to insert in the device

the intrusive information on the frontal teeth for the precise purpose of obtaining the correction of the PTM of the upper frontal teeth. The patient's maxillary inter-molar diameter (DIM) was 60 mm, and it was set by measuring the distance between the external sides of the distobuccal cusps of the upper first molars.

As mentioned, the appliance has a conformation based on the specific shape of the arches and the intermolar diameter of the upper arch. Device size of 60 mm DIM was deliberately chosen in order to obtain the levelling of the occlusal plane without an expansive effect in the upper alveolar but, on the contrary, with the therapeutic goal of restoring a correct neutron corridor and thus obtaining the re-entry of the two incisors with the relatively recent diastema #12 and #11. The aim was to take advantage of a single therapeutic approach to deal with the alteration of the correct occlusal scheme (PTM and diastema) and the alteration of the correct functional and motor patterns (trauma from occlusion, atypical swallowing, and oral breathing). This combined approach has a double rationale. The first one is the simplification of the treatment and the greater compliance of the patient concerning other differentials, multiple, in more times and more expensive treatments.

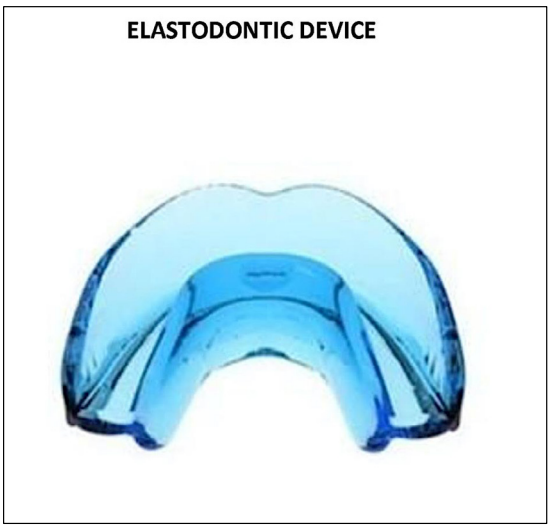

Fig. 2. *Detail of the Elastodontic device used in this case report.*

The second one is the clinical experience of the authors, who consider the problems mentioned above interconnected and potentially connected to the contextual problems of the periodontium; the latter, not by chance, was more damaged precisely in the frontal area where the dysfunctions were located. The appliance was initially worn for 30 minutes during the day (for the first 30 days) by practicing some myofunctional exercises explained to the patient to start to correct the functions of swallowing, breathing, and chewing by acting on the internally and externally. Immediately afterward, nocturnal use for 12 months was introduced, allowing these new, more correct motor engrams to become automatic (Fig. 3). The patient was observed monthly.

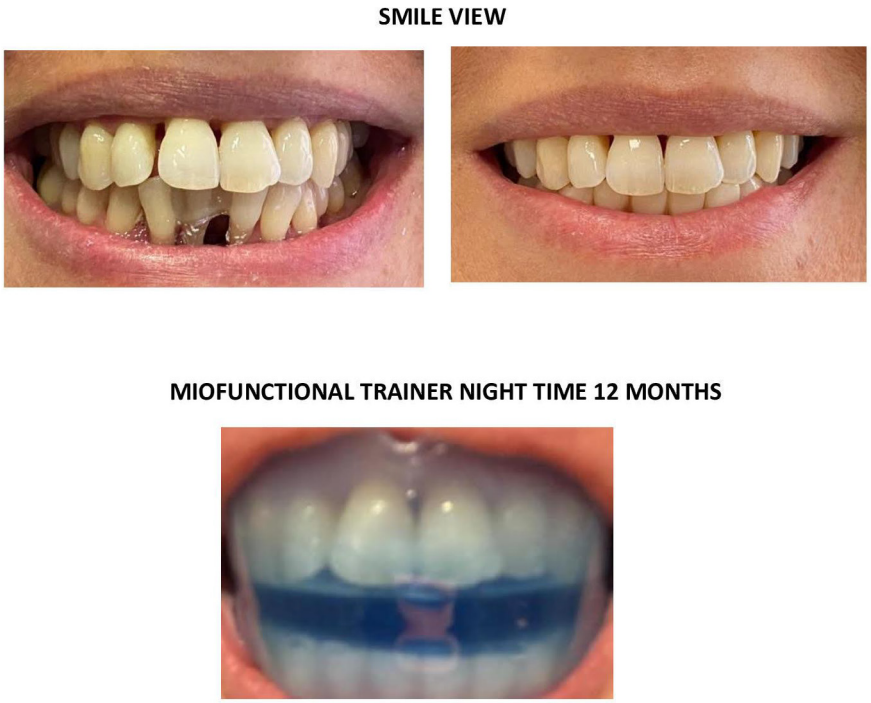

Fig. 3. *Case 1: Detail of the clinical case at the baseline and after 12 months of treatment.*

Clinical Case 2

A 45-year-old woman presented to our private practice with the complaint of "poor aesthetics due to periodontitis, pathologic tooth migration and diastema #11 #21", loss of interdental papilla #41, #31. The patient revealed the absence of systemic pathologies, no allergy, no trauma in the orofacial area, no smoking, and familiarity with periodontitis. On enquiring further, she was generally unhappy with the appearance of his front teeth and smile because of her PTM and diastema #11 #21.

Intraoral examination revealed sufficient oral hygiene, moderate periodontitis, with more severe localization on the lower and upper frontal sectors. Moreover, it was present a diastema between #11 and #21 and an anterior splaying of the upper incisors.

The presence of anterior splaying and grade 2 mobility on the upper central incisor #11, associated with the widening of the periodontal spaces and other signs and symptoms, highlights primary occlusal trauma. The examination of swallowing showed the presence of "atypical swallowing" with a low tongue posture and oral breathing. The patient reported two previous attempts to close the interincisal diastema using traditional fixed orthodontic therapy, both of which resulted in relapse. Based on data collection, the problem list is summarised as follows:

Periodontitis;
PTM #21;
Diastema #11, #21;
Loss of interdental papilla #41, #31;
reduced overjet and overbite;
Trauma of occlusion;
Atypical swallowing and mouth breathing.

Based on the problem list, the treatment goals for this patient were, at first, to eliminate periodontitis by etiologic periodontal therapy, followed by maintenance therapy by reinforcing meticulous oral hygiene. However, immediately after, it was necessary to face the "extra periodontal" problems already listed (PTM #11, 21, diastema #11, 21, trauma

Fig. 4. *Case 2: Detail of the clinical case at the baseline and after 12 months of treatment.*

of occlusion and parafunction); the latter were certainly responsible for part of the patient's symptoms and represented dangerous "mechanical" risk factors for periodontal tissues already reduced by the disease.

In regard to the extra-periodontal issues, the initial treatment planning provided action on the mandibular arch by applying four metal-free prosthetic crowns on 42,41,31,32 for the dual purpose of eliminating imperfections from the loss of the inter-incisive papilla between 41 and 31 and regularizing the overjet and overbite (altered) by acting on the length and inclination of the lower incisors. At the same time, an innovative myofunctional trainer was used (Fig. 4), with the same modalities, the same clinical procedure, and the same observation time of 12 months as case 1.

Clinical Case 3

A 33-year-old woman presented to our private practice with the complaint of "poor aesthetics due to periodontitis, pathologic tooth migration #11, #21 and diastema #21, #22". The anamnesis showed the absence of systemic pathologies, no allergy, no trauma in the orofacial area, no smoking, and familiarity with periodontitis. On enquiring further, she was generally unhappy with the appearance of his front teeth and smile because of her pathologic tooth migration and diastema #21 and #22.

Intraoral examination revealed sufficient oral hygiene, moderate periodontitis, with more severe localization on the lower and upper frontal sectors: diastema between #21, #22; anterior splaying of the upper incisors. The presence of anterior splaying and grade 2 mobility on the upper central incisors and #22, associated with the widening of the periodontal spaces highlights primary occlusal trauma. The examination of swallowing showed the presence of "atypical swallowing" with a low tongue posture and oral breathing. The patient reported the recent opening of the interincisal diastema between 21 and 22; based on data collection, the problem list is summarised as follows:

periodontitis,
PTM #11 #21,
diastema #21, #22,
trauma of occlusion,
atypical swallowing and mouth breathing.

Based on the problem list, this patient's treatment goals were to eliminate periodontitis by etiologic periodontal therapy

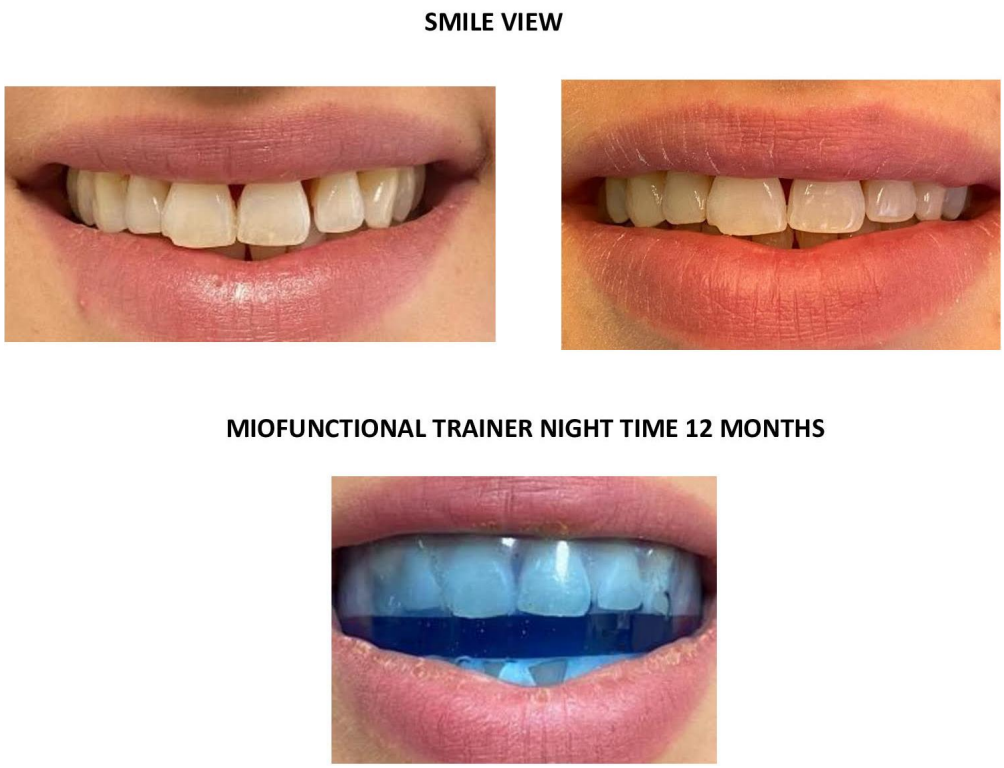

Fig. 5. *Case 3: Detail of the clinical case at the baseline and after 12 months of treatment.*

followed by maintenance therapy by reinforcing meticulous oral hygiene. Immediately after, it was necessary to face the "extra periodontal" problems already listed (PTM #11, 21; diastema #21, 22; trauma of occlusion and para-functions); the latter were undoubtedly responsible for part of the patient's symptoms and represented dangerous "mechanical" risk factors for periodontal tissues already reduced by the disease. To avoid extra-periodontal problems, they applied four metal-free prosthetic crowns on 42, 41, 31, and 32 for the dual purpose of eliminating the imperfection resulting from the loss of the inter-incisive papilla between 41 and 31 and regularizing the overjet and overbite (altered) by acting on the length and inclination of the lower incisors (Fig. 5). At the same time, they used an innovative myofunctional trainer as in clinical case 1 and 2 with the same modalities, the same clinical procedure, and the same observation time of 12 months.

Clinical Case 4

A 50-years old woman presented to our private practice with the complaint of "poor aesthetics due to periodontitis, pathologic tooth migration #11, #21 and diastema #41, #31". The anamnesis resulted in the absence of systemic pathologies, no allergy, no trauma in the orofacial area, soft smoking, and familiarity with periodontitis. The subject was unhappy with the appearance of her aesthetic frontal region due to pathologic tooth migration #11, #21 and diastema #41, #31.

Intraoral examination revealed sufficient oral hygiene, moderate periodontitis, with more severe localization on the lower and upper frontal sectors. In addition, a diastema between #41 #31 and PTM #11, #21 were present.

The presence of grade 2 mobility on the upper central incisors, associated with the widening of the periodontal spaces highlights primary occlusal trauma. The examination of swallowing showed the presence of "atypical swallowing" with a low tongue posture and oral breathing. The patient reported the recent opening of the interincisal diastema between 41 and 31. Based on data collection, the problem list is summarised as follows:

periodontitis,
PTM #11 #21
diastema #41, #31,
trauma of occlusion,
atypical swallowing and mouth breathing.

Based on the problem list, the treatment goals for this patient were, at first, to eliminate periodontitis by etiologic periodontal therapy, followed by maintenance therapy by reinforcing meticulous oral hygiene. However, immediately after, it was necessary to face the "extra periodontal" problems already listed PTM, diastema, dental trauma of occlusion, and para-functions. The latter was responsible for part of the patient's symptoms and represented dangerous "mechanical" risk factors for periodontal tissues already reduced by the disease.

At the same time, they used an innovative myofunctional trainer as in clinical cases 1, 2, and 3 with the same modalities, the same clinical procedure, and the same observation time of 12 months (Fig. 6).

Fig. 6. *Case 4: Detail of the clinical case at the baseline and after 12 months of treatment.*

RESULTS

From a clinical point of view, the consequences of this "integrated" therapeutic approach using the myofunctional trainer were multiple and early. After only 12 months, in all 4 cases presented, the return of the PTM

on the affected incisors was achieved. In addition, diastemas (Fig. 7-10) disappeared.

In cases 1 and 2, the PTM was also accompanied by fanning of the upper incisors supported by an excessive reduction of OVJ e OVB. The anterior splaying was also re-entered in these two cases where the length and shape of the lower incisors were aprosthodontically corrected.

The correct functions in swallowing and breathing have been regularized with the related effects on motor engrams and the harmony of occlusal relationships. A very satisfactory aesthetic appearance of the smile was also obtained, entirely in line with the best expectations of patients and able to improve their self-esteem and social life.

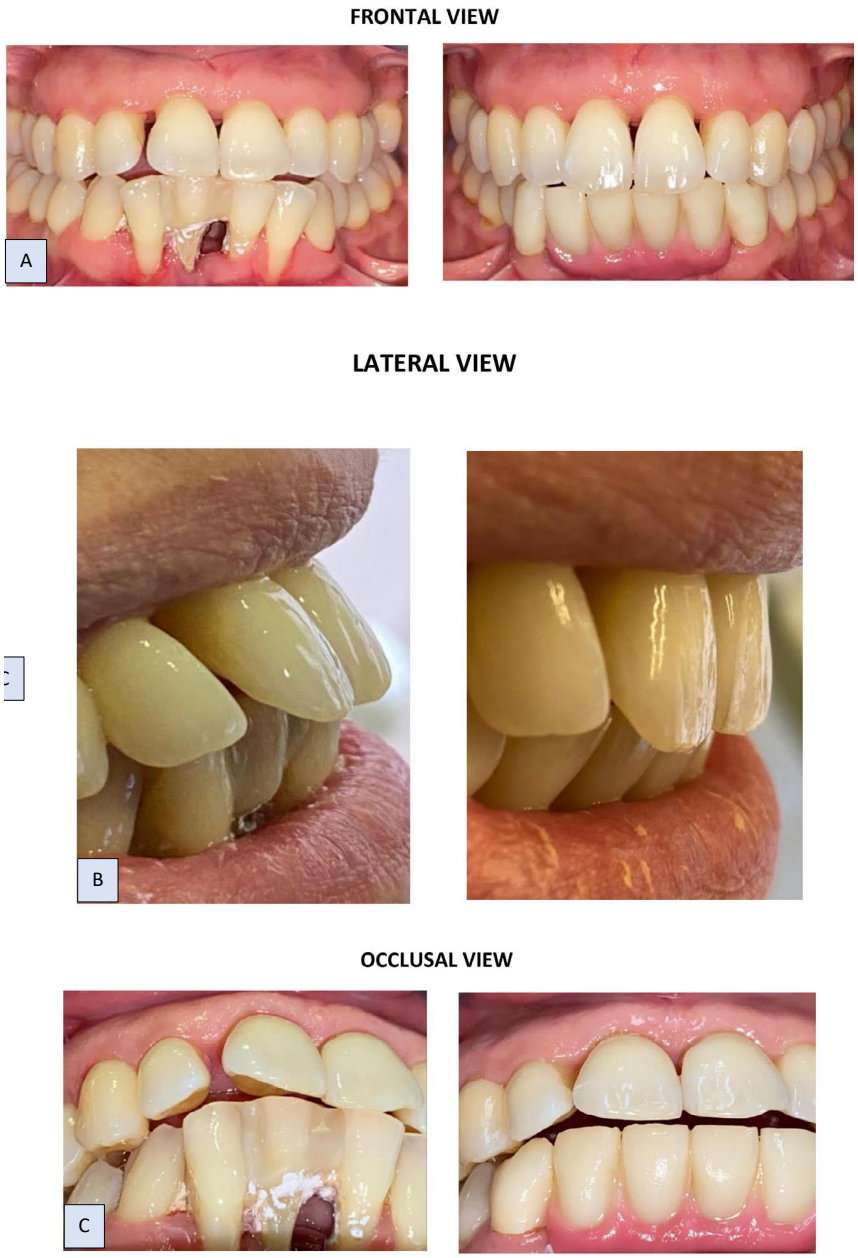

Fig. 7. *A): Case 1: Comparison of the clinical case at the baseline and after 12 months of treatment in frontal view; B): Case 1: Comparison of the clinical case at the baseline and after 12 months of treatment in lateral view; C): Case 1: Comparison of the clinical case at the baseline and after 12 months of treatment in occlusal view. Regularization of the overjet and overbite by acting on the length and inclination of the lower incisors.*

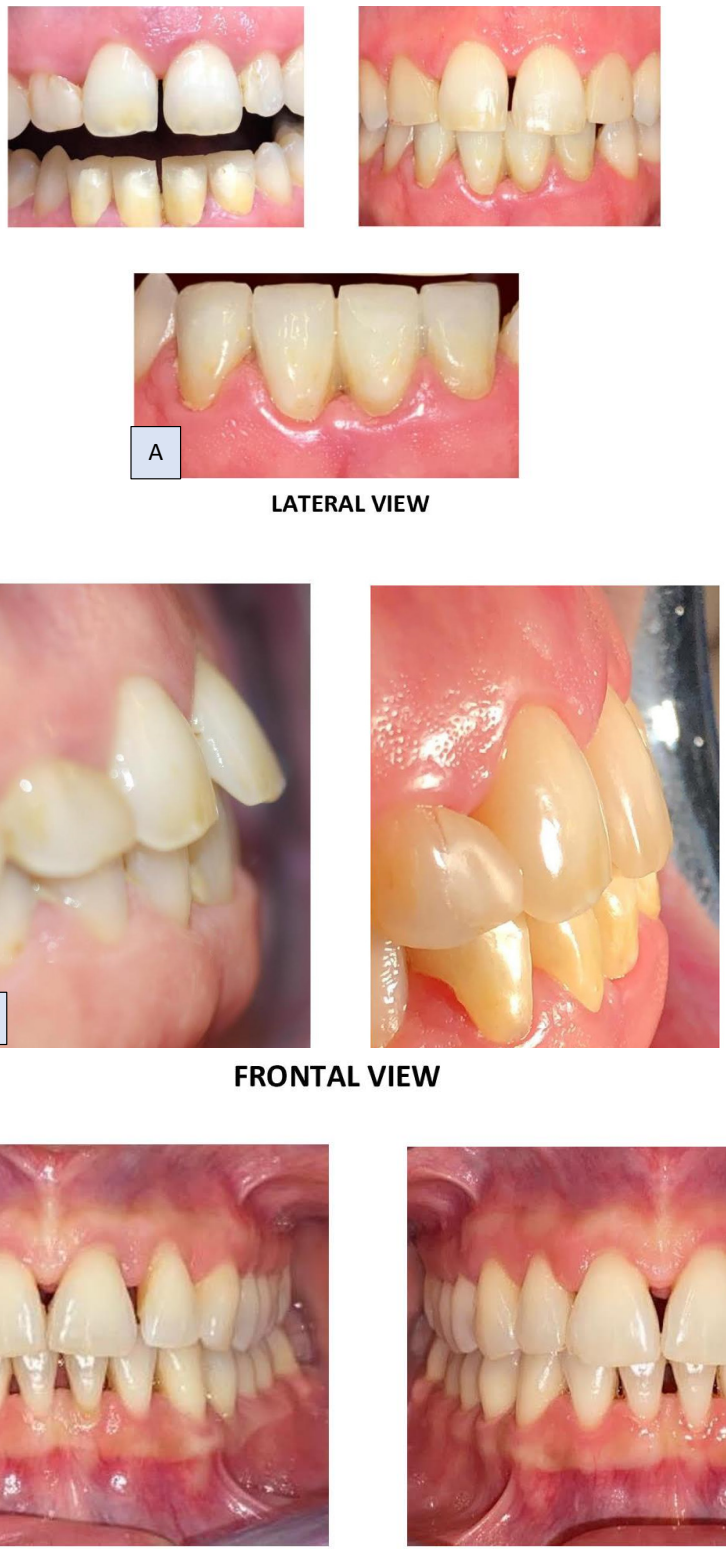

Fig. 8. *A): Case 2: Comparison of the clinical case at the baseline and after 12 months of treatment; B): Case 2: Comparison of the clinical case at the baseline and after 12 months of treatment in lateral view; C): Case 2: Comparison of the clinical case at the baseline and after 12 months of treatment in occlusal view.*

Fig. 9. *A): Case 3: Comparison of the clinical case at the baseline and after 12 months of treatment in frontal view; B): Case 3: Comparison of the clinical case at the baseline and after 12 months of treatment in lateral view; C): Case 3: Comparison of the clinical case at the baseline and after 12 months of treatment in occlusal view.*

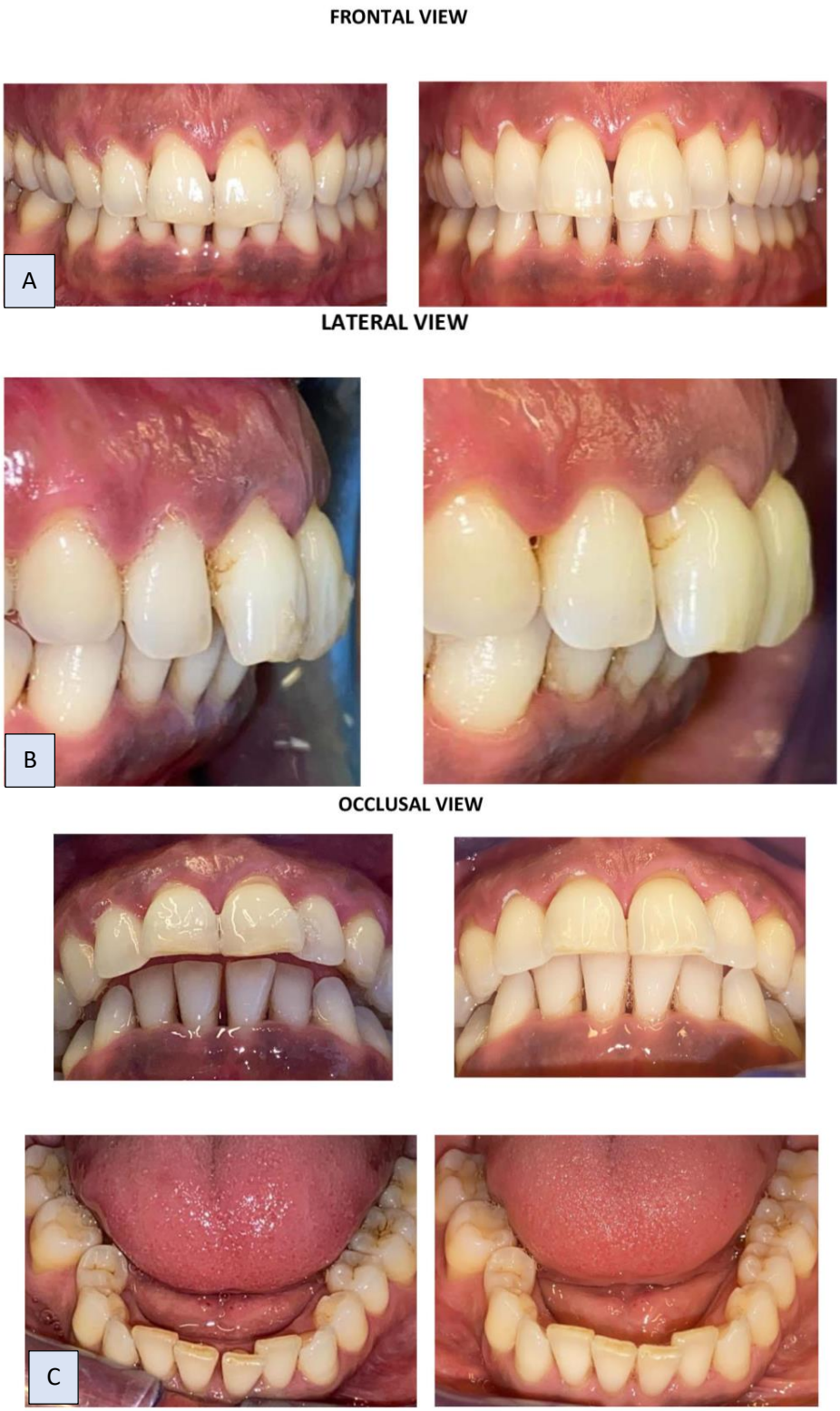

Fig. 10. *A): Case 4: Comparison of the clinical case at the baseline and after 12 months of treatment in frontal view; B): Case 4: Comparison of the case at the baseline and after 12 months in lateral view; C): Case 4: Comparison of the clinical case at the baseline and after 12 months of treatment in occlusal view.*

DISCUSSION

The authors observed improvement in dental and periodontal status in these clinical cases after elastodontic myofunctional therapy. After etiological therapy of periodontitis, it has been decided to implement an innovative myofunctional trainer.

Although more than a century has passed since the first publication of Karolyi, (27) which involved the forces of occlusion in the behavior of periodontal tissues, deep-rooted controversy about the role of occlusion in the development/progression of gingivitis and periodontitis remains. Some studies propose that traumatogenic occlusal forces are related to the initiation and/or progression of periodontal disease (28, 29). Conversely, other studies find no association between trauma from occlusion and periodontal disease (30-32).

During the 1960s and early 1970s, Glickman et al. (33, 34) proposed that occlusal trauma acted as a co-destructive agent, influencing the spread of inflammatory gingival exudate directly to the periodontal ligament, eliciting a combined lesion of trauma from occlusion and periodontitis. Despite extensive research over many decades, such defying question relates to the role of occlusion in the etiology and pathogenesis of periodontitis, is still not completely understood (6). By analyzing data from the literature, we can summarise the following to date:

- there is no definitive scientific evidence that trauma from occlusion causes or accelerates the progression of gingivitis or periodontitis;
- the periodontal ligament physiologically adapts to increased occlusal loading by resorption of the alveolar crestal bone, resulting in increased tooth mobility. This occlusal trauma is reversible;
- occlusal trauma is a cofactor that increases the rate of progression of an existing periodontal disease;
- there is a place for occlusal therapy in the management of periodontitis, especially when related to the patient's comfort and function;
- occlusal therapy is not a substitute for conventional methods of resolving plaque-induced inflammation.

The myofunctional trainer applied provided an effect of oral muscles re-education through a series of myofunctional exercises to start modifying and correcting the functions of swallowing, breathing, and chewing. In addition, it allowed muscular reprogramming and the modification of the previous motor engram (35, 36). The device presented a reference point for the tongue muscles to allow, during daily myofunctional exercises, but even at rest, a correct positioning up and behind the upper incisors (37, 38). The appliance showed its arch reconfiguration and intrusive effect, which have a decisive role in PTM improvement.

The elastic myofunctional trainer has restored a correct "neutral corridor" of the arches allowing the correct positioning of the teeth in a three-dimensional position not to receive oblique and deflecting forces. This result, thanks to the device's elastodontic action, was, in our opinion, due to the combined effect of the intrusive action by the horizontal plane, more rigid, on which the arches lay down, and the retraction action carried out by the vertical flanges.

The most relevant result has been achieved in the frontal sectors where the PTM and diastema disappeared, improving the smile with a very satisfactory aesthetic effect.

We want to point out that this therapeutic approach undoubtedly has advantages over other options (i.e., traditional orthodontics) that may be just as effective; first of all, the mini-invasiveness that, from the periodontal point of view, has no impact on the daily hygienic procedures (39, 40).

As for all medical acts (never 100% predictable), a value is also that of the reversibility of the treatment. Especially in cases like those presented, characterized by parafunctional habits, the action through traditional fixed orthodontic procedures, would certainly be less easily "reversible" than the removable device used at night (41, 42).

From the cost-benefit ratio point of view, which should always be considered in the ethics of our therapeutic choices, the simplified and mini-invasive device used here is undoubtedly brilliant.

CONCLUSION

Based on all the previous considerations, the authors want to focus their attention on the use of these new devices in cases where there is a possible traumatic and/or parafunctional component to support periodontal lesions like PTM and diastema.

"Three-dimensional byte": an elastic medical silicone device consisting of a monobloc that wraps both arches with a horizontal plane (more rigid) on which the two arches are leveled according to a predetermined anatomical plane and two vertical flanges, one internal and one external (softer); aimed at neutralizing the abnormal muscular forces that insist on the arches.

The use of three-dimensional silicone bytes during the night, without any impact on hygiene practice, could support and complete the anti-infective periodontal therapy with an occlusal stabilization activity, especially in occlusal trauma is evident and/or there are dental migrations, i.e., in stage 4 periodontitis.

The effect of this therapy additional is:

- greater stability of the result, the recovery of a harmonic occlusion, the recovery of acceptable aesthetics;
- the correction of long-time altered and never corrected muscle functions such as atypical swallowing and oral breathing that may have been the cause of the early onset and severity of periodontal lesions.

Further studies are needed to better investigate these innovative therapeutic procedures.

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Conflict of Interest

The authors declare no conflict of interest.

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Review

MYOSITIS OSSIFICANS: A REVIEW ON A BIOLOGICAL BASIS

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ABSTRACT

Myositis ossificans (MO) is a rare benign ossifying disease that most frequently affects young people. It is characterised by the localised production of heterotopic bone with cartilage in extraskeletal soft tissue. In most situations, it is impossible to pinpoint a cause. The patient's trauma history, imaging appearance, histological investigation and clinical symptoms are often used to diagnose MO. This review was performed to search the biological basis of MO. The research studies were collected from PubMed, Science Direct and Google Scholar. After proper assessment and evaluation, 14 articles were included in the study. The study also covers the diagnosis, management and treatment interventions that will be helpful in the understanding of MO.

KEYWORDS: *myositis ossificans, MO, skeletal muscles, chondrocytes, osteoblasts*

INTRODUCTION

In myositis ossificans (MO), lamellar bone forms around soft tissues, particularly the major skeletal muscles in the arms and thighs. Neurogenic and non-neurogenic acquired MO can be distinguished from one another. The latter can be further broken down into idiopathic/pseudomalignant as well as post-traumatic restricted MO (60–75% of patients). Especially severe direct injuries and persistent minor trauma, including maltreatment, can lead to post-traumatic MO. Although the pathophysiology is still not fully established, the current theory is that an "endothelial-mesenchymal transition" occurs. Following injury, ischemia, or inflammation, mesenchymal stem cells undergo this transformation, which is regulated by a cytokine cascade, into chondrocytes and osteoblasts (1).

In the first four weeks of its life, MO has a rapid overgrowth. In the centre of the lesion, osteoblasts and chondrocytes are now producing a new osteoid matrix. Whenever the lesion ceases progressing, in between the fourth and tenth week, the characteristic peripheral calcifications can be seen. The so-called "zonal pattern organisation" can be seen radiographically and histologically once the lesion has matured. They have a growing core region of fibroblasts with the potential for necrosis and bleeding. An "intermediate zone of immature osteoid tissue" and cartilage follows this.

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Enchondral ossification and a lamellar layer of mature bone promote this process (2, 3).

Clinically, the affected location swells painfully, and the surrounding joint's range of motion is limited. In most circumstances, a focused anamnesis enables a speedy diagnosis. However, the possibility of bone or soft tissue neoplasms must be considered when a tumour is developing without a history of trauma (4). The "centripetal calcifications" of the lesion can be identified via radiological imaging, bypassing the cortical bone; however, in the early weeks, these signs may not be present. The development of "pleomorphic osteoblasts" along with atypical nuclei and mitosis can be deceiving in ambiguous lesions if the biopsy is carried out too early or within the core lesion (5). As a result, MO might be difficult to distinguish from malignancies in the early stages. A review on MO is performed since this disease is not fully understood.

MATERIALS AND METHODS

The Science Direct and PubMed search engines and additional published articles from Google Scholar were used to conduct a database search. A specially created Performa was used to summarise the final publications.

RESULTS

Fourteen publications in all were taken into account for the systemic review and meta-analysis. Gender preference and age of engagement were incorporated in the forest mapping for demographics.

DISCUSSION

Pathophysiology

It is not fully understood how MO production occurs pathophysiologically. It is thought to happen due to fibroblasts diffusing improperly into osteogenic cells. Researchers have shown that the deregulated activity of local stem cells as a reaction to tissue injury with subsequent inflammation is the cause of the physiological response of heterotopic bone production. Recent research has shown that the "endothelial-mesenchymal transition" mechanism may be necessary for extraskeletal bone production. Injury to the skeletal muscles triggers a local inflammatory cascade. Cytokines are released as a result of this. These cytokines affect the vascular endothelial cells in skeletal muscle, causing them to undergo an "endothelial-mesenchymal transition". Whenever introduced to an "inflammatory-rich environment", these "endothelial-derived mesenchymal stem cells" may develop into chondrocytes or osteoblasts. The development of endochondral bone will then occur in extraskeletal tissue involving chondrocytes (6).

When a traumatic experience is evident, the term "traumatic MO" (TMO) is preferred. TMO makes up 60 to 75% of cases of MO and is the most prevalent kind (4). The diagnosis is relatively straightforward when a patient with TMO presents a typical history of trauma and an evident calcification on imaging. However, there have been several documented MO occurrences in individuals with no apparent history of trauma, which led some people to assume malignancy. As they mirror other benign or malignant lesions, such as abnormal parosteal osteochondromatous proliferation, melorheostosis, recurrent giant cell tumour, parosteal osteosarcoma, extraskeletal osteosarcoma, and soft tissue sarcoma, the imaging characteristics of MO are non-diagnostic (7).

Stages of myositis ossificans

Three distinct stages characterise MO. First, the proliferation comprises mesenchymal cells, secreting a myxoid matrix during the acute phase (i.e. first week). As fibroblasts undergo many mitoses at this stage, the mass appears pseudo-fibrosarcomatous. Histologically speaking, osteoblasts develop into fibroblasts during the subacute period (the next two weeks). They produce an osteoid matrix at the edge of the first myxoid zone. It seems pseudo-osteosarcomatous as a result. Finally, a precise histological diagnosis can be made during the maturation period (2–5 weeks) (8).

Osteosarcoma must be ruled out due to bone growth and similar epidemiology. Imaging is crucial for detecting MO in its early stages. Radiographs, however, are frequently negative early in the disease. An incorrect diagnosis of sarcoma may result from a biopsy performed early in MO. Conversely, a real sarcoma could go unnoticed if the biopsy is postponed.

The characteristic features of this condition, such as the detachment of the mass from the nearby cortex and the reduced attenuation of the mass's core, are best detected with computerised axial tomography (9).

Laboratory testing

Numerous writers have examined the usefulness of laboratory tests on serum. There is presently no diagnostic test, but a number of correlations have been found. Initial levels of "serum alkaline phosphatase (SAP)" remain normal. But after three weeks, it acutely elevates concurrently with bone growth. Particularly in people with clinically severe MO, this happens. During the initial phases of MO, acute phase reactants such as the prostagandin-E2 serum level, erythrocyte sedimentation rate, and C-reactive protein level are raised. Just before spike in SAP, the serum calcium value normally drops for a brief time before returning to normal. If muscle is involved, the amount of creatine phosphokinase is usually increased. And, unlike SAP, it might be able to forecast how severe and how soon MO will develop (10).

Imaging studies

Imaging investigations are a crucial component of the MO diagnosis procedure. In many circumstances, radiographic evidence are adequate to make the diagnosis. To make a definitive diagnosis, though, more advanced imaging techniques such a CT scan, MRI, or bone scintigraphy may be required (6). In order to accurately characterise the lesion prior to surgery and to better define the pattern of calcification, CT scans are preferred to radiographs. If requested quickly and early in the disease's progression, a bone scan can show higher uptake in the affected area and is thought to be particularly sensitive. However, there isn't enough support in the literature to prove how useful bone scintigraphy is in deciding when to perform surgery. Previously, it has been hypothesised that levels of SAP may peak 3 weeks after the primary injury in the context of traumatic MO. At around 10 weeks, it can take on any value that is more than 10 times the upper limit. By 18 weeks, it will have returned to normal levels. However, because the SAP level might remain normal even in active lesions, it cannot accurately assess the maturity as well as activity of a lesion. As a result, it's important to interpret SAP values in both the clinical as well as radiographic settings (11).

Diagnosis and treatment methods

Histopathological analysis is usually used to get a diagnosis. It could be challenging to distinguish a MO from a sarcoma based only on histology data. The clinical as well as radiological data' correlation is crucial in these situations. Once the confirmation of MO has been made by excision, additional treatment is not required. Understanding the aetiology and pathophysiology of MO, an uncommon clinical condition, helps spare the patient the concern of having a suspected neoplasm (9).

Surgical treatment

Surgery is not always the first course of treatment for MO ossificans because it is typically a self-limiting condition. The development of intractable pain, decreased range of motion compromising quality of life, neurovascular deterioration brought on by compressive impact, and failure of non-surgical approaches to treat the symptoms are all valid criteria for surgical care of MO. When surgery is necessary, the lesion is removed after it has fully developed. The laboratory (i.e., SAP level), clinical, plus radiographic elements should all be considered when making this choice (11).

Symptomatic MO lesions are typically the only ones that require surgical excision. It is advised to do an excision with precise resection margins because recurrence has been recorded. The diagnosis of MO is difficult when symptoms are not linked to trauma. The MRI results might point to a malignant fibrous histiocytoma-like mesenchymal tumour (12).

Non-surgical treatment

Nonsurgical intervention aims to reduce symptoms while maintaining function. Because MO is typically a self-limiting and self-resolving phase, nonsurgical therapy is frequently effective. Even though evidence is lacking, the finding that individuals with bleeding problems are more likely to have MO supports the idea that MO is linked to hematoma development, whether or not there is concurrent periosteal trauma. Therefore, it makes sense to treat muscle damage as soon as possible in order to prevent hematoma growth and preserve function.

It has been advise a brief period of relative immobilisation for 3 to 7 days together with rest, ice, compression, and

elevation for the first therapy of muscle damage. Crutches may help to reduce hematoma development by allowing the injured region to rest. Cryotherapy, which involves applying cold for 15 to 20 minutes every 30 to 60 minutes, can reduce intramuscular blood circulation by 50%. In the very earlier phases, aggressive physical treatment should be avoided to prevent symptom worsening (6).

Within a "pain-free arc of motion", supported range-of-motion activities can start as soon as 48 to 72 hours after surgery. An exercise programme that progresses gradually starts with isometric training, then moves on to isotonic training, isokinetic activities, and dynamic exercises. Aspiration could help large fluctuant hematomas that are symptomatic. Active range-of-motion as well as resistive strengthening activities are crucial to preserving and enhancing joint range of motion and functionality in more advanced lesions (13).

There is little pharmacological usage in the prevention of MO following injury. It was mostly inferred from research looking at the growth of heterotopic bone following hip surgery with pelvic trauma. Nevertheless, two doses of pamidronate were linked to recovery in both the clinical and radiographic symptoms reported in a case study of traumatic MO development in an athlete (14).

CONCLUSION

Although the cause of myositis ossificans is unknown, the clinical appearance is often marked by an ossifying soft-tissue tumour. Advanced cross-sectional imaging by itself can be vague and may resemble more nefarious causes. In order to provide an appropriate diagnosis, the study of a suspected soft-tissue tumour frequently requires the use of various imaging modalities. A biopsy may be necessary in cases where imaging is unable to provide a histologic diagnosis. On the other hand, histopathology differs according on evolutionary stage. Since a precise diagnosis is essential to a good outcome, myositis ossificans therapy is complicated and frequently undertaken in a multidisciplinary manner.

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that chronic MPS, which requires more difficult therapy, affects most patients who receive medical treatment. Therefore, a thorough history should be obtained from the patient. A thorough clinical assessment should be conducted to determine the best therapy strategy and, ultimately, deactivate TRPs (2).

When there is no definitive description, epidemiology, pathophysiology, or prognosis of MPS, there are basic problems with diagnosis and possible research (3). This paper aims to review MPS's empirical investigations and parts comprehensively. Since there is still some debate on a lot of the subject, publications and the medical literature were incorporated to create consensus on the MPS components.

MATERIALS AND METHODS

Multiple keyword combinations were searched for systematically across numerous databases. Included keywords: "pain from fascial tightness." Since 2013, "myofascial pain syndrome" has been searched in the title or abstract of systematic reviews, meta-analyses, and randomised controlled trials. PUBMED was one of the databases used. Between June 2013 and June 2021, all searches were conducted. There were only English-language publications listed. The scoping reviews in the research adhere to PRISMA principles. After a thorough examination, 20 studies were found relevant and were included in this study.

RESULTS AND DISCUSSION

Multiple sites of musculoskeletal pain and sensitivity linked to painful points are frequently used in clinical practice to identify MPS. Aching and intense pain may develop following trauma, excessive usage, or sedentarism. According to research, active employees are less prone than sedentary ones to experience MPS symptoms. The pain may be produced or made worse by palpating a TrP. These results, nevertheless, are not exclusive to MPS. They were also present in "normal" participants in controlled research. According to the literature, 54% of women and 45% of men in the general population have TrPs. Between 37% and 65% of people are thought to experience myofascial discomfort. All of this costs the United States $47 billion per year. One of the most commonly undiagnosed, untreated, and misunderstood causes of the common aches and pains that affect all people is MPS. Though it involves pain and lacks a distinct pathology, MPS is nevertheless often regarded as fiction or combined with psychosomatic diseases (4, 5).

Epidemiology

13.5 to 47% of people worldwide appear to experience chronic muscular pain. Chronic muscular pain is more common in the elderly, women than males, and Caucasians than Blacks. Additionally, it affects manual labourers and those from less wealthy areas more frequently than highly affluent regions (6).

The average MPS prevalence among people with musculoskeletal pain ranges from 30% to 93%. An estimated 46.1% to 27.4% of people have activated trigger sites, and the absence of MPS-defining criteria is to blame for this substantial heterogeneity (7). In addition, 85% of the elderly (those over 65) are affected. Compared to males, women are more susceptible to trigger point activation. The hormonal variations throughout a woman's menstrual cycle are to blame for this (2).

Aetiology

There is still much to learn about the aetiology of MPS. Adhesion could occur in muscles and fascia that have aseptic inflammation. According to current theories, the compression of inflammatory oedema tissues and the activation of sensory neurons by an algogenic chemical in the inflammatory environment cause MPS pain. MPS typically affects those who engage in prolonged low-intensity static activities, such as musicians, dentists, office employees, and other professionals. The residual strain created by the constant static pressure of long-term uncomfortable working positions disturbs the skin's blood circulation. As a result, metabolites build up and excite the nerve terminals in the periphery; this results in sensory nerve dysfunction, which includes allodynia, hyperalgesia, and the spread of referred pain.

Predisposing variables and risk factors are two categories into which the reasons for the onset of MTrP may be subdivided.

The following are some predisposing factors:
1). acute muscular damage or ongoing muscle tension;
2). mental stress, overexertion, or inadequate sleep;
3). muscle cooling to a great extent.
These are some risk factors:
1). metabolic abnormalities and hormonal changes, including hypothyroidism and menopause;
2). vitamin b and iron deficiencies;
3). chronic infection;
4). localised chronic instability of biomechanics;
5) immune disorders.

Pathogenesis

Myofascial pain and the development of TRPs have uncertain pathways. An irregular rise in acetylcholine at the motor end-plate may cause the TRPs and result in a regular muscular contraction; this can be made worse by localised acute or chronic overload in traumatic or micro-traumatic circumstances. Constant muscular contraction thus raises local ischemia and energy expenditure. The alterations may result in pain or hypersensitivity by boosting the local discharge of nociceptive chemicals. Substance P, calcitonin related peptides, and pro-inflammatory cytokines are some of these (8, 9). Sometimes the chemicals can move to nearby spinal cord segments and result in referred pain with TRPs (10). Refractory referred pain can be caused by central pain sensitisation, which can make neurons more excitable and cause the neuronal receptive fields to expand (11). Stecco et al. proposed that muscular fascia, under overload and trauma, may experience pathological alteration, resulting in the biomechanical modification of muscles (12). Eventually, this causes muscles' flexibility and force of contraction to decrease (13). The pathogenic change may be made worse by the inflammatory changes, resulting in or intensifying pain. The aberrant changes in myofibrils, fibroblasts, and extracellular matrix may be connected to the pathological transformation of the muscular fascia (14).

History and physical examination

Most MPS patients experience localised muscular pain and transferred pain in predictable patterns. For instance, myofascial pain in the infraspinatus muscle typically affects the anterior deltoid region and the radial side of the hand. Acute or gradual pain onset is also possible. After muscle strains or other overuse activities, symptoms can develop in some patients. On the contrary, other patients experienced symptoms without any obvious causes.

During a physical examination, the afflicted muscles typically have taut bands and TrPs. The palpable belly of constricted muscles is the taut band. TrP is a prominent tender point on the taut band that can be compressed to exacerbate local and transferred pain. TrPs are categorised as either active or latent. Patients without symptoms can nevertheless have latent TrPs, although active TrPs are only seen in symptomatic patients (7).

Clinical signs and symptoms typically identify MPS. For MPS, there are numerous clinical diagnostic standards. The majority of criteria have been agreed upon, including the following: TrP, recognition of pain while palpating the TrP, particular pain referral mechanism, and local twitch response.

Evaluation

MPS is a diagnosed medical disorder. However, one can confirm the diagnosis using medical technology (such as electromyography and ultrasound). Electromyography is typically used to identify end-plate noise in TrPs. When using diagnosis ultrasound, the region with TrPs may develop more hypoechoic compared to the surrounding muscles (15, 16).

The significance of employing electrophysiological tests and medical imaging is their ability to rule out other musculoskeletal problems. For example, bursitis and tendinopathy can be ruled out with diagnostic ultrasonography. Foraminal stenosis, spondylosis, and scoliosis are just a few structural bone flaws found with a plain radiograph. Neuromuscular illnesses can be examined with electromyography. Additionally, one can perform laboratory tests to find possible nutritional and hormonal deficiencies related to MPS, like hypothyroidism or vitamin D deficiency (16, 17).

Differential diagnosis

Regional pain is a common symptom of several illnesses, including MPS. The common illnesses that a clinical examination and assessment should rule out are tendinopathy, arthritis, bursitis, as well as nerve entrapment. The region and pattern of pain are key factors in the differential diagnosis. For instance, patients with medial elbow pain should be examined for cubital tunnel syndrome or medial epicondylitis.

Fibromyalgia needs to be taken into account for people with persistent multiple TrPs. A disorder known as fibromyalgia causes widespread chronic discomfort. Fibromyalgia and persistent MPS are different to fibromyalgia in two key ways. First, patients with fibromyalgia experience transferred pain and widespread muscle tender spots without taut bands. Physicians should, therefore, thoroughly palpate the location of the pain. Second, fibromyalgia patients frequently have comorbid diseases such as depression, sleeplessness, vertigo, dysmenorrhea, and numbness. Rarely do these symptoms appear with MPS (16, 17).

Treatment and management

Treatment for MPS aims to reduce discomfort and address contributing causative factors. There are numerous ways to treat MPS. Several treatments are being utilised to treat myofascial trigger points, including massage, electrical stimulation, stretching, dry needling/injections, cold laser therapy, and ultrasound. Myofascial trigger points can be relaxed with various massage techniques, including active rhythmic release, trigger point pressure release, and passive rhythmic release (18). The basic idea behind treating trigger points is to temporarily release them to lessen pain and temporarily improve muscular movement; this is frequently achieved with massage, heat (direct or by ultrasound), and needling and injection for persistent trigger points. Stretching and simulation, which effectively work the muscle, come next (16, 17).

Additionally, all patients should receive education on ergonomic modification, including stretching exercises. Muscle relaxants and nonsteroidal anti-inflammatory medications are frequently recommended. However, the available data on their efficacy are still conflicting. In MPS management, physical modalities play a significant part. In numerous studies, extracorporeal shockwave and low-power lasers were reported to lessen pain in MPS patients dramatically. Transcutaneous electrical nerve stimulation can temporarily reduce pain but not permanently. For the treatment of MPS, therapeutic ultrasonography is frequently employed. However, there is still conflicting information about its positive impact (18). Clinicians may need to utilise more invasive techniques to manage MPS in some patients.

In order to release TrPs, doctors can utilise the helpful technique of dry needling. To further reduce discomfort, doctors can inject TrP with a local anaesthetic. MPS may potentially be treated with acupuncture (19). Additionally, eliminating perpetuating factors is essential for effective MPS care, particularly in cases of chronic MPS. For instance, people with vitamin D deficiency may not respond well to standard therapies. Therefore, doctors should prescribe patients vitamin D supplements and other treatments (16, 17).

CONCLUSION

The pathological condition of imbalance in a natural process that results in MPS is thought to be caused by a disturbed biomechanical interaction and manifested in the fundamental characteristics of the fascia. Reports show that trigger points, tension, and pain characterise MPS, and myofibroblasts influence myofascial tension that persists. Furthermore, sedentary living predisposes to MPS and its recurrence, whereas movement and mechanical interventions manage and protect from MPS.

Recent advancements in experimental research have yielded copious information which can be used to comprehend the molecular pathways underlying myofascial pain syndrome. Therefore, the only way to find novel therapies is to understand the molecular and subcellular mechanisms underlying this condition fully. This increased understanding might also help current treatment plans be optimised. However, numerous unanswered questions regarding the signalling mechanisms are still required, demanding more research.

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tivity, the muscle releases irisin, IL-15, leukaemia inhibitory factor (LIF), brain-derived neurotrophic factor (BDNF), fibroblast growth factor-21 (FGF-21), and SPARC, counteracting the synthesis of adipose tissue.
Myokines such as IL-6, IL-8, IL-15, IL-4, IL-7, myostatin, FGF, LIF, BDNF, erythropoietin (EPO), and brain-like growth factor insulin-1 (IGF-1) regulate the energy process by acting on carbohydrate and lipid metabolism and induce the production of biologically active molecules. Myokines protect us from cardiovascular diseases, obesity, and diabetes (15-18). The synthesis of myokines is reduced in physical inactivity, worsening the quality of life and the immune response. Physical exercise causes the synthesis of myokines, improving brain function. BDNF, upregulated by muscle-produced cathepsin B, is a well-studied myokine that regulates neurogenesis and synaptic function, although the exact mechanisms are still unclear. Skeletal muscle activity requires adenosine triphosphate (ATP), regulates myokine expression, increases oxidative stress, and mediates the neurobiological response. The production of myokines leads to an endocrine effect on metabolism, thermogenesis, inhibition of inflammation, mitochondrial biogenesis, and fatty acid oxidation. Myokines promote angiogenesis and represent a potential therapeutic target, although further investigation is needed.

CONCLUSION

In conclusion, myokines are a new class of functional molecules connected from a metabolic point of view to muscle, bone and adipose tissues and represent a new chapter in the physiology and pathology of human medicine.

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Letter to the Editor

GORHAM-STOUT SYNDROME

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ABSTRACT

Gorham-Stout syndrome (GSS) is a relatively rare condition with no known cause. It is distinguished by the breakdown of osseous matrices and the growth of vascular structures, leading to bone loss and subsequent fractures. Even though there has been much research on the disease's pathogenetic pathways, its aetiology is still unclear, and there are a few different views about what caused it. The disease can affect the patient's head, lower and upper extremities, vertebrae, and pelvis to varying degrees. The syndrome can also affect numerous bones at the same time. Pain, impaired functioning, and inflammation of the affected region are the hallmarks of a patient's clinical picture of GSS. However, asymptomatic cases have been described, as have cases in which the diagnosis was confirmed after pathologic fractures. In this concise review, we will discuss the hypotheses concerning the disease's origin, the clinical manifestations, the diagnostic strategy, and the therapy choices available for this extremely uncommon condition.

KEYWORDS: *lymphatic, osteolysis, bone, resorption, vanishing disease*

INTRODUCTION

A rare ailment distinguished by spontaneous and increasing bone resorption is referred to as Gorham-Stout syndrome (GSS), enormous osteolysis, phantom bone disease, and vanishing disease. Each of these terms is a synonym for the other. It has not been determined what causes the condition, despite the significant research that has been done on the disease's pathogenetic pathways. Jackson, in the year 1838, was the first person to describe this phenomenon. He did so in the context of a case involving a young man whose humerus was slowly wasting away (1). In addition, Gorham and Stout authored a study in 1955 that associated the severe osteolysis observed in the condition with hemangiomatosis. This paper appears to have played a significant part in vanishing bone disease, also known as "Gorham-Stout syndrome" (2).

It is a sickness that has an unpredictable progression and might lead to serious problems. There is no connection between gender, ethnic background, environmental elements, or contagious or environmental health conditions. It is not known what causes the pathophysiology. One of the hypotheses claimed that osteoclasts play a significant role as well as endothelial cells (3). In a systematic review, Faruqi T. et al. (3) reported that TNFα and IL-6 are implicated in GSS since

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they stimulate osteoclast formation with excessive osteolysis. Macrophages also produce VEGF, which stimulates the proliferation of endothelial cells. Furthermore, the levels of IL-6 were significantly higher in the serum of GSS patients.

Clinically GSS could manifest itself in several bones, most frequently those in the craniofacial region and the upper arms, but any bone can be affected. The location of the affected area is directly related to the complaints. In most cases, the disease manifests with swelling, discomfort, and a restriction in the affected region's functional capacity. However, the condition can sometimes be asymptomatic unless a pathological fracture occurs (4).

According to Hardegger et al. (5), of the five kinds of osteolysis, this illness is classified as type IV: Type I is a monocentric illness with autosomal dominant inheritance, Type II is a monocentric disease with autosomal recessive inheritance, Type III is nonhereditary multicentric osteolysis with nephropathy, and Type V is Winchester syndrome. Osteolysis and increasing bone resorption are both characteristics that are indicative of the condition. Ribs, vertebrae, pelvis, cerebral vault, clavicle, and mandibular are some typical sites impacted by this condition. In normal circumstances, the bones involved are more likely to have osteopenia and fractures, in addition to swelling and pain. Depending on the degree of the condition, patients might anticipate experiencing both disfigurement and impaired functioning. Most diagnoses are made in patients under 40, and the symptoms and complications can range from moderate to life-threatening. The prognosis is difficult to predict, and GSS can sometimes be accompanied by several catastrophic complications (6).

Etiopathology

In 1987, Dickson et al. (7), after researching the cytochemistry of both alkaline and acid phosphatase, concluded that mononuclear phagocytes, multinuclear osteoclasts, and the vascular endothelium are all involved in bone resorption in this condition. Furthermore, in 1996, Devlin et al. (8) attributed this massive osteolysis to the increased activity of the osteoclasts. In this process, interleukin-6 plays a critical role, as its levels are elevated in the serum of patients suffering from GSS in early stages (8). In addition, an interesting finding made by Korsi et al. in 1998 was that the disease manifested itself in a patient who lacked calcitonin, a hormone that possesses antiosteoclastic activity; this was a consequence of the absence of C-cells in the thyroid gland that the patient possessed (9). On the other hand, Moller et al. (10) mentioned the unprecedented frequency of stimulated osteoclasts as a factor responsible for the development of GSS. At the same time, Hirayama et al. (11) concluded that the increased number of circulating osteoclasts is the repercussion of the heightened susceptibility of their precursors to humoral factors that contribute to osteoclast formation.

Clinical features

Patients, whose age ranges from 1 month to 75 years, can have the condition in one or more of their bones (12). The disease typically affects people under 40 (13), and there does not appear to be an epidemiologic association between race, gender, or geography (14). However, they found that men had a "predilection" for the illness (14). Although GSS can affect many bones, most case reports focus on the upper extremity and the craniofacial region (15). The femur, however, was the primary damaged bone in a case series (14). Initial x-rays show radiological alterations that resemble patchy osteoporosis. Later, an appendicular skeleton in the upper and lower limbs experiences concentric shrinking and bone mass loss, resulting in bone deformity. Eventually, the bone begins to resorb almost entirely, giving rise to the known "vanishing bone" disease (16).

The most common symptoms of vanishing bone disease among patients are pain, impaired functioning, and swelling in the affected area, while asymptomatic cases and situations in which the diagnosis was confirmed after a pathological fracture have also been reported (14). Furthermore, the syndrome's complications risk being fatal, especially when chest complications arise. Pulmonary oedema and chylothorax, which are complications of GSS in a proportion as high as 17%, are two conditions that can significantly affect respiratory function. Chylothorax can happen due to the afflicted thoracic bone intrusion of the thoracic duct or by the extension of lymphangiectasia into the pleural cavity (17). Additionally, there have been few reports, bone infections leading to septic shock (18), spinal cord participation and paraplegia from vertebral lesions, cerebrospinal fluid leaking, and meningitis from damaged skull bones (19).

Diagnosis

The syndrome is difficult to diagnose and requires the assistance of multiple diagnostic examinations. A diagnosis cannot be made based on blood tests because they are typically normal, except for alkaline phosphatase, which may have a modest elevation (17).

Plain radiographs, bone scans, computed tomography (20), and magnetic resonance imaging (i.e. MRI) may also contribute to the diagnostic process. In the beginning, plain X-rays show radiolucent foci in the intramedullary or

subcortical regions. Later, a slowly progressive dissolution, fracture, fragmentation, and disappearance of a portion of a bone become visible, along with constriction or "pointing" of the surviving osseous tissue. CT and MRIs better define the extension of lesions (21).

The histological evaluation affirms the disease, and the biopsy reveals nonmalignant overexpression of small vessels. Heffez et al. proposed the eight diagnostic criteria of GSS: (A) presence of angiomatous tissue; (B) absence of atypia; (C) lack of dystrophic calcifications; (D) indication of local bone progressive remineralization; (E) nonexpansive, non-ulcerative lesion; (F) loss of visceral involvement; (G) osteolytic computed tomography pattern; and (H) lack of hereditary, energy metabolism, neoplastic, autoimmune, and contagious pattern. The diagnosis of GSS should only be considered after other possible reasons for osteolysis, such as infection, malignancy, inflammatory and endocrine problems, have been ruled out (22, 23).

Hereditary multicentric osteolysis, osteolysis with nephrotic syndrome, osteomyelitis, rheumatoid, osteolysis due to eosinophilic granuloma, intracoronary malignancies, hyperparathyroidism, and osteolysis due to disorders affecting the central nervous system, such as syringomyelia and tabes dorsalis are all included in the differential diagnosis of the disease (24).

Treatment

Numerous therapeutic options have been proposed, the effectiveness of which varies depending on the aetiology of the condition, which is why treatment is still a matter of research. Three primary approaches can be used to treat the syndrome: medical therapy, radiation therapy, and surgical procedures (25, 26).

In the first area, bisphosphonates, which have an antiosteolytic action, have been employed to treat the illness (27). In addition, some additional pharmacologic drugs, such as vitamin D, calcium, interferon, adrenal extracts, and androgens, have been proposed.

Patients with substantial symptomatic lesions with chronic debilitating functional instabilities are preferable candidates for radiation therapy and surgical intervention. The use of radiotherapy in therapeutic doses considered on the lower end of the spectrum appears to produce excellent results, with only a limited number of long-term problems (23). However, radiation may cause major adverse effects, such as secondary malignancies and growth limitations in children and adolescents who get high-dose radiation treatments. Therefore, in the final stage, especially when fractures arise, orthopedic and maxillofacial surgery is needed, the lesion is removed, and then bone grafts and/or prostheses are used to reconstruct the affected area. Also, general surgeons are involved, especially for chest drainage, thorax duct conjugation, and pleural treatment (28).

CONCLUSION

GSS is an extremely uncommon condition that can grow in ways that are difficult to anticipate and can cause serious problems. At this time, their osteoclast activation and endothelial cell proliferation are the main targets of current studies on the onset of GSS. The exclusion of other causes is the main axis to reach the diagnosis. In addition, there is no established treatment protocol, and research is still ongoing in this area.

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