European Journal of Musculoskeletal Diseases
ISSN 2038-4106/2022

Article

CALCIFIC POST-EPIDURAL STEROID INFILTRATION EPIDURITIS, WHEN AND IF TO TREAT WITH OZONE THERAPY

M. Bonetti[1], G. Bragaglio[2], G. Guarino[2], I. Marchina[2], G. Ottaviani[3] and M. Moretti[2]

[1]Neuroradiology Service of the Clinical Institute of the City of Brescia, Via Bartolomeo Gualla 15, 25128 Brescia, Italy;
[2]Oberdan Specialist Clinic, Via Guglielmo Oberdan 126, 25128 Brescia, Italy;
[3]Department of Emergency and Urgency Spedali Civili of Brescia, Piazzale Spedali Civili 1, 25123, Brescia, Italy.

Correspondence to:
Matteo Bonetti, MD
Neuroradiology Service of the Clinical Institute of the City of Brescia
Via Bartolomeno Gualla 15, 25128 Brescia, Italy
E-mail: dottorbonetti@gmail.com

ABSTRACT

Epidural administration of steroids in the treatment of acute or chronic low back pain has been taking place for over 30 years. Despite this, it is still a very controversial topic. Meta-analysis studies document the effectiveness of steroid procedures, although very serious complications can occur. The authors report their experience in the treatment with oxygen-ozone in three cases of calcific epiduritis post epidural infiltrations perform as a second-line treatment due to the ineffectiveness of this steroid therapy.

KEYWORDS: *oxygen ozone, epidural steroid infiltration, side effects, steroid infiltration, ozone therapy*

INTRODUCTION

Epidural steroid infiltrations are used in clinical practice in case of low back pain caused by sciatica (1-3). The main goal of the injection is to relieve pain. In fact, no action is taken on the main cause of the symptomatology which, in the majority of treated cases, consists of protrusions or herniated discs. Almost all doctors who use this practice agree that, while the effects of the injection are generally temporary, they can reduce symptoms for a period ranging from a week to a year. If the initial injection is effective for a patient, a maximum of three infiltrations per year can be delivered.

Although many studies document the short-term benefits of epidural steroid injections, the data on long-term efficacy are less convincing. Indeed, the results of lumbar epidural steroid injections continue to be a topic of debate.

The therapy, in most cases, is well tolerated by the patient, although minor, sometimes very serious complications are reported in the literature (4-26). Contraindications to carrying out this surgery are clotting disorders, pregnancy, local infections at the presumed entry site (osteomyelitis and spondylodiscitis), and overt allergy to local anesthetics and cortisone.

Received: 07 March, 2022
Accepted: 12 May, 2022

ISSN: 2038-4106

The epidural infiltration procedure is performed under local anesthesia through a percutaneous approach, and a 20 -25 G (gauge) spinal needle is inserted into the epidural space. After verifying the exact positioning of the needle, a mixture of anesthetic and cortisone is injected to obtain the therapeutic effect. In the thirty minutes following the procedure, the patient is kept lying down and under observation, then discharged in the absence of complications.

MATERIALS AND METHODS

In the period October 2019 - January 2021, three female patients aged between 59 and 66 years with a neuroradiological picture of calcific epiduritis post epidural steroid infiltrations came to our observation. In two of these patients, antalgic treatment with oxygen-ozone therapy under Computer Tomography (C.T.) guidance was performed.

Infiltration Technique

All treatments were done under C.T. guidance. After being informed about the procedure and possible complications, the patient signs the informed consent. Then, preliminary CT scans are performed with the patient prone to confirm the pathology and the level to be treated. At this point, the skin is disinfected using special preparations for general skin antisepsis (Citro jod 100 registration No. 1805 of the Italian Ministry of Health based on iodine polyvinylpyrrolidone).

A preliminary C.T. scan is performed to identify the skin approach point. Next, local anesthesia is delivered with ethyl chloride spray, and then, again using the C.T. guide, a spinal needle is inserted normally using needles of varying caliber between 22 and 25 G. The perfect positioning of the needle is checked with a C.T. scan. A 10 ml syringe in polyethylene is then filled with the gaseous mixture at 25 µg / ml concentration.

The gaseous mixture is then injected. Generally injecting a variable volume from 3 cc to 5 cc of the O2-O3 gaseous mixture. After the infiltration, other C.T. scans are performed to document the correct distribution of the gaseous mixture. All material used must be sterile and single use.

Case 1

B.G., a 66-year-old female, came to our observation requesting possible treatment with oxygen-ozone for discopathies L4-L5 and L5-S1. The CT survey in October 2019, highlights the presence of degenerative discopathies in L4-L5 and L5-S1 with associated circumferential protrusions of the partially calcified interposed annulus (Fig. 1, 2A-D).

The C.T. survey also highlights the presence of widespread calcifications along the dura case extended from L2 to S1, the result of previous infiltrative treatment with steroid epidurals (Figs. 1 - 2A-D). In fact, in the ten months preceding our recruitment, the patient had undergone three epidural infiltrations of steroids. The first infiltration was carried out in December 2018, the second one month later in late January, and the third in late April.

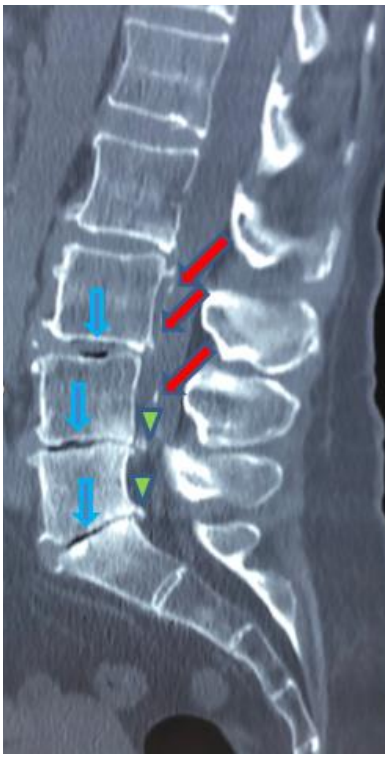

Fig. 1. *Lumbosacral CT sagittal reconstruction with bone algorithms: calcific epiduritis (red arrows), degenerative disc diseases L3-L4, L4-L5 and L5-S1 with vacuum disk (blue arrows) and partially L4-L5 and L5-S1 protrusions calcifications (arrowheads).*

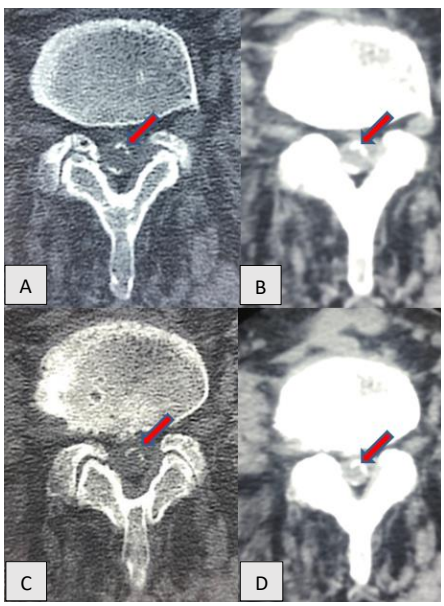

Fig. 2. *(A-D) Lumbosacral CT: axial scans with algorithms for both bone and parenchyma: calcific epiduritis (arrows).*

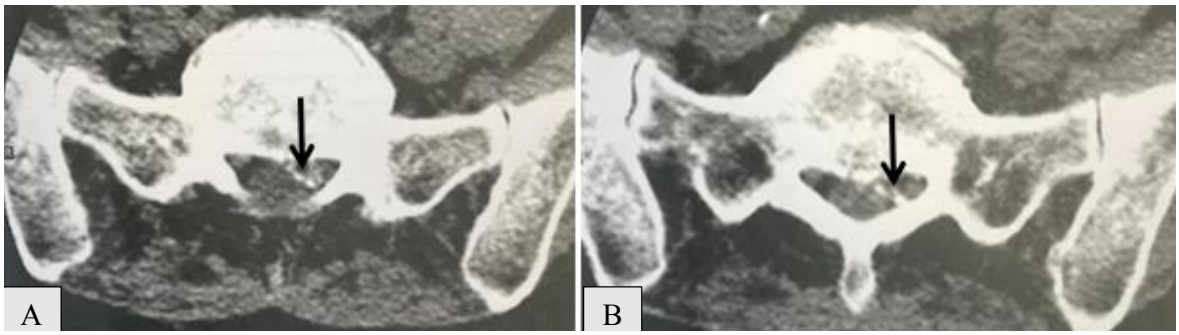

Fig. 3. *(A-B) Lumbosacral CT after three epidural steroid infiltrations: calcific epiduritis (arrows).*

The patient came to our attention in October 2019 due to the persistence of painful symptoms characterized by acute low back pain complicated by right sciatica in the distribution area of L5, despite previous steroid treatments.

At the time of our clinical evaluation, we decided to perform a lumbosacral C.T. scan before any therapeutic decision. On October 17, 2019 the patient underwent the Computerized Tomography exam requested by us, which highlights a picture of calcified epiduritis after epidural steroid infiltrations and the presence of multiple partially calcified lumbar discopathies in particular at L4- L5 and L5-S1. With the evidence of the C.T. picture, we decided to send the patient to a physiatrist colleague for an evaluation, temporarily avoiding a therapeutic approach with oxygen-ozone therapy.

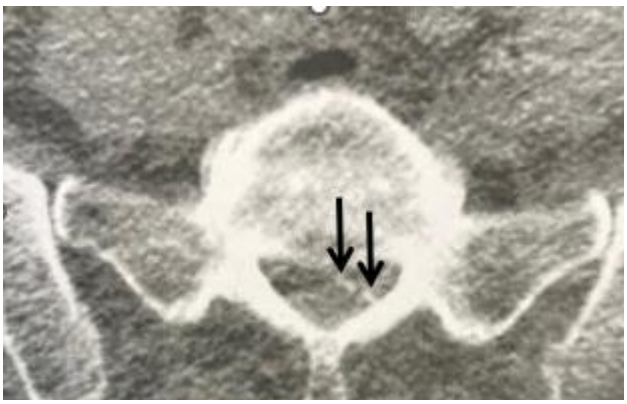

Fig. 4. *Lumbosacral CT scan for post-zone therapy. The findings appear unchanged compared to the previous check, confirming the picture of calcific epiduritis (arrows)*

Case 2

F.S. 59-year-old female. Following left acute lumbosciatica in the distribution area of left S1, she undergoes three epidural steroid infiltrations in May 2020-January 2021. The patient reports that after each treatment, the sciatica symptomatology partially regresses for a short time, almost nothing after the first session and after the second and third infiltration. The well-being lasted twenty / thirty days, then returned to a similar entity to the pre-treatment period.

In September 2021, the patient came to our attention for a possible attempt to resolve sciatica symptoms with oxygen-ozone therapy under a C.T. scan. Having examined the lumbosacral C.T. scan carried out on September 115, 2021 (Fig 3A-B), which documents a calcific epiduritis L5-S1 on the left side. The patient was offered three infiltrative sessions under C.T. scan with oxygen-ozone, carried out with prior informed consent, fifteen days from each other, were proposed to the patient.

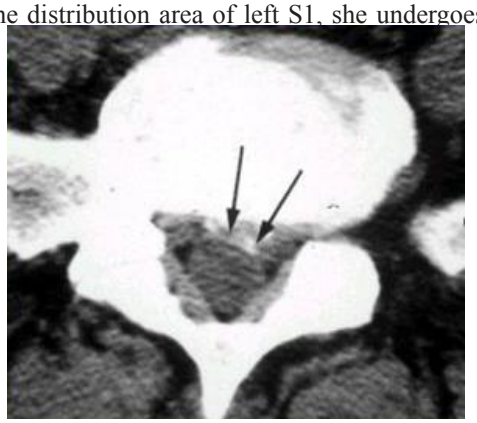

Fig. 5. *Lumbosacral CT: left paramedian disc herniation L5-S1 with situation of radicular disc conflict with the left S1 root (arrows)*

The patient reported significant clinical improvement from the first therapy session with the almost total disappearance of the sciatica symptoms and well-being that remains constant after the second and third infiltration. Therefore, in January 2022, we expected to perform a clinical check and a C.T. scan of the picture (Fig. 4). Clinically, the patient did not present any neurological deficit, and the sciatica symptoms appeared completely resolved, while the C.T. picture appeared unchanged compared to the previous investigation.

Case 3

A sixty-three-year-old female came to us following left lumbosciatalgia as from radicular disc conflict due to the presence of paramedian left L5-S1 sublegamentous disc herniation, which determines an imprint on the emergence of the ipsilateral S1 root. It was initially managed everywhere with pharmacological therapy: ibuprofen CPR 600 mg plus thiocolchicoside cps 4 mg. for 7 days.

In the persistence of painful symptoms, there was congruence between the clinical and the neuroradiological picture. The C.T. survey documents, in fact, a left paramedian sublegamentous disc herniation at L5-S1 with a compressive effect on the left S1 root (Fig. 5). The practitioner requests neurosurgical consultation. The neurosurgeon first recommended a microdiscectomy. The patient refused, asking if there were temporarily non-surgical alternatives to resolve the painful symptoms. In response to patient request, the neurosurgical colleague envisaged the idea of carrying out three infiltrations of steroid epidurals delayed over three months. After the first treatment, the patient reported little clinical benefit, so much so that she was advised to anticipate the second infiltration by about ten days. However, this session produced a clinical benefit lasting about 15 days with partial regression of sciatica symptoms. The third session was thus carried out as scheduled one month later, and, in this case, there was a clinical temporal improvement of short duration.

The patient, therefore, began a targeted physiotherapy program under the supervision of the neurosurgeon: Tecar therapy (10 therapeutic sessions) and a postural rehabilitation program. Unfortunately, the clinical benefits are minimal, and in the following six months, the patient undergoes another three epidural steroid infiltrations, thus making a total of six sessions. After two months with chronic symptoms, the patient undergoes a second C.T. scan (Fig. 6) which documents a picture of calcific epiduritis at L5-S1 prevalent on the left side. During this period, the patient came to our attention, and we proposed a treatment aimed at L5-S1 with oxygen-ozone. We carried out three sessions with the guided intraforaminal C.T. technique and obtained a notable reduction in lumbosciatica symptoms. Three months after the last treatment, we performed a control C.T. This confirmed the calcified images' persistence at the epidural level (Fig. 7).

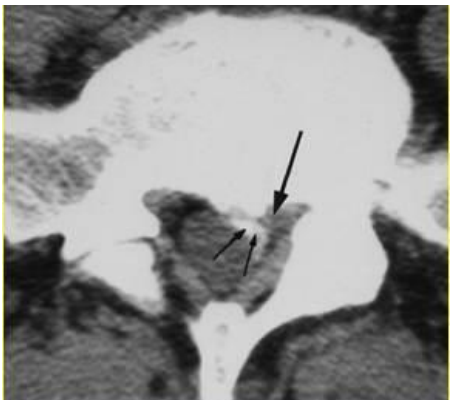

Fig. 6. *Lumbosacral CT after six epidural steroid infiltrations, appearance of calcific epiduritis (small arrows), and persistence of the left paramedian disc herniation (arrow)*

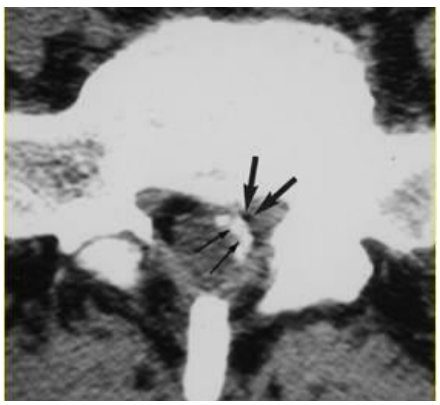

Fig. 7. *Lumbosacral CT after Treatment with oxygen ozone therapy: the picture of calphic epiduritis persists while a minimal volumetric reduction of the L5-S1 disc herniation seems to be appreciated (arrows)*

DISCUSSION

The presence of soft tissue calcifications is a possible complication of the injection of corticosteroids. In literature, however, reports of this occurrence are rare; in particular, the evidence is reported above all in the treatment with steroids of the shoulder, elbow, and foot, while as regards epidural infiltrations, there are no reports in this regard (27-30).

The fact of not finding articles that report the presence of calcifications after epidural steroid infiltrations, such as in our cases at the epidural level, we believe is mainly attributable to the fact that neuroradiological examinations are hardly carried out in the short and medium term to control patients treated with this technique.

In our opinion, certainly, steroid treatment leads to a clinical benefit in the short term, but this benefit is not long-lasting, so much so that many patients repeat these sessions. In our case series, a patient even went so far as to carry out six epidural steroid infiltrations, even if in a long over 1 year.

In our experience, post steroid infiltration calcific epiduritis is not an isolated case. This finding, although the number

of cases we report is only 3 who presented epidural calcifications to post epidural steroid infiltration, underlines the need of taking into account this possibility. Therefore, this data is very important for the subsequent therapeutic strategy.

In the face of a request for a second-line treatment with oxygen-ozone therapy, two of us decided to proceed according to this therapeutic indication, foreseeing a possible clinical benefit. In contrast, in one case, given the complexity of the symptoms, we considered this option a treatment with little chance of success, thus giving up oxygen-ozone treatment. Although there are no contraindications to oxygen-ozone treatment in such patients, it is never possible to guarantee patient results such as those obtained with oxygen-ozone therapy reported in the literature (31-35), equal to 75-80% therapeutic success in correctly recruited patients.

CONCLUSIONS

In conclusion, we believe oxygen-ozone therapy should always be preferred as a first approach therapy for affected patients, if the steroid treatment has already been carried out and resulted in calcific epiduritis due to complications. As confirmed by numerous randomized and controlled studies, ozone therapy can give a lasting clinical result over time, without any side effect, such as calcific epiduritis, unlike steroid therapy.

Conflict of interest

The authors declare that they have no conflict of interest.

REFERENCES

1. Conger A, Cushman DM, Speckman RA, Burnham T, Teramoto M, McCormick ZL. The Effectiveness of Fluoroscopically Guided Cervical Transforaminal Epidural Steroid Injection for the Treatment of Radicular Pain; a Systematic Review and Meta-analysis. *Pain Medicine (Malden, Mass)*. 2020;21(1):41-54. doi:10.1093/pm/pnz127
2. Gegel BT, Floyd JP, Hart DW, Barnhill WK, Maye JP. A Review of the Analgesic Benefits and Potential Complications Related to Epidural Corticosteroid Injections. *AANA journal*. 2019;87(1):71-79. https://pubmed.ncbi.nlm.nih.gov/31587747/
3. Mordhorst TR, McCormick ZL, Presson AP, Collier WH, Spiker WR. Examining the relationship between epidural steroid injections and patient satisfaction. *The Spine Journal: Official Journal of the North American Spine Society*. 2020;20(2):207-212. doi:10.1016/j.spinee.2019.09.024
4. Abdallah MA, Xie C, Ahmed KM, Hericks AJ. Chemical Meningitis and Status Epilepticus Caused by Accidental Epidural Administration of Digoxin. *South Dakota Medicine: The Journal of the South Dakota State Medical Association*. 2019;72(7):310-312.
5. Ali SS, Shaw AE, Oselkin M, Bragin I. Iatrogenic Spinal Epidural Hematoma Associated with Intracranial Hypotension. *Cureus*. 2019;11(3). doi:10.7759/cureus.4171
6. Amoretti N, Baqué J, Litrico S, Stacoffe N, Palmer W. Serious Neurological Complication Resulting from Inadvertent Intradiscal Injection During Fluoroscopically Guided Interlaminar Epidural Steroid Injection. *Cardiovascular and Interventional Radiology*. 2019;42(5):775-778. doi:10.1007/s00270-018-2151-5
7. Banik RK, Chen Chen CC. Spinal Epidural Hematoma after Interlaminar Cervical Epidural Steroid Injection. *Anesthesiology*. 2019;131(6):1342-1343. doi:10.1097/aln.0000000000002896
8. Bao C, Bao S. Hemorrhagic Infarction of Cerebellum and Brainstem Due to Cervical Epidural Steroid Injection - Case Report and Review of the Literature. *Academic Forensic Pathology*. 2018;8(4):952-956. doi:10.1177/1925362118821494
9. Berthelot JM, Le Goff B, Maugars Y. Side effects of corticosteroid injections: What's new? *Joint Bone Spine*. 2013;80(4):363-367. doi:10.1016/j.jbspin.2012.12.001
10. Carreon LY, Ong KL, Lau E, Kurtz SM, Glassman SD. Risk of Osteoporotic Fracture After Steroid Injections in Patients With Medicare. *American Journal of Orthopedics (Belle Mead, NJ)*. 2017;46(5):E293-E300.
11. Colorado B, Decker G. Persistent Hiccups After an Epidural Steroid Injection Successfully Treated With Baclofen: A Case Report. *PM & R: the journal of injury, function, and rehabilitation*. 2017;9(12):1290-1293. doi:10.1016/j.pmrj.2017.04.013

12. Gharibo CG, Fakhry M, Diwan S, Kaye AD. Conus Medullaris Infarction After a Right L4 Transforaminal Epidural Steroid Injection Using Dexamethasone. *Pain Physician*. 2016;19(8):E1211-E1214.
13. Kaydu A, Kılıç ET, Gökçek E, Akdemir MS. Unexpected Complication after Caudal Epidural Steroid Injection: Hiccup. *Anesthesia, Essays and Researches*. 2017;11(3):776-777. doi:10.4103/aer.AER_90_17
14. Kauffman CA, Malani AN. Fungal Infections Associated with Contaminated Steroid Injections. *Microbiology Spectrum*. 2016;4(2). doi:10.1128/microbiolspec.EI10-0005-2015
15. Kim SI, Lee DH, Kim SH, Cho YH. Spinal epidural hematoma occurring at a distance from the transforaminal epidural injection site. *Medicine*. 2019;98(30):e16654. doi:10.1097/md.0000000000016654
16. Krätzig T, Dreimann M, Mende KC, Königs I, Westphal M, Eicker SO. Extensive Spinal Adhesive Arachnoiditis After Extradural Spinal Infection–Spinal Dura Mater Is No Barrier to Inflammation. *World Neurosurgery*. 2018;116:e1194-e1203. doi:10.1016/j.wneu.2018.05.219
17. Lee DY, Park YJ, Kim KT, Lee JH, Kim DH. Acute lumbosacral hemorrhagic ganglion cyst after transforaminal epidural steroid injection. *Acta Orthopaedica Et Traumatologica Turcica*. 2018;52(6):475-479. doi:10.1016/j.aott.2017.07.003
18. Lee JK, Chae KW, Ju CI, Kim BW. Acute Cervical Subdural Hematoma with Quadriparesis after Cervical Transforaminal Epidural Block. *Journal of Korean Neurosurgical Society*. 2015;58(5):483-486. doi:10.3340/jkns.2015.58.5.483
19. Li WF, Kovacs K, Fisayo AA. Pneumocephalus and Sixth Nerve Palsy after Epidural Steroid Injection: Case Report and Review of the Literature. *The Journal of Emergency Medicine*. 2017;53(5):e89-e92. doi:10.1016/j.jemermed.2017.08.021
20. Loomba V, Kaveeshvar H, Dwivedi S. Paraplegia After Thoracic Epidural Steroid Injection. *A & A Case Reports*. 2016;7(5):118-121. doi:10.1213/xaa.0000000000000402
21. Page J, Moisi M, Oskouian RJ. Lumbar Epidural Hematoma Following Interlaminar Fluoroscopically Guided Epidural Steroid Injection. *Regional Anesthesia and Pain Medicine*. 2016;41(3):402-404. doi:10.1097/aap.0000000000000387
22. Palmer E. Management of Cervical Epidural Hematoma After Cervical Epidural Steroid Injection Using a Catheter Technique. *Pain Medicine*. 2019;21(6). doi:10.1093/pm/pnz220
23. Petrin Z, Marino RJ, Oleson CV, Simon JI, McCormick ZL. Paralysis After Lumbar Interlaminar Epidural Steroid Injection in the Absence of Hematoma: A Case of Congestive Myelopathy Due to Spinal Dural Arteriovenous Fistula and a Review of the Literature. *American Journal of Physical Medicine & Rehabilitation*. 2020;99(9):e107-e110. doi:10.1097/PHM.0000000000001325
24. Sanders RA, Bendel MA, Moeschler SM, Mauck WD. Epidural Hematoma Following Interlaminar Epidural Injection in Patient Taking Aspirin. *Regional Anesthesia and Pain Medicine*. 2018;43(3):1. doi:10.1097/aap.0000000000000730
25. Schneider BJ, Maybin S, Sturos E. Safety and Complications of Cervical Epidural Steroid Injections. *Physical Medicine and Rehabilitation Clinics of North America*. 2018;29(1):155-169. doi:10.1016/j.pmr.2017.08.012
26. Shah AK, Bilko A, Takayesu JK. Epidural Steroid Injection Complicated by Intrathecal Entry, Pneumocephalus, and Chemical Meningitis. *The Journal of Emergency Medicine*. 2016;51(3):265-268. doi:10.1016/j.jemermed.2016.05.040
27. Sorber J, Levy D, Schwartz A. Pneumocephalus and seizures following epidural steroid injection. *The American Journal of Emergency Medicine*. 2017;35(12):1987.e1-1987.e2. doi:10.1016/j.ajem.2017.09.030
28. Stout A, Friedly J, Standaert CJ. Systemic Absorption and Side Effects of Locally Injected Glucocorticoids. *PM&R*. 2019;11(4):409-419. doi:10.1002/pmrj.12042
29. Turel MK, Kerolus MG, Deutsch H. Intradural spinal arachnoid cyst - A complication of lumbar epidural steroid injection. *Neurology India*. 2017;65(4):863-864. doi:10.4103/neuroindia.NI_56_17
30. Urits I, Viswanath O, Petro J, Aner M. Management of dural puncture headache caused by caudal epidural steroid injection. *Journal of Clinical Anesthesia*. 2019;52:67-68. doi:10.1016/j.jclinane.2018.09.004
31. Wang G, Liang J, Jia Z, Wan L, Yang M. Spinal cord infarction caused by sacral canal epidural steroid injection: A case report. *Medicine*. 2018;97(11):e0111. doi:10.1097/MD.0000000000010111
32. Beaudreuil J. Intradiskal Treatments for Active Degenerative Disk Disease. *Joint Bone Spine*. 2019;87(3). doi:10.1016/j.jbspin.2019.06.008
33. Darmoul M, Bouhaouala MH, Rezgui M. Calcifications post-nucléorthèse, un problème toujours d'actualité? *La Presse Médicale*. 2005;34(12):859-860. doi:10.1016/s0755-4982(05)84064-3

34. Bonetti M, Fontana A, Cotticelli B, Volta GD, Guindani M, Leonardi M. Intraforaminal O(2)-O(3) versus periradicular steroidal infiltrations in lower back pain: randomized controlled study. *AJNR American journal of neuroradiology*. 2005;26(5):996-1000. https://pubmed.ncbi.nlm.nih.gov/15891150/
35. Costa T, Linhares D, Ribeiro da Silva M, Neves N. Ozone therapy for low back pain. A systematic review. *Acta Reumatologica Portuguesa*. 2018;43(3):172-181.

European Journal of Musculoskeletal Diseases
ISSN 2038-4106/2022

Review

CORRELATION BETWEEN ORAL DYSBIOSIS AND ORAL PATHOLOGIES

R.A. Assanti[1] and P. Daliu[2]

[1]Multidisciplinary Department of Medical-Surgical and Dental Specialties, University of Campania "Luigi Vanvitelli", Naples, Italy;
[2]Dental School, Albanian University, Tirana, Albany

**Correspondence to:*
Remo Antonio Assanti, DDS
Multidisciplinary Department of Medical-Surgical and Dental Specialties,
University of Campania "Luigi Vanvitelli",
Naples, Italy
e-mail: remoantonio.assanti@unicampania.it

ABSTRACT

Numerous microorganisms inhabit the human oral cavity, including bacteria, viruses, fungi, archaea, and protozoa, forming a complex ecological community that impacts oral and systemic health. Microbiota-associated diseases are the most dominant oral diseases, such as dental caries and periodontal diseases. Furthermore, increasing shreds of evidence have sustained that many systemic diseases are associated with alterations in the oral ecosystem, like tumors. The present control of dental plaque-related diseases is nonspecific and focuses on removing plaque by mechanical means. Due to this actuality of the oral microbiome, new strategies founded on the microbiome's modulation that aim to support and reestablish a healthy oral ecosystem are gaining ever greater importance. The present review aims to describe the concept of dysbiosis and its correlation with pathological processes that can affect the oral cavity.

KEYWORDS: *bacterium, fungi, viruses, protozoa, archaea, microbioma, microbiota*

INTRODUCTION

The oral microbiome consists of microbial groups in different habitats in our mouth, such as teeth, cheeks, tongue, palates, gingiva, and tonsils. It is the second most diverse habitat of the human body after the gut microbiome, prevalently residing bacteria besides fungi, viruses, protozoa, and archaea (1). More than 700 bacterial species are colonizing in the mouth (2) with a specific bacterial composition based on its location. The hard palate represents the site with the least relevant bacterial composition, while the bacterial presence is increased in the gingival plaque. Bacteria such as Eubacterium and Prevotella are significantly associated with the back of the tongue. The papillary structure and the low redox potential of its surface could explain its distinctive specific bacterial association (3). The anaerobic environment of subgingival plaque may explain the bacteria site-specific association. In the oropharynx, the distribution of Firmicutes,

Received: 02 March, 2022
Accepted: 17 July, 2022

ISSN: 2038-4106

Proteobacteria, and Bacteroidetes were similar to that of saliva, and the presence of Proteobacteria was increased compared to the mouth (4). Moreover, the bacteria present in the oral cavity can undergo continuous mutations dictated by factors that can be external or internal. Furthermore, their evolution is related to age/dentition stages (5,6) and lifestyles (7,8).

Although the oral microbiome plays an essential role in maintaining health, specific ecological changes in the microbiome can driveway some bacteria to cause various oral diseases (9).

The present review aims to describe the concept of dysbiosis and its correlation with pathological processes that can affect the oral cavity.

Method of bacterial cohabitation

The oral microbiome keeps the oral cavity healthy by preventing the expansion of pathogens (however already present in the environment) rather than preventing their invasion. Through the structural, metabolic, and chemical interactions that are triggered between bacteria equilibrium and stability are maintained in the resident microbial community in favor of non-pathogenic bacterial species (10).

Symbiosis can be mandatory, meaning that one or both symbiotics depend entirely on each other for survival, or optional when they can generally live independently. Symbiosis is also classified by physical attachment; the symbiosis in which organisms have a bodily union is called conjunctive symbiosis, and the symbiosis in which they are not in a union is called disjunctive symbiosis (11). Inside the oral cavity, bacteria can coexist with each other in three ways:

- mutualism: the particular relationship between species that mutually benefit from coexistence and are unable to live in isolation;
- commensalism: it is a non-obligatory interaction between two living beings in which one takes advantage of the other's nourishment or waste without causing suffering or disturbance. One organism between the two benefits from the other, and the other is neither harmed nor helped;
- parasitism: it is a form of biological interaction, generally of a trophic nature, between two species of organisms, one of which is called a parasite and the other a host. Unlike mutualistic symbiosis, the parasite benefits at the host's expense, creating biological damage to it.

Oral dysbiosis

Dysbiosis identifies an alteration of the human bacterial flora, and it is usually followed by an adjective that specifies the body district concerned (oral dysbiosis, vaginal dysbiosis, skin dysbiosis). Biofilm and other oral surfaces can be affected by what happens in the mouth, leading to an alteration of the balance between "good" and "bad" bacteria.

Any dental intervention can represent a disturbance of the normal oral microbiota. Even the diet can have a significant impact on the microbial environment: foods rich in sugar, acidic drinks (those without sugar), and smoking can all contribute to changing the oral environment, potentially making it more difficult for bacteria "the good overwhelm the bad" (12). As a result, maintaining good oral hygiene becomes more complicated than previously thought. Rather than simply fighting all bacteria indiscriminately, it is better to work towards supporting a healthy oral environment and maintaining natural balance (12).

It is clear to understand that a state of bacterial imbalance can negatively affect the oral district and the whole organism's health (13). The causes of this imbalance, as already mentioned, can be traced back to diet, drugs, incorrect lifestyles (smoking, alcohol, smog, little or no physical activity), and toxins. Exposure to these factors leads to the intestinal growth of non-beneficial bacterial strains at the expense of those beneficial to human health (13).

Toxins are invisible chemical compounds in the air, water, and food. Still, naturally, others are produced by the body itself and are the waste substances of the metabolic processes through a highly efficient internal chemical laboratory, which works constantly, or bacterial waste derived from the organism (13).

Dysbiosis occurs when the virulent microorganisms, which are often the same "friendly" organisms that, in a balanced state, are beneficial, transform into a pathogenic state without homeostasis. The problem, therefore, lies not in the presence of bacteria in the oral cavity but in their balance (14).

Oral dysbiosis and oral diseases

Interesting evidence emerges in the literature on the ability of the microbiota to educate the human immune system, for

example, by allowing it to recognize pathogens or by directly stimulating various components of the innate and adaptive immune response (10).

The role of the oral microbiota on the immune system is not as well-known as that of other microbial communities in other human ecosystems. However, today it is possible to state, for example, that bacteria in the oral cavity selectively regulate the expression of the cytokine CXCL2 by determining the increase in neutrophils that "prepare" healthy gingival tissue (10).

In recent decades, research on the microbiota has focused on the role it plays in oral diseases rather than on the possible benefits for human health (as it has been done for the bacteria that reside in the intestine, genitourinary tract, and respiratory system). Recalling that it is possible to prevent diseases even by maintaining a good state of health, Kumar & Mason (10), therefore, stressed the importance of exploring the oral ecosystem and investigating the possible benefits that would arise from the presence of microorganisms in the oral cavity.

As mentioned above, with the interruption of microbiological homeostasis, a pathological process is triggered that sees the diversity of "healthy" populations decrease, and the prevalence of "pathological" populations increase. This way, the host's inflammatory/immune responses are established (14). The presence of an imbalance in the oral ecosystem can lead to the possible development of pathologies such as dental caries, periodontal diseases, and carcinoma.

Dental caries

Dental caries is the dissolution of the tooth structure by the acid produced as a result of the fermentation of dietary carbohydrates by oral bacteria (15). In individuals who repeatedly ingest high levels of carbohydrates, the frequency of acid production leads to a decrease in the buffering capacity of saliva. This, in turn, changes the composition of the oral microbiota, favoring aciduric microbial species. These species, notably Streptococcus mutans and Lactobacilli, continue to produce acid under acidic conditions, thus exacerbating the damage to dental hard tissues. Streptococcus mutans has been extensively studied for its cariogenic properties and has also been considered a specific pathogen (15).

To date, many bacterial species are recognized both in the biofilm and in the plaque, intent on producing acidogenic substances derived from the fermentation of dietary carbohydrates. Among these are present in addition to Streptococcus mutans and Lactobacilli, also Bifidobacterium, Propionibacterium and Scardovia (10).

However, in addition to acid production, some bacteria can raise the pH by producing ammonia from urea and arginine, which provide a mechanism to balance acid production and thus maintain homeostasis. What counts in developing a pathological process is not the identification of bacterial species but the consideration that the environmental characteristics pour on them (15).

Periodontal diseases: gingivitis

Gingivitis is, perhaps, the most common bacterial disease in humans, with a prevalence in adults of over 90%, where bacterial plaque through stratification processes due to the presence of primary (Gram + aerobic) and secondary (Gram- anaerobic) colonizing bacteria adhere on the tooth surface through the interposition of the acquired film. The failure in constant removal of this bacterial biofilm produce the consequent microbial accumulation with an increase in gram-anaerobic species, endotoxins, and enzymes which, with their pro-inflammatory function, cause irritation and inflammation of the gums with subsequent increase in volume and spontaneous or induced bleeding. The disease is entirely reversible, and thanks to professional hygiene sessions and reasonable home control of the plaque, it is possible to obtain a "restitutio ad integrum" of the tissues, thus eliminating the clinical signs.

Periodontal diseases: periodontitis

Periodontitis is a common oral disease, the manifestation of which increases with increasing age (16). Often one gets the impression that it is a natural, almost inevitable, and physiological consequence of the aging process. It is essential to change this obsolete perception. It is mandatory to understand that periodontitis is an inflammatory disease linked to the oral microbiome and the individual's immune system (16).

It is also clear that the oral microbiota changes concerning different diseases. For example, in periodontitis, anaerobic bacteria are abundant in the oral cavity; these include Porphyromonas gingivalis, Tannerella forsythia, and Treponema denticola (the three members of the " red complex "). Furthermore, these bacteria are associated with

the pathogenesis of some systemic diseases (16). The pathology manifests with deepening the physiological sulcus between the tooth surface and the marginal/free gingiva.

The onset and the course are also attributable to the host's susceptibility as bacterial plaque represents the leading cause but is not sufficient for developing the disease. As a consequence of the bacterial plaque's action, there is the alveolar bone's reabsorption with an accentuated mobility of the dental element and possible loss. The disease is irreversible, characterized by alternating periods of quiescence and activity (15).

Oral squamous cell carcinoma

Several mechanisms of action have been hypothesized regarding the role of the oral microbiota in cancer pathogenesis. Activation of inflammatory-driven cellular pathways of proliferation may have an essential role in the progression of oral carcinoma. Inflammatory mediators in this process cause or facilitate mutagenesis, cell proliferation, oncogene activation, and angiogenesis.

Martilla et al. (17) showed that oral microbial cultures can produce acetaldehyde (ACH), a carcinogenic agent, and that cultures from smokers generated significantly higher levels of ACH. *In vitro* characterization of the oral microbiome indicates that *Neisseria* species and *Candida* species are among the considerable microbial producers of ACH (18). The influence of OSCC risk factors on the carriage of ACH-generating microorganisms needs additional investigation. Microbially derived *N*-nitrosamine compounds are another potential carcinogen. Commensal bacteria and Candida spp can generate N-nitrosamines *in vitro* from nitrite and secondary amines (19). Community-level metabolomics strategies are required to define whether disturbances in the normal microbiota can form these and other toxic metabolites.

CONCLUSIONS

In conclusion, the oral microbial ecosystem plays an essential role in maintaining human health. The altered oral microbiota may be intimately associated with oral and systemic diseases. The balance of the microbiome is closely linked to that of the immune system: alterations of the former lead to disproportionate reactions of the latter, promoting inflammation and increasing exposure to oncological pathologies (20).

Furthermore, the salivary microbiome seems to be more sensitive to environmental factors and lifestyle habits rather than to genetically determined factors, thus confirming that a correct lifestyle can keep the pathogenicity of the salivary microbiome under control, thus also influencing the trend of dental diseases (21).

A more feasible and clinically practical goal would be to create a "hostile" environment for pathogenic strains and healthy for non-pathogenic bacteria, thus favoring disease control, modulating the microbiome, for example, with probiotics. The use of targeted probiotics could reduce the use of drug therapies, especially antibiotics, preventing drug resistance phenomena and adverse reactions.

Another prospect could be the early diagnosis of pathologies such as oral carcinoma through the analysis of the salivary microbiome profile, characteristically altered in these pathologies, just as is being done for the intestinal microbiome where for example, any alterations of the same can influence immune responses both locally and in organs distant from the intestine (21). The knowledge of oral microbiota's role in disease occurrence and development is far from complete. Forthcoming research exactly identifying the critical oral microbiota in health and disease will help to develop better practical tools for therapies.

Funding

This research received no external funding.

Conflict of Interest

The authors declare no conflict of interest.

REFERENCES

1. Zhang Y, Wang X, Li H, Ni C, Du Z, Yan F. Human oral microbiota and its modulation for oral health. *Biomedicine & Pharmacotherapy*. 2018;99:883-893. doi:10.1016/j.biopha.2018.01.146
2. Palmer Jr RJ. Composition and development of oral bacterial communities. *Periodontology 2000*. 2013;64(1):20-39. doi:10.1111/j.1600-0757.2012.00453.x
3. Huse SM, Ye Y, Zhou Y, Fodor AA. A Core Human Microbiome as Viewed through 16S rRNA Sequence Clusters. Ahmed N, ed. *PLoS ONE*. 2012;7(6):e34242. doi:10.1371/journal.pone.0034242
4. Lemon K. Comparative Analyses of the Bacterial Microbiota of the Human Nostril and Oropharynx. *mBio*. 2010;1(3). doi:10.1128/mbio.00129-10
5. Dewhirst FE, Chen T, Izard J, et al. The Human Oral Microbiome. *Journal of Bacteriology*. 2010;192(19):5002-5017. doi:10.1128/jb.00542-10
6. Gomez A, Nelson KE. The Oral Microbiome of Children: Development, Disease, and Implications Beyond Oral Health. *Microbial Ecology*. 2016;73(2):492-503. doi:10.1007/s00248-016-0854-1
7. Nasidze I, Li J, Quinque D, Tang K, Stoneking M. Global diversity in the human salivary microbiome. *Genome research*. 2009;19(4):636-643. doi:10.1101/gr.084616.108
8. Fan X, Peters BA, Jacobs EJ, et al. Drinking alcohol is associated with variation in the human oral microbiome in a large study of American adults. *Microbiome*. 2018;6(1). doi:10.1186/s40168-018-0448-x
9. Jenkinson HF, Lamont RJ. Oral microbial communities in sickness and in health. *Trends in Microbiology*. 2005;13(12):589-595. doi:10.1016/j.tim.2005.09.006
10. Kumar PS, Mason MR. Mouthguards: does the indigenous microbiome play a role in maintaining oral health? *Frontiers in Cellular and Infection Microbiology*. Published online May 6, 2015. doi:10.3389/fcimb.2015.00035
11. Ptasiewicz M, Grywalska E, Mertowska P, et al. Armed to the Teeth-The Oral Mucosa Immunity System and Microbiota. *International Journal of Molecular Sciences*. 2022;23(2):882. doi:10.3390/ijms23020882
12. Valm AM. The Structure of Dental Plaque Microbial Communities in the Transition from Health to Dental Caries and Periodontal Disease. *Journal of Molecular Biology*. 2019;431(16):2957-2969. doi:10.1016/j.jmb.2019.05.016
13. Clark GC, Casewell NR, Elliott CT, et al. Friends or Foes? Emerging Impacts of Biological Toxins. *Trends in Biochemical Sciences*. 2019;44(4):365-379. doi:10.1016/j.tibs.2018.12.004
14. Curatola GP. Oral Microbiome Homeostasis: The New Frontier in Oral Care Therapies. *Journal of Dentistry Oral Disorders and Therapy*. 2013;1(1). doi:10.15226/jdodt.2013.00105
15. Wade WG. The oral microbiome in health and disease. *Pharmacological research*. 2013;69(1):137-143. doi:10.1016/j.phrs.2012.11.006
16. Holmstrup P, Damgaard C, Olsen I, et al. Comorbidity of periodontal disease: two sides of the same coin? An introduction for the clinician. *Journal of Oral Microbiology*. 2017;9(1):1332710. doi:10.1080/20002297.2017.1332710
17. Marttila E, Uittamo J, Rusanen P, Lindqvist C, Salaspuro M, Rautemaa R. Acetaldehyde production and microbial colonization in oral squamous cell carcinoma and oral lichenoid disease. *Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology*. 2013;116(1):61-68. doi:10.1016/j.oooo.2013.02.009
18. Moritani K, Takeshita T, Shibata Y, Ninomiya T, Kiyohara Y, Yamashita Y. Acetaldehyde production by major oral microbes. *Oral Diseases*. 2015;21(6):748-754. doi:10.1111/odi.12341
19. Healy CM, Moran GP. The microbiome and oral cancer: More questions than answers. *Oral Oncology*. 2019;89:30-33. doi:10.1016/j.oraloncology.2018.12.003
20. Gholizadeh P, Eslami H, Yousefi M, Asgharzadeh M, Aghazadeh M, Kafil HS. Role of oral microbiome on oral cancers, a review. *Biomedicine & Pharmacotherapy*. 2016;84:552-558. doi:10.1016/j.biopha.2016.09.082
21. Shaw L, Ribeiro ALR, Levine AP, et al. The Human Salivary Microbiome Is Shaped by Shared Environment Rather than Genetics: Evidence from a Large Family of Closely Related Individuals. Fraser CM, ed. *mBio*. 2017;8(5). doi:10.1128/mbio.01237-17

European Journal of Musculoskeletal Diseases
ISSN 2038-4106/2022

Case series

ORAL HYGIENE IN PATIENTS WITH AUTOIMMUNE BULLOUS DISEASES

R.A. Assanti[1] and P. Daliu[2]

[1]Multidisciplinary Department of Medical-Surgical and Dental Specialties, University of Campania "Luigi Vanvitelli", Naples, Italy;
[2]Dental School, Albanian University, Tirana, Albany

Correspondence to:
Remo Antonio Assanti, DDS
Multidisciplinary Department of Medical-Surgical and Dental Specialties,
University of Campania "Luigi Vanvitelli", Naples, Italy
e-mail: remoantonio.assanti@unicampania.it

ABSTRACT

Pemphigus vulgaris (PV) and mucous membrane pemphigoid (MMP) are immunologically mediated mucocutaneous disorders denoted by blistering mucous membranes, skin, and oral cavity lesions. The buccal mucosa, soft palate, and lips are often the first sites involved in PV and MMP patients. The oral blisters blasted fast, exiting painful erosions and ulcers. Gingival involvement (desquamative gingivitis) consists of an erythematous lesion accompanied by dryness, desquamation, and bullae. Although gingivitis desquamative is autoimmune e non induced by the accumulation of plaque and tartar, careful oral hygiene prevents secondary inflammation, with consequent clinical worsening of the primary pathology. The present work aims to review the recent literature regarding oral hygiene protocols applied to patients suffering from vesiculo-bullous diseases, with a critical evaluation of the advantages and limitations of the therapy.

KEYWORDS: *vesicle, pain, gingival, inflammation, hygiene, protocol*

INTRODUCTION

Pemphigus and pemphigoid are two of a group of autoimmune bullous diseases affecting oral mucosa and skin. "Pemphigus" is defined as a group of vesiculo-bullous pathologies of an autoimmune nature involving the skin and mucous membranes covered by stratified paving epithelium, characterized by keratinocyte dissociation. This phenomenon is called acantholysis (1).

There are two varieties: low acantholysis pemphigus (vulgar, vegetative) and high acantholysis pemphigus (foliaceus, erythematosus). In low acantholysis, cell detachment is the lower half of the spinous layer with frequent oral injuries; on the contrary, in high acantholysis, cell detachment is found in the upper half of the spinous layer with cutaneous lesions (2).

In particular, the most common and most represented form of pemphigus in the oral cavity is Pemphigus Vulgaris. It mainly affects female patients aged between the third and sixth decade.

Received: 14 June 2022
Accepted: 12 August 2022

ISSN: 2038-4106

In genetically predisposed subjects, triggering agents, such as drugs, viruses, neoplasms, and pregnancy, can cause the onset of pemphigus. Autoantibodies, belonging to the IgG class, directed against adhesion proteins such as Desmoglein 3 (auto-ab anti Dsg3), would induce plasmin synthesis, an effector molecule of acantholysis typical of this pathology (1).

The intraepithelial fissures, due to acantholysis, are filled with transudative fluid, with the consequent formation of vesicles. The intraepithelial vesicle represents the elementary lesion of the pemphigus. The basement membrane constitutes its floor, while the other epithelial layers form its roof. Inside is a serous liquid rich in leukocytes and dysmorphic epithelial cells and a fair presence of eosinophilic granulocytes. The blister, however, inside the oral cavity does not persist for long. It readily undergoes rupture, becoming an erosion. There is also notable salivation and fetor ex ore. Clinical diagnosis is carried out with an objective examination in which the presence of vesicles or erosions and positivity to Nicolsky's sign must be accompanied by cytological, histological, direct, and indirect immunofluorescence tests (1,3). In most cases, the prognosis is benign, following cortisone or immunosuppressive therapy; in 10% of cases, the prognosis is poor, mainly due to dehydration and secondary systemic infections (4).

Benign mucous membranous pemphigoid is an autoimmune disease that mainly affects the mucous membranes and, in a few cases, the skin. There is a predilection for women starting from the fifth decade of life. The most accredited pathogenetic hypothesis suggests that the lesions are caused by antibodies of the IgG and IgM type directed against a series of antigens (i.e. BP180, BP230, Laminin-5, Laminin-6, beta4-integrin, alpha6- integrin) located at the level of the basement membrane, in particular the lower portion of the lamina lucida. The chorion-epithelial detachment causes the infiltration of exudate with the formation of sub-epithelial vesicles (5).

The lesions predominantly affect the gum. The tissues are erythematous and shiny because the epithelium flakes quickly show a bleeding and painful surface (3); in other areas of the mouth, such as cheeks, soft palate, and tongue, blisters that erode causing the formation of ulcers, filled with flaking material and fibrin.

In most cases, the extraoral lesions involve the ocular mucous membranes. The formation of blisters occurs, which, by healing, can determine the union between the conjunctival mucosa and the eyelid or the union between the two eyelids. Differential diagnosis is made with pemphigus using direct immunofluorescence testing and laboratory tests to search for circulating autoantibodies. Therapy involves the administration of topical and/or systemic cortisone and immunosuppressants (6).

Vesiculo-bullous diseases, with the onset of erosions and/or ulcers, determine inaccurate oral hygiene in most patients due to the burning and/or pain due to the lesions, with consequent plaque accumulation (7). This accumulation causes inflammation of the periodontal tissues, halitosis, and possible candidiasis, with consequent clinical worsening of the primary pathology.

The present work has the purpose of reviewing the recent literature regarding oral hygiene protocols applied to patients suffering from vesiculo-bullous diseases, with a critical evaluation of the advantages and limitations of the therapy.

MATERIALS AND METHODS

The search engine used is PUBMED, and the search has been refined using MESH terms. No filters were used. The following search terms (MeSH terms) were utilized: (“’Root Planing” AND “Dental Scaling” AND “Pemphigus”), (“Root Planing” AND “Dental Scaling” AND “oral lichen planus”), (“Root Planing” AND “Dental Scaling” AND “Pemphigoid”), (“Oral Hygiene” AND “Pemphigus”), (“Oral Hygiene” AND “Pemphigoid”), (“Oral Hygiene” AND “oral lichen planus”), (“periodontal status” AND “Pemphigoid”), (“periodontal status” AND “Pemphigus”), (“periodontal status” AND “oral lichen planus”).

Qualitatively different scientific works were examined: case-control studies, case report studies, randomized controlled experimental studies, case series, and pilot studies.

RESULTS

The initial electronic search turned out 79 results. Titles and abstracts derived from the investigation were independently screened. Comparing the labels of the initial 79 results, 16 were duplicates, and 37 were eliminated after having screened the titles and the abstract. Then, 26 full-text articles were obtained for all titles agreed upon, and disagreements were resolved by discussion. A total of 9 studies were excluded because they were not related to aspects concerning hygiene protocols. Finally, 17 studies were included in the present study, as reported in Table I.

DISCUSSION

The periodontal state of patients suffering from vesiculo bullous diseases, such as pemphigus and mucous membranous

Table I. *Characteristics of the 17 included studies.*

Reference (First Author + Year)	Cases and controls (n)	Study design
Akman et al.[8] 2008	20 PV; 20 healthy subjects.	*Case-control study*
Arduino et al.[9] 2011	29 MMP; 30 healthy subjects.	*Case-control study*
Arduino et al.[10] 2012	12 MMP	*Case*–series *study*
Azizi et al.[11] 2012	32 OLP; 32 healthy subjects.	*Case-control study*
Ertugrul et al.[12] 2013	27 OLP; 30 healthy subjects.	*Case-control study*
Guiglia et al.[13] 2007	30 OLP	Clinical trial
Holmstrup et al.[14] 1990	11 erosive OLP	Clinical trial
Lo Russo et al.[15] 2010	8 OLP; 4 MMP	Pilot study
López-Jornet et al.[16] 2012	80 OLP; 40 healthy subjects.	*Case-control study*
Nagao et al.[17] 2011	9 OLP-HCV	Clinical trial
Orrico et al.[18] 2010	1 MMP	Case report
Ramón-Fluixá et al.[7] 1999	90 OLP; 52 healthy subjects.	*Case-control study*
Scattarella et al.[19] 2010	1 OLP	Case report
Schellinck et al.[20] 2009	10 MMP; 10 healthy subjects.	*Case-control study*
Stone et al.[21] 2013	82 OLP	Randomized controlled study
Thorat et al.[22] 2010	50 PV and 50 healthy subjects.	*Case-control study*
Tricamo et al.[23] 2006	20 MMP 20 healthy subjects.	*Case-control study*

Abbreviations: PV, Pemphigus Vulgaris; PMM, Mucous Membrane Pemphigoid; OLP, Oral Lichen Planus; HCV, Hepatits C Virus.

pemphigoid, is compromised. Several authors have carried out scientific research in this regard, carrying out clinical studies and laboratory analyses (8) to verify the hypothesis that vesiculo-bullous pathologies may influence the onset or progression of periodontal disease. Almost all the studies confirmed the hypothesis: subjects suffering from vesiculo-bullous diseases have more compromised periodontal conditions than control patients. The results can be interpreted as follows: due to the painful symptoms caused by the vesiculo-bullous lesions, these patients tend not to follow a scrupulous home oral hygiene and do not even undergo professional oral hygiene sessions; moreover, the unstable immune system, typical of autoimmune diseases, does not protect against the onset or worsening of periodontal disease (9).

Some Authors (10), on the other hand, do not value the hypothesis of a more compromised periodontal state in patients suffering from vesiculo-bullous diseases. This study explains that there are no significant differences between case and control patients from a periodontal point of view: the highest gingival inflammation values found in the cases are not the result of inflammation due to periodontal disease but the outcomes of nature erythematous of the PMM itself.

Faced with these results, several authors have conducted clinical studies to prove the efficacy of non-surgical periodontal therapy and home oral hygiene instructions: the protocols applied to prove to be a valid resource as an adjunct therapy to drug therapy. Arduino et al. (11) use only oral hygiene protocols, not drug therapy, to measure the effective

contribution of non-surgical periodontal therapy in the remission of vesiculo-bullous lesions. After three weeks, patients undergo supragingival and subgingival scaling, use a soft filament brush performing the modified Bass technique, and a medium filament toothbrush and interdental brush. The contribution of periodontal therapy proves to be effective but insufficient for the complete remission of the lesions, for which it is necessary to support pharmacological therapy.

The professional oral hygiene protocols used vary according to the authors, but the scaling and polishing procedures are constant.

Polishing is carried out with a rubber cup. In particular, Orrico et al. (12) specify the use of the cup at low speeds with non-abrasive polishing paste and recommend carrying out the procedures in a very delicate manner to avoid laceration of the gingival tissues compromised by vesiculo-bullous lesions. Therefore, the only ones to carry out root-planing are Orrico et al. (12) and Scattarella et al. (13).

As for the home oral hygiene protocols, all the authors follow the same guiding thread: traumatic procedures but effective in removing plaque accumulations and disinfecting the mucous membranes.

Recommended brushing techniques range from modified Bass (11, 14) to Stillman's (12). The toothpaste should be non-abrasive (12), free of flavourings, and high in fluoride (13).

The use of interdental brush varies according to the studies: Guiglia et al. (14) recommend its use from the beginning of therapy. Other authors, Arduino et al. (11) and Otrico et al. (12), on the other hand, recommend using the brush following the re-epithelialization of the lesions to prevent further lesions of the mucous membranes.

In principle, chlorhexidine-based mouthwash is recommended in different formulations, 0.12% (12) and 0.20% (14). In particular, according to Orrico et al. (12) and Scattarella et al. (13), chlorhexidine can be used in an alcohol-free formulation following re-epithelialization of the lesions, except for Guiglia et al. (14), which recommends its use, in a formulation at 0.20% twice / day for seven days, at the beginning of therapy. In the initial phase, however, they recommended bicarbonate rinses (13), which are less traumatic than a strong antibacterial agent, such as chlorhexidine.

To promote patient motivation, Scattarella et al. (13), in addition to recommending the use of an electric toothbrush with an ultra-soft filament head, proposes plaque-revealing substances, also used by Guglia et al. (14) in giving home oral hygiene instructions.

In addition, Scattarella et al. (13) recommend a diet free of spices and alcohol, substances considered aggressive in patients affected by pemphigus and pemphigoid, and provide anti-smoking counselling.

CONCLUSIONS

The present review aimed to report and describe evidence in the scientific literature about which oral hygiene protocols for plaque and tartar removal should be used in patients with oral pemphigus and oral pemphigoid. In particular, from the analysis of the literature, it was possible to deduce the following indications:

professional oral hygiene sessions must be gently performed in order to avoid laceration of the gingival tissues already compromised by vesiculo-bullous lesions;

perform scaling and polishing sessions using inserts and materials suitable for the patient, such as low-speed rubber cups and non-abrasive polishing paste;

home oral hygiene instructions must be suitable for the patient, preferring soft or extra-soft toothbrushes, non-abrasive toothpaste without aromas, floss, and extra-soft brush recommended following the re-epithelialization of the lesions, rinsing with bicarbonate in the phases acute lesions and subsequently rinsing with 0. 12% chlorhexidine-based mouthwashes;

motivate the patient to oral hygiene, proposing, as appropriate, an electric toothbrush with soft filaments and plaque-revealing substances;

recommend diets free of foods irritating the oral mucosa, such as spicy, spicy, too hot, and too cold foods;

motivate the patient to avoid and/or limit the consumption of alcohol as, in addition to being irritating to the oral mucosa, it is a predisposing factor to the onset of oral cancer, especially in subjects who, having ulcerative lesions, are more prone to degeneration malignant;

carry out anti-smoking counselling since, in addition to being extremely harmful to general health, it slows down tissue healing and is also an irritant for the oral mucosa and a risk factor for the onset of malignant degeneration.

In conclusion, considering that the accumulation of plaque and tartar causes gingival inflammation and, in the long run, in predisposed subjects, causes periodontitis and that patients suffering from vesiculo-bullous diseases have a destabilized immune system, in addition to following a pharmacological therapy based on corticosteroids and/or immunosuppressants, it is strongly recommended that the latter, undergo professional oral hygiene sessions. In addition, the patient must follow the most suitable home oral hygiene instructions for the case to achieve faster healing of the lesions and avoid enlargement of periodontal involvement.

REFERENCES

1. Batistella EÂ, Sabino da Silva R, Rivero ERC, Silva CAB. Prevalence of oral mucosal lesions in patients with pemphigus vulgaris: A systematic review and meta-analysis. *J Oral Pathol Med*. 2021 Sep;50(8):750-757. doi: 10.1111/jop.13167. Epub 2021 Apr 15.
2. Pisani M, Ruocco V. Drug-induced pemphigus. *Clin Dermatol.* 1986 Jan-Mar;4(1):118-32. doi: 10.1016/0738-081x(86)90015-5.
3. Buonavoglia A, Leone P, Dammacco R, Di Lernia G, Petruzzi M, Bonamonte D, Vacca A, Racanelli V, Dammacco F. Pemphigus and mucous membrane pemphigoid: An update from diagnosis to therapy. *Autoimmun Rev.* 2019 Apr;18(4):349-358. doi: 10.1016/j.autrev.2019.02.005. Epub 2019 Feb 7.
4. Robinson JC, Lozada-Nur F, Frieden I. Oral pemphigus vulgaris: a review of the literature and a report on the management of 12 cases. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 1997 Oct;84(4):349-55. doi: 10.1016/s1079-2104(97)90030-5.
5. Otten JV, Hashimoto T, Hertl M, Payne AS, Sitaru C. Molecular diagnosis in autoimmune skin blistering conditions. *Curr Mol Med.* 2014 Jan;14(1):69-95. doi: 10.2174/1566524013136660079. PMID: 24160488; PMCID: PMC3905716.
6. Du G, Patzelt S, van Beek N, Schmidt E. Mucous membrane pemphigoid. *Autoimmun Rev.* 2022 Apr;21(4):103036. doi: 10.1016/j.autrev.2022.103036. Epub 2022 Jan 4. PMID: 34995762.
7. Ramón-Fluixà C, Bagán-Sebastián J, Milián-Masanet M, Scully C. Periodontal status in patients with oral lichen planus: a study of 90 cases. *Oral Dis.* 1999 Oct;5(4):303-6
8. Akman A, Kacaroglu H, Yilmaz E, Alpsoy E. Periodonial status inpatients with pemphigus vulgaris. *Oral Dis.* 2008 Oct;14(7):640-39.
9. Arduino PG, Farci V, D'Aiuto F, Carcieri P, Carbone M, Tanteri C, Gardino N, Gandolfo S, Carrozzo M, Broccoletti R. Periodontal status in oral mucous membrane pemphigoid: initial results of a case-control study. *Oral Dis.* 2011 Jan;17(1):90-411.
10. Arduino PC, Lopetuso E, Carcieri P, Giacometti S, Carbone M, Tanteri C. Broccoletti R. Professional oral hygiene treatment and detailed oral hygiene instructions in patients affected by mucous membrane pemphigoid with specific gingival localization: a pilot study in 12 patients. *Int J Dent Hyg.* 2012 May;10(2):138-41
11. Azizi A, Rezace M. Comparison of periodontal status in gingival oral lichen planus patients and healthy subjects. *Dermatol Res Prach.* 2012:2012:561232
12. Ertugrul AS, Dursun R, Dundar N, Avunduk MC, Hakki SS. MMP1, MMP-9, and TIMP-1 levels in oral lishen plans talichs with gingivitis or periodontitis. *Arch Oral Biol.* 2013 Jul;58(7):843-52
13. Guiglia R, Di Liberto C, Pizzo C, Picone L, Lo Muzio L, Gallo PD, Campisi C, D'Angelo M. A combined trealment regimen for desquamative gingivitis in patients with oral lichen planus. *J Oral Pathol Med.* 2007 Feb;36(2): 110-6
14. Holmstrup P, Schietz AW, Westergaard J. Effect of dental plaque control on gingival lichen planus. *Oral Surg Oral Med Oral Pathol.* 1990 May;69(5):585-90
15. Lo Russo L, Guiglia R, Pizzo G, Fierro G, Ciavarella D, Lo Muzio L, Campisi G. Effect of desquamative gingivitis on periodontal status: a pilot study. *Oral Dis.* 2010 Jan;16(1):102-716.
16. Lopez-Joret P, Camacho-Alonso F. Application of a motivation behavioral skills protocol in gingival lichen planus: a shor-term stud). *Periodontol.* 2010 Oct:81(10):1449-54.
17. Nagao Y, Sata M. Effect of oral care gel on the quality of life for oral lichen planus in patients with chronic HCV infection. *Virol J.* 2011 Jul 12;8:348.
18. Orrico SR, Navarro CM, Rosa FP, Reis FA, Salgado DS, Onofre MA. Periodontal treatment of benign mucous membrane pemphigoid. *Dent Today.* 2010 Jul;29(7):100-2;
19. Scattarella A, Petruzzi M, Ballini A, Grassi F, Nardi G. Oral lichen planus and dental hygiene: a case report. *Int J Dent Hyg.* 2011 May; 9(2):163-6
20. Schellinck AF, Rees TD, Plemons JM, Kessler HP, Rivera- Hidalgo F, Solomon ES. A comparison of the periodontal status in Patients with mucous membrane pemphigoid: a 5-year follow-up. *J Periodontol.* 2009 Nov:80(11):1765-73
21. Stone SJ, McCracken Cl, Heasman PA, Staines KS. Pennington M. Cost-effectiveness of personalized plaque control for managing the gingival manifestations of oral lichen planus: a randomized controlled study. *J Clin Periodontol.* 2013 Sep:40(9):859-67.
22. Thorat MS, Raju A, Pradeep AR. Pemphigus vulgaris: effects on periodontal health. *J Oral Sci.* 2010 Sep;52(3):449-54.
23. Tricamo MB, Rees TD, Hallmon WW, Wright JM, Cueva MA, Plemons JM. Periodontal status in patients with gingival mucous membrane pemphigoid. *J Periodontol.* 2006 Mar;77(3):398-405

European Journal of Musculoskeletal Diseases
ISSN 2038-4106/2022

Clinical Trial

CT GUIDED INFILTRATION OF THE TMJ WITH OXYGEN-OZONE IN TEMPOROMANDIBULAR JOINT OSTEOARTHROSIS. OUR EXPERIENCE.

M. Bonetti[1], G. Bragaglio[2], G. Guarino[2], I. Marchina[2], G. Ottaviani[3], M. Moretti[2] and A. Majorana[4]

[1]Department of Neuroradiology, Clinical Institute, Città di Brescia, Brescia, Italy
[2]Specialist Outpatient Clinic Oberdan, Brescia, Italy
[3]Department of Emergencies and Urgencies, Civil Hospitals of Brescia, Brescia, Italy
[4]Operating Unit of Odontostomatology, Civil Hospitals, University of Brescia, Brescia, Italy

**Correspondence to:*
Matteo Bonetti, MD
Department of Neuroradiology, Clinical Institute, Città di Brescia, Brescia, Italy
e-mail: dottorbonetti@gmail.com

ABSTRACT

In recent years, there have been an increasing number of reports on the use of oxygen-ozone therapy in the treatment of acute and chronic inflammatory diseases of small and large joints.

In this study, we report our experience in the treatment of temporomandibular joint (TMJ) osteoarthrosis with oxygen-ozone therapy performed with CT control.

From January 2018 to April 2021, we treated 86 patients (48 females and 38 males aged from 52 to 78 years, mean 66.9 years) afflicted with TMJ osteoarthrosis with oxygen-ozone therapy using a guided CT technique.

A first and second clinical check-ups were performed three months after treatment. At the first check, 71 patients (82.5%) reported an almost complete disappearance of painful symptoms, while at the second control, 63 (73.2%) confirmed a good clinical result.

Based on our experience, CT-guided oxygen-ozone therapy is a valid therapeutic option in the treatment of pain in TMJ osteoarthrosis.

KEYWORDS: *oxygen, ozone, therapy, TMJ, arthrosis, temporomandibular, joint*

INTRODUCTION

Arthrosis-degenerative pathology ranks second in incidence among temporomandibular joint (TMJ) pathologies, with greater prevalence in women and advanced age. It occurs in disc dislocation of any origin, such as trauma and infection, and as a consequence of rheumatism or other conditions that cause polyarthritis. The latter condition includes osteoarthritis, rheumatoid arthritis, psoriasis, lupus erythematosus, scleroderma, Sjogren's syndrome, and hyperuricemia (1-5).

TMJ osteoarthrosis is a degenerative disease characterized by a deterioration of the joint tissue concomitant with bone

Received: 12 May, 2022
Accepted: 23 August, 2022

ISSN: 2038-4106

changes at the condyle and/or joint eminence level. Symptoms are frequently characterized by pain on palpation, joint noises, crackles, reduced mandibular motility, and pain in the execution of normal movements.

Mechanical and biological events associated with this condition - overload, bruxism, and the tendency to ipsilateral chewing - as well as the presence of genetic factors, are responsible for the onset of this condition. The traditional treatment of this condition is based on the use of non-surgical procedures such as physiotherapy, administration of non-steroidal anti-inflammatory drugs, and arthrocentesis (1-17).

These interventions aim to control symptoms, stop the progression of the disease and restore correct joint function. Over the years, arthrocentesis has been increasing to improve jaw function and reduce pain in TMJ dysfunction, thereby improving the opening of the mouth. However, this technique's effectiveness is temporary and cannot restore the joint's microarchitecture.

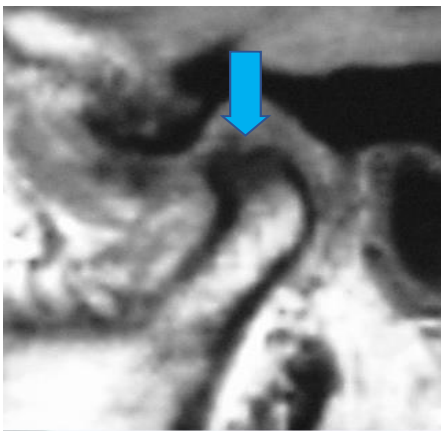

Fig 1. *Sagittal MRI scan with mouth closed: there is advanced osteoarthritis of the apex of the mandibular condyle (arrow).*

In recent years, several studies have been presented on the use of hyaluronic acid to improve TMJ's range of motion (1, 13, 15, 16, 17). Although osteoarthritis is classified as a non-inflammatory arthropathy, inflammation - of modest entity - plays an important role in the pathogenesis of joint damage, leading to progressive structural and functional changes. Initially, there is a dislocation of the articular disc or temporomandibular click. Subsequently, the pathology is complicated by the phenomena of wear of the articular disc up to its perforation and profound modification of the articular fibrocartilage with the formation of osteophytes and osteosclerosis, which determine alterations of the articular surfaces and formation of bone spurs. In the end, the articular disc is practically absent, except for residues, often observed near the anterior pole of the condyle visible on MRI.

TMJ arthrosis inevitably creates a bone contact surface between the joint heads, which generates a typical "sand" noise during the opening movement and is clinically detectable on TMJ palpation. The most frequent symptom is pain accentuated with movement and reduced with rest. Pain has a double origin: inflammatory pain is derived from the release of inflammatory mediators, and neuropathic pain is caused by degeneration of the sensory nerve endings.

In this study, we report our experience in the treatment of pain for TMJ arthrosis treated with oxygen-ozone therapy under CT scan control.

MATERIALS AND METHODS

From January 2018 to April 2021, 86 patients (48 females and 38 males aged from52 to 78 years, mean 66.9 years) affected by TMJ osteoarthrosis were treated with oxygen-ozone therapy using a guided CT technique. All patients previously did a dynamic MRI of TMJ, which confirmed the diagnosis of degenerative lesions of osteoarthritis in one (27 patients 31.4%) or both (59 patients 68.6%) TMJ (Fig. 1).

Dynamic MRI is currently the best method for the detailed study of joint areas such as bone structures, muscles, and ligaments. The examination, supplemented by dynamic sequences, starts from the intercuspidation phase (contact relationship between the posterior teeth of the upper and lower arches) to reach the maximum mouth opening. Dynamic MRI is the complete technique for studying TMJ, providing morpho-structural information on the articular bone heads and the articular menisci (Fig. 2 A-D).

The main advantages of other dental and skull imaging methods are high contrast resolution and the possibility to distinguish different, in addition to the absence of radiation.

Infiltration technique

All treatments were performed under CT guidance. After being informed about the procedure and possible complications, the patient signed the informed consent. First, preliminary CT scans were performed to confirm the pathology. The skin was then disinfected using special preparations for general skin antisepsis (Citro jod 100 registration No. 1805 of the Italian Ministry of Health based on iodine polyvinylpyrrolidone).

A preliminary CT scan with an open mouth was performed to identify the skin approach point (Fig 3). Next, local

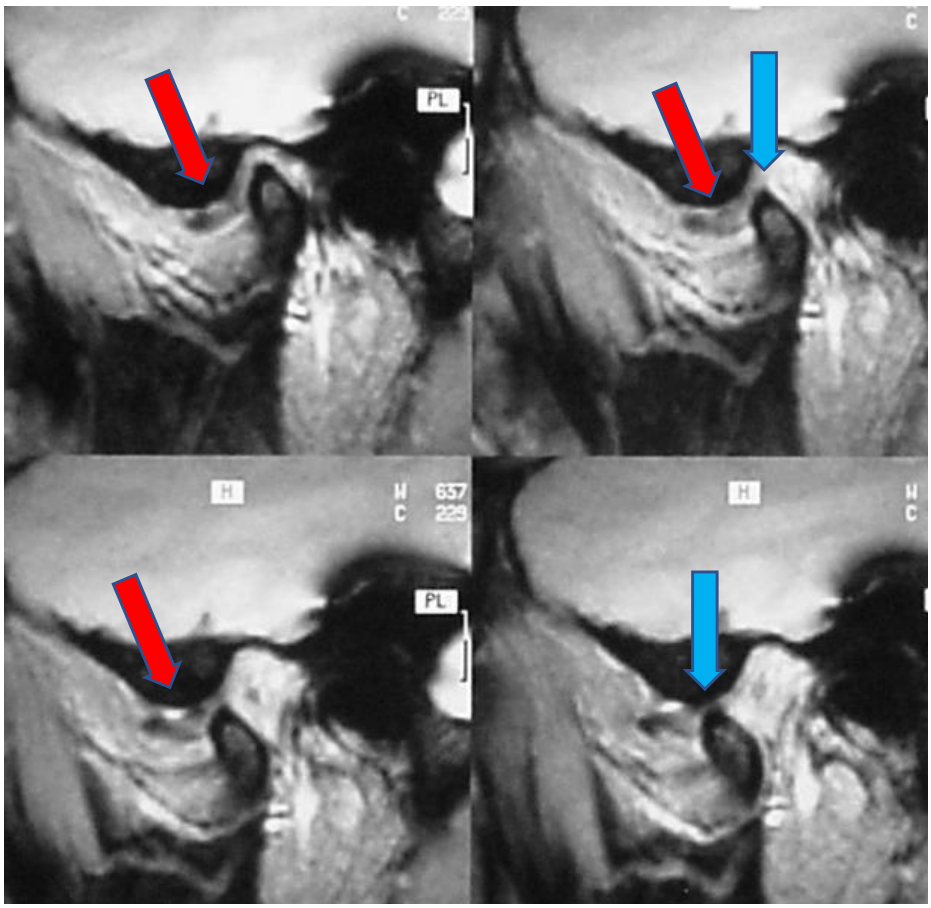

Fig. 2. *(A-D): Dynamic Magnetic Resonance Imaging: irreducible dislocation of the articular meniscus during the condyle excursion manoeuvre (red arrows), with initial arthritic degeneration of the apex of the condyle (blue arrows)*

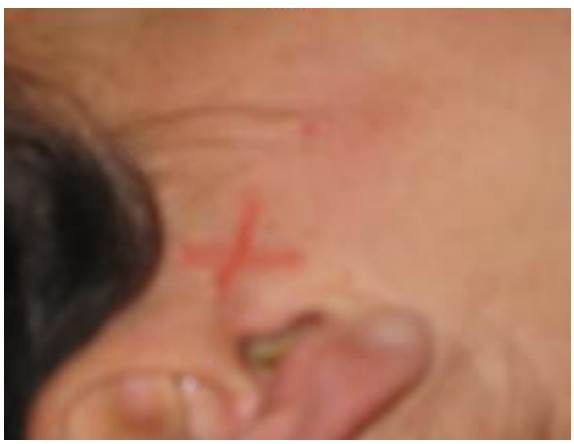

Fig 3. *The point of skin approach to TMJ is marked with a dermographic pencil.*

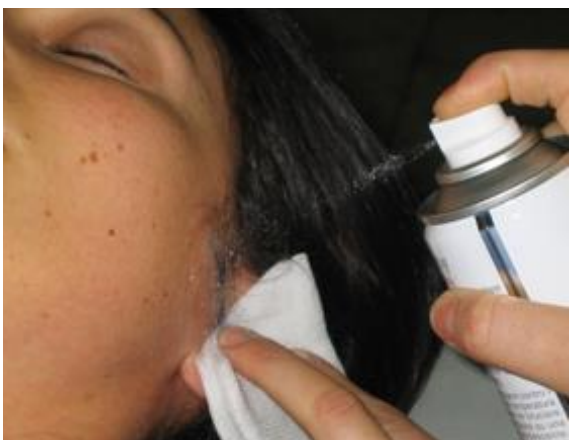

Fig. 4. *Local anesthesia with ethyl chloride.*

anesthesia was performed with ethyl chloride spray (Fig 4), and then, again, under the CT guide, a 25G needle was inserted (Fig 5). Finally, the corrected position of the needle was checked with a CT scan (Fig 6). A 5 ml syringe in polyethylene was filled with the gaseous mixture at a 25 µg / ml concentration.

The gaseous mixture was injected using a variable volume from 3 cc to 5 cc of the O2-O3 gaseous mixture. After the infiltration, another CT scan was performed to document the correct distribution of the gaseous mixture (Fig 7). All material used was sterile and single use.

RESULTS

At the clinical check-up one month after treatment, 71 patients (82.5%) reported an almost complete disappearance of painful symptoms, while the remaining 15 (17,5%) had no significant improvements. In 38 of the 71 patients with a good outcome, oral anti-inflammatory therapy was associated the week after guided CT infiltration.

The 15 patients without satisfactory clinical results were referred to their dentist to evaluate other therapeutic approaches. Seventy-one patients with clinical benefits were then re-evaluated after an additional three. Of these, 63 (73.2%) confirmed the good clinical result, while 8 had a relapse of the symptoms that had recurred; this group was sent back to a dental specialist (Table I).

DISCUSSION

TMJ can be affected by arthrosis (degenerative disease), usually in people over 50 years. Women are prevalent (1-17), and this data is confirmed in the present study, where 48 (55.8%) women out of 86 patients were treated.

Occasionally, patients complain of stiffness, an abnormal sound in jaw movement, or mild pain. Crepitus can result from degeneration or perforation of the disc, producing friction between bone and bone. Joint involvement is usually bilateral.

In general, even a simple X-ray of the joint can provide good diagnostics. However, for a more precise and complete

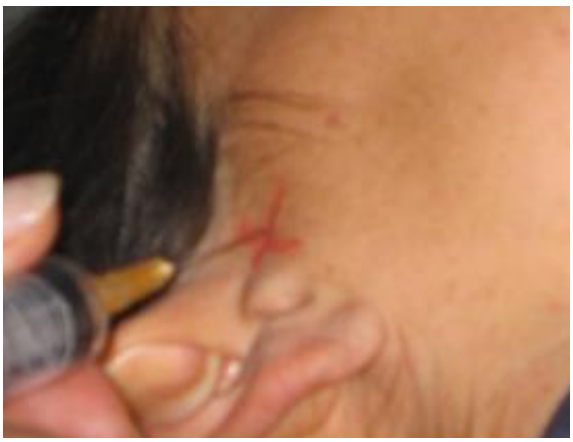

Fig. 5. *Infiltration with 25 G needle, orange color code.*

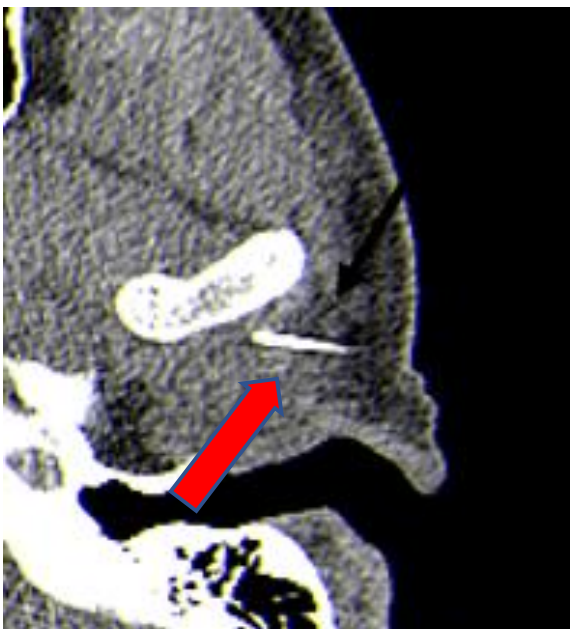

Fig. 6. *Open-mouth CT scan that documents the correct positioning of the needle in the joint cavity (arrow).*

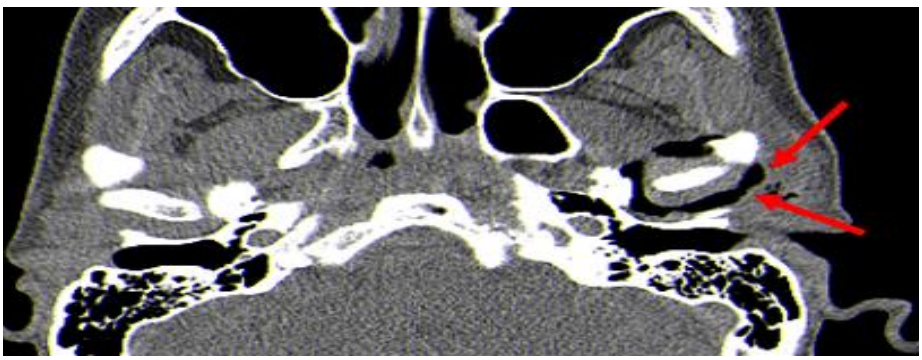

Fig. 7. *Post infiltration CT scan to check the correct distribution of the gas mixture in the joint cavity (arrows).*

Table I. *Clinical outcome.*

	one month check	three months check
excellent clinical outcome	71/86 (82,5%)	63/86 (73,2%)
poor clinical outcome	15/86 (17,5%)	23/86 (26,8%)

diagnosis, it is useful to carry out the investigation with a CT scan or an MRI performed with dynamic sequences. This latter method is currently considered the most effective in providing a detailed study of the degenerative pathology of the TMJ. In our study, all patients enrolled did a dynamic MRI scan of the TMJs for diagnostic purposes, which confirmed the diagnosis of TMJ osteoarthritis.

The standard treatment of TMJ osteoarthritis is based on non-surgical approaches such as physiotherapy, administration of non-steroidal anti-inflammatory drugs, and arthrocentesis. The combination of arthrocentesis with visco-supplementation with hyaluronic acid appears to be more effective than arthrocentesis alone (1, 13, 15-17). Given the brilliant therapeutic results reported in literature proving the efficacy of oxygen-ozone in the treatment of acute and chronic inflammatory pathologies of small and large joints (18-31), 86 patients affected by TMJ pain were treated.

Patients were re-evaluated one and three months after treatment. The clinical outcome was excellent in 71 patients (82.5%) at the one-month follow-up and 63 patients (73.2%) at the three-month follow-up. The mechanisms of action of the oxygen-ozone gas mixture are well known and widely documented in the literature (18-31). The rationale for anti-inflammatory treatment by intra-articular oxygen-ozone infiltration is based on anti-inflammation and analgesic action. The oxygen-ozone gas mixture normalizes the level of cytokines and prostaglandins, increases superoxide dismutase, minimizes reactive oxidant species, and improves local circulation with a eutrophic effect.

CONCLUSION

The good results obtained in our series are linked to the biological activities of oxygen-ozone therapy. In particular, to the improvement of intra and trans tissue oxygenation determine the improvement of hypoxia in addition to anti-inflammatory, analgesic, and eutrophicating activities of ozone. In conclusion, oxygen-ozone therapy can be considered an excellent therapeutic approach for patients afflicted with arthrosis of the TMJ.

Author Contributions

G.C. and F.C. designed the research study. G.C. performed the research. P.C. and G.C. wrote the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

Funding

This research received no external funding.

Conflict of Interest

The authors declare no conflict of interest.

REFERENCES

1. Gurung T, Singh R, Mohammad S, Pal U, Mahdi A, Kumar M. Efficacy of arthrocentesis versus arthrocentesis with sodium hyaluronic acid in temporomandibular joint osteoarthritis: A comparison. *National Journal of Maxillofacial Surgery*. 2017;8(1):41. doi:10.4103/njms.njms_84_16
2. Ibi M. Inflammation and Temporomandibular Joint Derangement. *Biological & Pharmaceutical Bulletin*. 2019;42(4):538-542. doi:10.1248/bpb.b18-00442
3. Tamimi D, Jalali E, Hatcher D. Temporomandibular Joint Imaging. *Radiologic Clinics of North America*. 2018;56(1):157-175. doi:10.1016/j.rcl.2017.08.011
4. Derwich M, Mitus-Kenig M, Pawlowska E. Interdisciplinary Approach to the Temporomandibular Joint Osteoarthritis—Review of

the Literature. *Medicina*. 2020;56(5):225. doi:10.3390/medicina56050225

5. Al-Ani Z. Temporomandibular Joint Osteoarthrosis: A Review of Clinical Aspects and Management. *Primary Dental Journal*. 2021;10(1):132-140. doi:10.1177/2050168420980977
6. Marotte H. Les articulations temporomandibulaires et les pathologies rhumatismales inflammatoires. *Revue de Stomatologie, de Chirurgie Maxillo-faciale et de Chirurgie Orale*. 2016;117(4):223-227. doi:10.1016/j.revsto.2016.07.011
7. Tanaka E, Detamore MS, Mercuri LG. Degenerative Disorders of the Temporomandibular Joint: Etiology, Diagnosis, and Treatment. *Journal of Dental Research*. 2008;87(4):296-307. doi:10.1177/154405910808700406
8. Aiken A, Bouloux G, Hudgins P. MR Imaging of the Temporomandibular Joint. *Magnetic Resonance Imaging Clinics of North America*. 2012;20(3):397-412. doi:10.1016/j.mric.2012.05.002
9. Yin Y, He S, Xu J, et al. The neuro-pathophysiology of temporomandibular disorders-related pain: a systematic review of structural and functional MRI studies. *The Journal of Headache and Pain*. 2020;21(1). doi:10.1186/s10194-020-01131-4
10. Beinarovich SV, Filimonova OI. Morphometric features of the temporomandibular joints according to MR studies in adult patients with dislocations of the articular discs and malocclusion of the anterior teeth. *Stomatologiya*. 2020;99(6):44. doi:10.17116/stomat20209906144
11. Toshima H, Ogura I. Characteristics of patients with temporomandibular joint osteoarthrosis on magnetic resonance imaging. *Journal of Medical Imaging and Radiation Oncology*. 2020;64(5):615-619. doi:10.1111/1754-9485.13054
12. Gharavi SM, Qiao Y, Faghihimehr A, Vossen J. Imaging of the Temporomandibular Joint. *Diagnostics*. 2022;12(4):1006. doi:10.3390/diagnostics12041006
13. Marzook HAM, Abdel Razek AA, Yousef EA, Attia AAMM. Intra-articular injection of a mixture of hyaluronic acid and corticosteroid versus arthrocentesis in TMJ internal derangement. *Journal of Stomatology, Oral and Maxillofacial Surgery*. 2020;121(1):30-34. doi:10.1016/j.jormas.2019.05.003
14. Castaño-Joaqui OG, Cano-Sánchez J, Campo-Trapero J, Muñoz-Guerra MF. TMJ arthroscopy with hyaluronic acid: A 12-month randomized clinical trial. *Oral Diseases*. 2020;27(2):301-311. doi:10.1111/odi.13524
15. GUARDA-NARDINI L, FERRONATO G, FAVERO L, MANFREDINI D. Predictive factors of hyaluronic acid injections short-term effectiveness for TMJ degenerative joint disease. *Journal of Oral Rehabilitation*. 2010;38(5):315-320. doi:10.1111/j.1365-2842.2010.02164.x
16. Wang XW, Fang W, Li YJ, Long X, Cai HX. Synovial fluid levels of VEGF and FGF-2 before and after intra-articular injection of hyaluronic acid in patients with temporomandibular disorders: a short-term study. *British Journal of Oral and Maxillofacial Surgery*. 2021;59(1):64-69. doi:10.1016/j.bjoms.2020.07.013
17. Yilmaz O, Korkmaz YT, Tuzuner T. Comparison of treatment efficacy between hyaluronic acid and arthrocentesis plus hyaluronic acid in internal derangements of temporomandibular joint. *Journal of Cranio-Maxillofacial Surgery*. 2019;47(11):1720-1727. doi:10.1016/j.jcms.2019.07.030
18. Andreula CF, Simonetti L, De Santis F, Agati R, Ricci R, Leonardi M. Minimally invasive oxygen-ozone therapy for lumbar disk herniation. *AJNR American journal of neuroradiology*. 2003;24(5):996-1000.
19. Bonetti M, Fontana A, Cotticelli B, Volta GD, Guindani M, Leonardi M. Intraforaminal O(2)-O(3) versus periradicular steroidal infiltrations in lower back pain: randomized controlled study. *AJNR American journal of neuroradiology*. 2005;26(5):996-1000.
20. Costa T, Linhares D, Ribeiro da Silva M, Neves N. Ozone therapy for low back pain. A systematic review. *Acta Reumatologica Portuguesa*. 2018;43(3):172-181.
21. Bonetti M, Cotticelli B, Raimondi G, Valdenassi L, Richelmi P, Bertè E. Ossigeno-ozono terapia vs infiltrazioni epidurali cortisoniche. *Rivista di Neuroradiologia*. 2000;13(2):203-206. doi:10.1177/197140090001300207
22. Gallucci M, Limbucci N, Zugaro L, et al. Sciatica: treatment with intradiscal and intraforaminal injections of steroid and oxygen-ozone versus steroid only. *Radiology*. 2007;242(3):907-913. doi:10.1148/radiol.2423051934
23. Gaulandi G, Bonetti M. Ossigeno-ozonoterapia nel trattamento della patologia dolorosa del rachide lombare: esperienza preliminare. *Acta Toxic Therap*. 1996;17(2-3):261-264.

24. Iliakis E. Ozone treatment in low back pain. *Orthopaedics*. 1995;1:29-33.
25. Iliakis E, Valadakis V, Vynios DH, Tsiganos CP, Agapitos E. Rationalization of the Activity of Medical Ozone on Intervertebral Disc A Histological and Biochemical Study. *Rivista di Neuroradiologia*. 2001;14(1_suppl):23-30. doi:10.1177/19714009010140s105
26. Lehnert T, Naguib NNN, Wutzler S, et al. Analysis of Disk Volume before and after CT-guided Intradiscal and Periganglionic Ozone–Oxygen Injection for the Treatment of Lumbar Disk Herniation. *Journal of Vascular and Interventional Radiology*. 2012;23(11):1430-1436. doi:10.1016/j.jvir.2012.07.029
27. Magalhaes FNDO, Dotta L, Sasse A, Teixera MJ, Fonoff ET. Ozone therapy as a treatment for low back pain secondary to herniated disc: a systematic review and meta-analysis of randomized controlled trials. *Pain Physician*. 2012;15(2):E115-129.
28. Muto M, Andreula C, Leonardi M. Treatment of herniated lumbar disc by intradiscal and intraforaminal oxygen-ozone (O2-O3) injection. *Journal of Neuroradiology*. 2004;31(3):183-189. doi:10.1016/s0150-9861(04)96989-1
29. Perri M, Grattacaso G, Di Tunno V, et al. MRI DWI/ADC signal predicts shrinkage of lumbar disc herniation after O2–O3 discolysis. *The Neuroradiology Journal*. 2015;28(2):198-204. doi:10.1177/1971400915576658
30. Steppan J, Meaders T, Muto M, Murphy KJ. A metaanalysis of the effectiveness and safety of ozone treatments for herniated lumbar discs. *Journal of vascular and interventional radiology: JVIR*. 2010;21(4):534-548. doi:10.1016/j.jvir.2009.12.393
31. Zhang Y, Ma Y, Jiang J, Ding T, Wang J. Treatment of the lumbar disc herniation with intradiscal and intraforaminal injection of oxygen-ozone. *Journal of Back and Musculoskeletal Rehabilitation*. 2013;26(3):317-322. doi:10.3233/bmr-130386

European Journal of Musculoskeletal Diseases
ISSN 2038-4106/2022

Case Report

INTRAMUSCULAR OEDEMA AFTER TRUNCULAR ANALGESIA DIAGNOSED BY MRI: A CASE REPORT AND DIFFERENTIAL DIAGNOSIS OF MOUTH OPENING LIMITATION

F. Cecchetti[1], M. Di Girolamo[2], L. Baggi[1], D. Mazza[1]

[1]Department of Social Dentistry and Gnathological Rehabilitation, National Institute for Health, Migration and Poverty (NIHMP), Roma, Italy;
[2]Department of Clinical Sciences and Translational Medicine, Tor Vergata University, Roma, Italy.

Correspondence to:
Dario Mazza, DDS
Department of Social Dentistry and Gnathological Rehabilitation,
National Institute for Health, Migration and Poverty (NIHMP), Roma, Italy
e-mail: mzzdra@hotmail.com

ABSTRACT

Mouth opening limitation (MOL) is an important clinical sign generally referred to as temporomandibular disorders (TMD) but MOL can also be due to other pathologies as neoformations. The first level's radiological exam is an orthopantomography that helps the clinician choose the most appropriate second-level exam. MRI is the gold standard for TMD, while multislices CT generally investigates maxillofacial pathologies. Cone beam CT (CBCT) with an appropriate FoV is recommended if a contrast agent is not indicated. Muscle contractures frequently cause MOL as prolonged mouth opening during dental treatment, antalgic contractures due to any infectious-inflammatory process, or after surgery. An MRI investigation of a case of intramuscular oedema after troncular analgesia has never been documented in the literature.

A 36-year-old female with MOL (21 mm) with midline deflection to the left side since the last 15 days is presented. The patient reported that she had endodontic therapy on 4.6 after troncular analgesia at the ipsilateral ascending mandibular ramus just before the onset of symptoms. She had never experienced symptoms of TMJ dysfunction a before T2/DP-weighted TMJ MRI with T1/T2-weighted scans of the pterygoid muscles in axial and coronal planes with a dedicated coil was performed. The images demonstrate the presence of a reducing disc displacement in the right TMJ and a non-reducing disc displacement in the left TMJ with a limitation of condyle translation. An inhomogeneous area of isointense in T1 and hyperintense in T2, referable to intramuscular oedema resulting from troncular analgesia, was appreciated At the right internal pterygoid muscle, at the level of the spine of Spix.

MRI is an essential method in the differential diagnosis of MOL and allows targeted and resolutive therapy.

KEYWORDS: *MRI, pterygoid muscles, temporomandibular disorders*

Received: 23 May 2022
Accepted: 19 August 2022

ISSN: 2038-4106

INTRODUCTION

During oral examination (OE) mouth opening limitation (MOL) is one of the most important clinical signs to be detected. In most cases, MOL is related to chronic trauma of the temporomandibular joints (TMJ). More rarely, the cause is related to specific arthritis, malformations, trauma outcomes, or neoformations.

Functional alterations may result from intraarticular adhesions (1) or extraarticular causes that determine a limitation of mandibular movements (2).

Intraarticular causes could be a joint lock, neoformations, chronic arthritis (post-traumatic, infectious, specific arthritis), intracapsular fracture outcomes, and ankylosis. In contrast, extraarticular ones are neoformations, dysplastic lesions, malformations or fractures of the facial bones that can cause an impediment to mandibular movements, muscular contractures (post-traumatic, infectious, antalgic, and in dysfunctional patients), scarring (post-traumatic or following burns), progressive systemic sclerosis, connective tissue diseases and outcomes of demolition resective surgery with reconstruction of the jaws tissues and systemic diseases leading to a deficit of the neuromuscular system. Therefore, the differential diagnosis of MOL is mainly performed by anamnestic investigation and oral examination and completed by imaging.

The first level's radiological exam is an orthopantomography (OPT) of the dental arches, which helps the clinician choose the most appropriate second-level exam.

MRI is the gold standard for temporomandibular disorders (TMD), while multislices CT generally investigates maxillofacial pathologies (fractures, malformations, dysplastic and neoplastic lesions). CBCT with an appropriate FoV is recommended if a contrast agent is not indicated. Among the intraarticular causes are the TMJ lock, usually caused by chronic inflammation resulting from a non-reducible disc dislocation clinically manifested by a limitation of the mouth opening (1). The lock is defined as chronic when condylar hypomobility remains after several episodes of remission and exacerbation of symptoms. The mandibular kinetics shows a limitation of mouth opening of less than 30mm. Clinically, non-specific symptoms such as cervicalgia, headache, tinnitus, and vertigo may also be present. On OE, there is a deviation of the mandible towards the locked TMJ both during opening and protrusion. On palpation of the locked joint, no clicks can be appreciated, and rarely can a crackling be perceived. The joint compression test causes vivid pain. The end-feel test does not increase the mouth opening and causes severe pain in the locked joint. MRI shows a condylar hypomobility with the articular disc displaced anteriorly. It is also easy to find T2W hyperintense intra-articular joint effusion, retrodiscal fibrosis, and remodeling of the articular surface of the condyle (3). CBCT is only useful in cases of gross remodelling of the condyle. Here a case of intramuscular oedema resulting from troncular analgesia is reported, and the pertinent literature is discussed.

CASE REPORT

A 36-year-old female patient presented with MOL (21 mm) with midline deviation to the left side since the last 15 days. At the time of her medical history, she reported that she had undergone endodontic therapy on 4.6 after troncular analgesia at the ipsilateral ascending mandibular ramus just before the onset of symptoms. She had never experienced symptoms of TMJ dysfunction before the MOL had started after dental treatment and had progressively worsened in about 10 days.

She reported pain in the right temporomandibular region, at the level of the right internal pterygoid muscle and right masseter, which were painful on palpation (80 VAS), and limited pain in the left temporomandibular area (40 VAS). The end-feel test did not allow an increase in maximum mouth opening and caused pain in the left TMJ. The patient presented an occlusal class I. She also reported frequent teeth clenching. Rx OPT was negative.

A TMJ MRI with T1/T2-weighted scans of the pterygoid muscles in axial and coronal planes with a dedicated coil was performed. The images demonstrate the presence of a reducing disc displacement in the right TMJ and a non-reducing disc displacement in the left TMJ with a limitation of condyle translation. Furthermore, at the right internal pterygoid muscle, at the level of the spine of Spix, an inhomogeneous area of isointense in T1 and hyperintense in T2 scans referable to intramuscular oedema probably resulting from troncular analgesia, was detected (Fig. 1-3).

DISCUSSION

Frequently, dental therapies requiring very long sessions, such as endodontic treatment of a molar, result in muscle spasms and/or antalgic contractures that resolve spontaneously or with appropriate medical therapy within a couple of weeks. In some cases, these muscle spasms can lead to joint dysfunction or worsen the prognosis of an already pre-

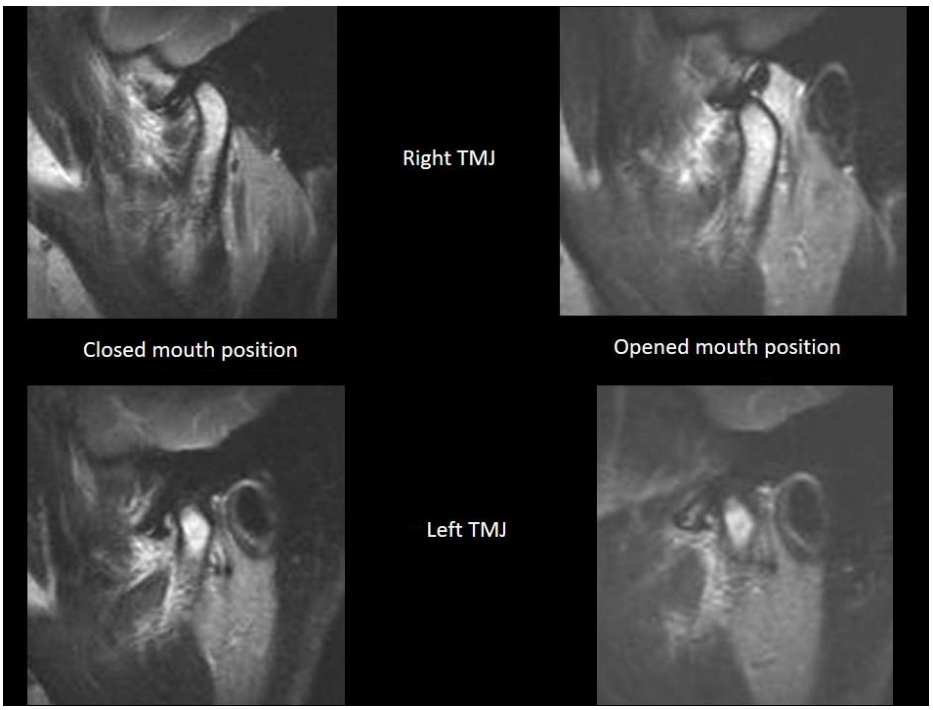

Fig. 1. *Turbo spin-echo T2-weighted MRI with parasagittal scans: top images of the right TMJ, bottom images of the left TMJ; left with mouth closed and right with mouth open.*

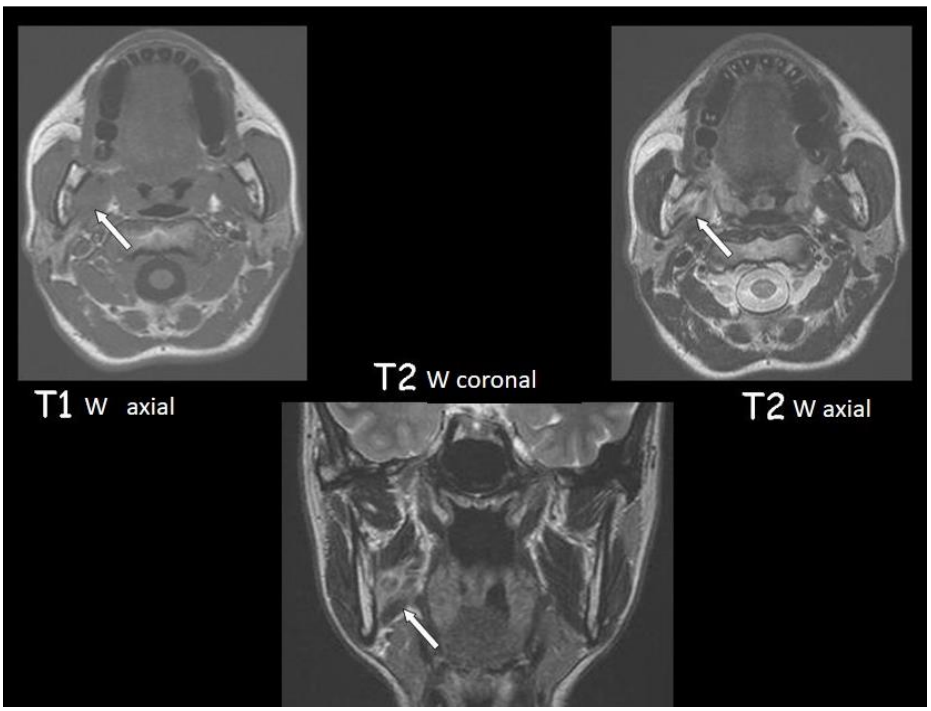

Fig. 2. *MRI of the maxillofacial structures with axial T1- and T2-weighted and coronal T2-weighted scans. The white arrow indicates the lesion inside the right internal pterygoid muscle which is isointense in T1 and hyperintense in T2.*

existing dysfunction. Troncular analgesia alone may also lead to muscle contracture due to oedema at the injection site and, thus, to MOL. In order to make a proper diagnosis, an MRI scan to evaluate both the muscles and the TMJ is needed. In the MRI request the clinician must to point out the suspicion of a lesion in a specific muscle to allow the radiologist to perform an adequate MRI examination. To perform the correct diagnosis several pathological condition has to be excluded in differential diagnosis. In addition, MOL can be due to several conditions.

A benign neoformation (4) such as a chondroma, osteoma or osteochondroma and synovial chondromatosis (5) can cause inflammation and alteration of the joint tissues such as adhesions and thus functional limitations but is unlikely to cause MOL on its own.

Regarding chronic arthritis, the patient often reports a previous trauma (fracture, whiplash) leading to osteoarthritis and thus to chronic inflammation, or, more rarely, recurrent infections (in debilitated, immunocompromised patients) or with psoriasis, rheumatoid arthritis and other autoimmune diseases.

In the case of outcomes of intracapsular fracture, imaging is essential to understand the cause of the MOL. OPT may show remodelling of the condylar head, but CBCT scan is the elective study; dynamic MRI is equally essential to evaluate the condylar-discal complex and to exclude the presence of other pathologies (6, 7).

TMJ ankylosis is the last stage of diseases such as TMJ dysfunction, condyle fractures and chronic arthritis that evolve into fibrosis and then bony ankylosis. The patient's clinical history will differ depending on the etiopathogenesis of the ankylosis and a simple OPT could be sufficient to make the diagnosis. A CBCT scan of TMJ will be used to describe the extent of the ankylotic block and to plan TMJ surgery (8).

Among the extraarticular causes that could lead to MOL we find dysplastic alterations as fibrous dysplasia (9), ossifying fibroma, cherubism (10) and leontiasis.

Malignant tumours can cause a MOL either directly by causing adhesions with the mandible (parotid lodge) or a mechanical block to mandibular movements (infratemporal fossa) or indirectly by involving the masticatory elevator muscles (temporalis, masseter and internal pterygoid) causing trismus (11).

In our report, clinical history shows a sudden onset of MOL without a previous history of joint dysfunction. Generally, the patient may be asymptomatic or report pain; in addition to MOL , signs such as intra- and/or extra-oral swellings, swelling of the cervico-facial lymph nodes, erythro/leukoplasic lesions (even ulcerated) in the oral cavity in particular on the retromolar trigone, soft palate and tonsillar lodge, epistaxis, sudden tooth mobility, visual changes and more generally neurological symptoms related to cranial nerve or central nervous system alterations and signs of endocranial hypertension can be appreciated.

The OPT may be negative or show the absence of rear wall of the maxillary sinus (12) or alterations of the ascending

Fig. 3. *Maximum mouth opening and lateral right movement, protrusive movement, and lateral left movement.*

branch of the mandible. Multislices CT with contrast agent and MRI (13) are indicated.

In case of maxillofacial fractures (14) which cause an impairment of mandibular movements, CBCT are used for diagnosis and to plan surgical therapy.

The hypertrophy of the coronoid processes cause an increase in the height of the coronoid processes, which impacts against the posterior wall of the zygoma, resulting in a MOL (15). An OPT or a CBCT is sufficient for a diagnosis.

Muscle contractures can be caused by a prolonged opening of the mouth such as during dental treatment, antalgic contractures due to any infectious-inflammatory process (abscesses and odontogenic phlegmons involving the masseter or internal pterygoid), the outcome of trauma with skin ecchymosis, intramuscular hemangioma (16) and intramuscular oedema, surgery such as the extraction of a third molar (17);

Scarring outcomes as a result of facial skin burns, can limited the mouth opening as well as progressive systemic sclerosis (18) and connectivopathies result in a progressive sclerosis of the connective tissues, particularly the perioral tissues (tobacco bag mouth) that reduces the mouth opening. The diagnosis is clinical and a referral to a specialist is recommended for a general assessment of the patient's health.

Among the connectivopathies, scleroderma and in particular the Parry-Romberg syndrome, especially when it occurs during development, determines a localised atrophy of connective tissues (cutaneous and muscular) that blocks skeletal growth resulting in facial asymmetry and, in severe cases, even MOL.

Pedicled or revascularized flaps in maxillofacial surgery can lead to scar retractions that, together with submandibular muscle deficits caused by laterocervical emptying, can lead to MOL.

Systemic diseases leading to a deficit of the neuromuscular system can give rise to a spastic paresis of the masticatory muscles or a deficit of the trigeminal efferences. Hypercalcemia can also lead to 'tetanic' trismus of the masticatory muscles.

CONCLUSION

MRI is an essential method in the differential diagnosis of MOL and by highlighting intramuscular and articular lesions, it allows targeted and resolutive therapy.

For the first time, an MR imaging of a case with a MOL caused by intramuscular oedema at the injection site after mandibular nerve troncular analgesia is presented.

REFERENCES

1. Nitzan DW. "Friction and Adhesive Forces" – Possible Underlying Causes for Temporomandibular Joint Internal Derangement. *Cells Tissues Organs*. 2003;174(1-2):6-16. doi:10.1159/000070570
2. De Laat A, Horvath M, Bossuyt M, Fossion E, Baert AL. Myogenous or arthrogenous limitation of mouth opening: correlations between clinical findings, MRI, and clinical outcome. *Journal of Orofacial Pain*. 1993;7(2):150-155.
3. Mazza D, Di Girolamo M, Cecchetti F, Baggi L. MRI findings of working and non-working TMJ during unilateral molar clenching on hard bolus. *Journal of Biological Regulators and Homeostatic Agents*. 2020;34(3 Suppl. 1):1-8.
4. Izzo L, Caputo M, Buffone A, et al. [Benign tumors and pseudotumors of temporo-mandibular joint: radiologic aspects]. *Il Giornale Di Chirurgia*. 2005;26(8-9):314-317.
5. Testaverde L, Perrone A, Caporali L, et al. CT and MR findings in synovial chondromatosis of the temporo-mandibular joint: Our experience and review of literature. *European Journal of Radiology*. 2011;78(3):414-418. doi:10.1016/j.ejrad.2009.11.015
6. Mazza D, Karrub Z, Stasolla A, et al. Qualitative comparison of MR TSE T2 and HASTE in temporomandibular disorders. Clinical observations. *Minerva Stomatologica*. 2005;54(4):219-226.
7. Barchetti F, Stagnitti A, Glorioso M, et al. Static and dynamic MR imaging in the evaluation of temporomandibular disorders. *European Review of Medical and Pharmacological Sciences*. 2014;18(20):2983-2987.
8. Tanaka H, Westesson PL, Larheim TA. Juxta-articular ankylosis of the temporomandibular joint as an unusual cause of limitation of mouth opening: Case report. *Journal of Oral and Maxillofacial Surgery*. 1998;56(2):243-246. doi:10.1016/s0278-2391(98)90878-3
9. Mazza D, Primicerio P, Ambesi Impiombato F, Impara L. Studio TC e RM in un caso di fibro-displasia ossea. *Italian Oral Surgery*. Published online May 2008:21-25.

10. Mazza D, Ferraris L, Galluccio G, Cavallini C, Silvestri A. The role of MRI and CT in diagnosis and treatment planning of cherubism: a 13-year follow-up case report. *European Journal of Paediatric Dentistry*. 2013;14(1):73-76.
11. Weber C, Dommerich S, Pau HW, Kramp B. Limited mouth opening after primary therapy of head and neck cancer. *Oral and Maxillofacial Surgery*. 2010;14(3):169-173. doi:10.1007/s10006-010-0220-2
12. Mazza D, Bontempi E, Guerrisi A, et al. Paranasal sinuses anatomic variants: 64-slice CT evaluation. *Minerva Stomatologica*. 2007;56(6):311-318.
13. Perrone A, Guerrisi P, Izzo L, et al. Diffusion-weighted MRI in cervical lymph nodes: Differentiation between benign and malignant lesions. *European Journal of Radiology*. 2011;77(2):281-286. doi:10.1016/j.ejrad.2009.07.039
14. Hwang K, Kim DH. Analysis of Zygomatic Fractures. *Journal of Craniofacial Surgery*. 2011;22(4):1416-1421. doi:10.1097/scs.0b013e31821cc28d
15. Kim SM, Lee JH, Kim HJ, Huh JK. Mouth opening limitation caused by coronoid hyperplasia: a report of four cases. *Journal of the Korean Association of Oral and Maxillofacial Surgeons*. 2014;40(6):301-307. doi:10.5125/jkaoms.2014.40.6.301
16. Mazza D, Impiombato F, Luppi G, Primicerio P. Magnetic resonance imaging of intramuscular hemangioma: a literature review. *Doctor OS*. 2006;17(7):1-5.
17. Mazza D, Di Girolamo M, Cecchetti F, Baggi L. Appearance of normal MRI anatomy of the lingual nerve using steady-state free precession sequences at 3-T. *Journal of Biological Regulators and Homeostatic Agents*. 2020;34(3 Suppl. 1):19-26.
18. Alantar A, Cabane J, Hachulla E, et al. Recommendations for the care of oral involvement in patients with systemic sclerosis. *Arthritis Care & Research*. 2011;63(8):1126-1133. doi:10.1002/acr.20480.

European Journal of Musculoskeletal Diseases
ISSN 2038-4106/2022

Case Report

TREATMENT OF AMALGAM TATTOO WITH MUCOABRASION ASSOCIATED WITH A BILAMINAR TECHNIQUE AND A SUBEPITHELIAL CONNECTIVE TISSUE GRAFT: A CASE REPORT

L. Parma Benfenati[1]

[1]Private practice, Ferrara, Italy

Correspondence to:
Lucrezia Parma Benfenati, DDS
Private practice
Corso della Giovecca 155, 44121 Ferrara, Italy
e-mail: lucrezia.parmabenfenati@hotmail.it

ABSTRACT

An amalgam tattoo is an iatrogenic lesion that may lead to aesthetic problems. A 47-year-old woman complained of very unattractive dark pigmentations and a flat macule adjacent to a restored tooth (amalgam tattoo) on the first and second maxillary premolars with a mild gingival recession at the first bicuspid. Following muco-abrasion to eliminate the oral pigmented lesion, a bilaminar mucogingival procedure was planned to treat the gingival recession. At the 8-year follow-up, gingival color and texture blended well with adjacent soft tissue areas, the periodontal tissues appeared healthy, and no scar tissue was present. The patient was very pleased with the final result. Therefore, a one-stage procedure should be considered an effective treatment of amalgam tattoo, providing positive morphologic and cosmetic outcomes over an 8-year follow-up period.

KEYWORDS: *tattoo, mucosa, gingival, tissue graft, pigmentation*

INTRODUCTION

Regarding soft tissue colour, in 1999, the American Academy of Periodontology (AAP) drew up a classification system of developmental or acquired mucogingival deformities and conditions based on clinical and morphologic criteria (1). The abnormal colour of the gingiva was included in this classification (1). Furthermore, the amalgam tattoos are also included in the new periodontal classification of non–plaque-induced gingival diseases and conditions approved by AAP and European Federation of Periodontology members in 2018 (2).

Although amalgam discoloration of the oral mucosa does not represent a pathological entity per se and is usually asymptomatic, it can still create cosmetic dissatisfaction for the patient, leading to treatment, especially in anterior areas (3, 4). With an approximate incidence of 18.9% among pigmented lesions of the oral mucosa, amalgam tattoo usually appears as a bluish-blue, black, or grayish spot of different diameters and is most frequently located at the level of the keratinized gingiva or alveolar mucosa, often related by evident cause-and-effect: adjacent amalgam restorations (5).

Received: 7 May 2022
Accepted: 23 July 2022

ISSN: 2038-4106

Metal particles can become incorporated into the oral mucosa in different manners: by condensation of the material to adjacent tissues during ortho- or retro-grade obturation; injury to the adjacent mucosa during replacement of old amalgam restoration; fracture of the material during extractions of the previously amalgam-treated tooth or leakage of the material to the alveolus; corrosion of the apical retrograde obturation (6). A radiograph is recommended to confirm the presence of metallic particles, but the absence of radiographic evidence does not rule out the possibility since particles are often too fine or widely dispersed to be visible on radiographs (6). Depending on the diameter of the leaked particles, aluminium in amalgam may be phagocytosed by macrophages or encapsulated by connective tissue fibres. The cellular mobility of macrophages may be why many of these pigmentations appear to grow over time (6). As anticipated, the localization of the particles may result in aesthetic complaints.

Microscopic examination reveals that amalgam is present in the tissues in two forms: as irregular dark, solid fragments of metal or as numerous, discrete fine, brown, or black granules dispersed along collagen bundles and around small blood vessels and nerves, also disclosing the presence of metal fragments immersed in connective tissue (3, 7, 9). These stains are not associated with inflammatory responses, although in some cases, they can generate fibrosis, chronic inflammation, and even granulomas by foreign body reactions (8).

In the absence of correlation with pre-existing restoration, or evident cause-related factors, a biopsy is recommended to rule out an early melanoma or to exclude association with other pathologies by differential diagnosis (3, 7).

If the pigmentation is cosmetically unacceptable, surgical excision and transplantation of oral mucosal tissue have been suggested, with or without soft tissue harvesting from the palate associated or not with new technologies, such as laser (3, 4, 10-17). Therefore, diagnosis is crucial; assessment of the lesion and appropriate understanding of the patient's aesthetic expectations will be essential to select the most proper technique.

CASE REPORT

A 47-year-old, non-smoking patient complaining of cosmetic dissatisfaction in the right upper maxillary area was referred by a general practitioner. During the first visit, the patient reported that 10 years earlier, she had undergone a prosthetic rehabilitation with single crowns on the first and second maxillary bicuspids. Following endodontic treatment and amalgam restorations, abutments were restored with single metal-ceramic crowns. However, the patient stated that a black pigmentation began to emerge on the buccal aspect of the maxillary premolar area shortly after.

Clinically, the amalgam tattoo presented as a dark grey or blue macula with undefined borders, immobile and flat, at the keratinized mucosa of the first and second upper right bicuspids (Fig. 1a). The periodontal biometric parameters were within normal limits. A periapical x-ray was taken to evaluate pre-existing treatments and confirm the diagnosis of periodontal and endodontic health (Fig. 1b).

The diagnosis thus seemed obvious, as the medical history indicated that the black pigmentations were probably the result of metal fragments released during abutment preparation.

A fine-grain diamond football bur mounted on a high-speed handpiece removes the epithelium and the underlying connective tissue (Fig. 2a) with the simultaneous goal of removing the cosmetic problem and creating a bleeding recipient bed for the planned soft tissue reconstruction (Fig. 2b). The size of the macula will dictate the extension and depth of the bleeding wound site. Nonpigmented periosteal fibres were left in place.

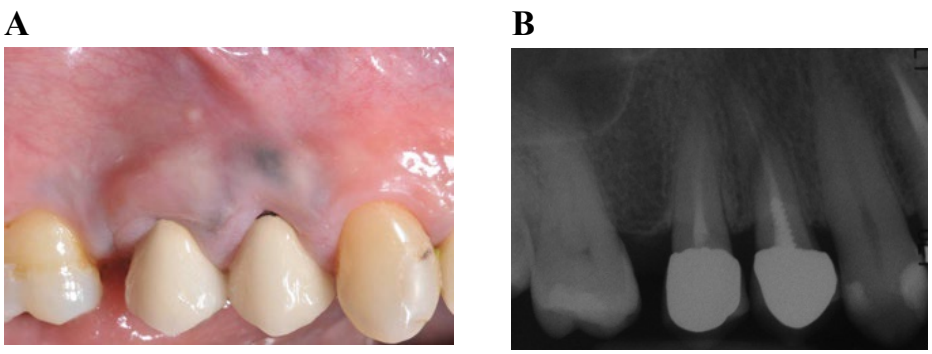

Fig. 1. *A) Clinical aspect of the extended discoloration at teeth 1.4 and 1.5, B) Periapical x-ray of the maxillary right sextant*

A 45-degree beveled ‘’C’’ shaped release incision was then performed mesial at the right maxillary canine. A partial-thickness flap is raised, starting from the most apical portion of the release incision and connecting the muco-abrasive area (Fig. 3a). The objective was to move the flap laterally and distally. The pedicled flap was meticulously passivated, removing muscle insertions, and laid on the periosteal bed, slightly coronal to the cemento-enamel junction (Fig. 3b). The not-abraded tissue by the diamond bur and the interproximal papillae were then de-epithelialized to receive a sub-epithelial connective tissue graft harvested from the palate, with the “L” incision technique (18). The connective tissue graft was immediately placed underneath the buccal flap (Fig. 3c). The donor site is sutured with horizontal mattress sutures, crossed in the palate, and tied buccally. The graft is then stabilized using a resorbable suture material with a combination of single sling sutures at the cementum-enamel junction and horizontal periosteal stabilizing mattress sutures apically to the graft for both premolars, to achieve intimate contact with the underlying periosteal bleeding bed (fig. 4a).

The laterally sliding pedicle flap was positioned and sutured coronally to the graft and the cementum-enamel junction using a simple ‘’sling’’ suspended suture. Part of the graft was left exposed at the canine and second premolar but nourished by the underlying periosteal bed. Vertical compressive mattress sutures were implemented to achieve steady, intimate adaptation (Fig. 4b-c).

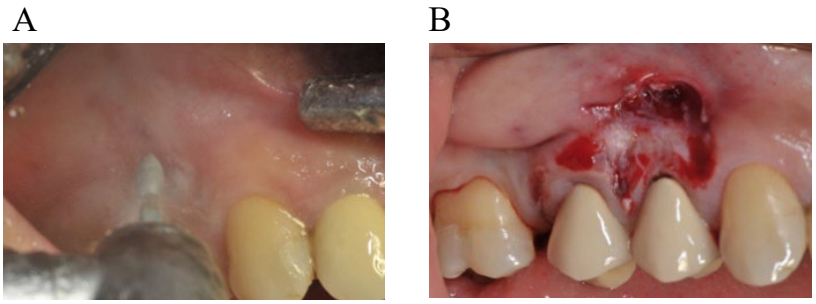

Fig. 2. *A) Fine-grain diamond football burr is used to remove the amalgam discoloration; B) A bleeding recipient bed for the planned soft tissue reconstruction is prepared.*

Fig. 3. *A) Buccal flap design with “C” mesial release incision; B) Raised and tension-free partial-thickness buccal flap; C) The connective tissue graft is covering the exposed periosteum.*

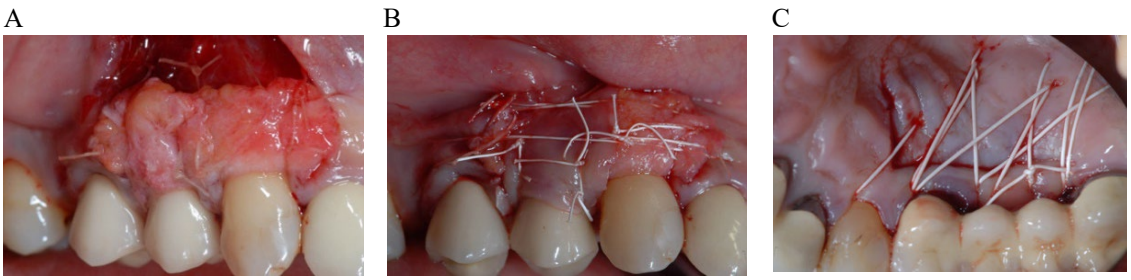

Fig. 4. *A) The connective tissue graft was stabilize with resorbable suture material; B) The laterally sliding pedicle flap was positioned and sutured coronally to the graft and to the cemento-enamel junction; C) The donor site was sutured with crossed horizontal mattress, buccally knotted, stitches.*

The medication protocol included Amoxicillin 500 mg every 8 hours for 7 days, Ibuprofen 600 mg every 8 hours for 3 days, and 0.12% Chlorhexidine Di-gluconate every 12 hours for 7 days. Sutures were removed two weeks following surgery. The healing was uneventful, and 3 weeks later, the patient was allowed to resume mechanical tooth cleaning of the treated area using a soft toothbrush with the roll technique.

The referring dentist carried out postoperative follow-up visits every 4 months for the first year. The treated area was pink, had an adequate amount of keratinized tissue with no pigmentation, and was perfectly integrated with the adjacent tissues without scars.

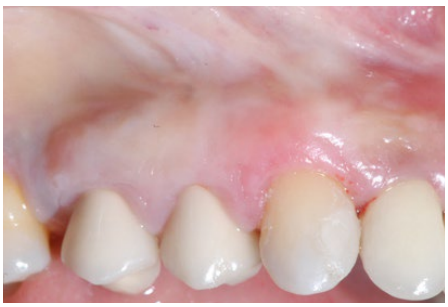

Fig. 5. *8-year follow-up clinical view*

After 8 years, the periodontal tissues appeared healthy, and no pigmentation was present in the treated area; the tissues were stable with no signs of gingivitis, and the cosmetic result completely satisfied the patient (Fig. 5). The previous mild gingival recession on the first premolar was covered entirely, and an improvement in quantity and quality of the keratinized tissue was detected.

DISCUSSION

Amalgam tattoos are due to the deposition of a mixture of silver, tin, mercury, copper, and zinc, which are components of an amalgam filling, into the oral soft tissues. Nowadays, the shift from amalgam to composite filling materials and the use of metal-free restorations (such as zirconia, disilicates, or feldspathic ceramic instead of metal-ceramic) have reduced the onset of iatrogenic gingival pigmentation.

There is little documentation in the literature regarding treating these oral mucosal alterations. Surgical treatment with the preparation of a bleeding wound site and soft tissue harvesting from the palate appears to be the most reported case reports with long follow-ups (3, 4, 10). Different types of lasers have also shown good efficacy in amalgam tattoo removal when present in the most superficial tissues or for the preparation of a bleeding bed for a soft tissue graft placement (12-16). Although less invasive therapeutic solutions are proposed in the literature through the use of ER:YAG lasers (12, 15, 16) or through the use of diode lasers (17), the clinician must always consider the width and depth of the cosmetic lesion. Indeed, the cited articles report encouraging evidence and satisfactory cosmetic results when using these devices, emphasizing minor morbidity for the patient, preventing risks related to surgical procedures, and avoiding sutures. Despite this, the extent of amalgam tattoo appears to be particularly limited and confined to the keratinized mucosa.

A recent paper by Aguirre-Zorzano et al. (10) summarizes 11 articles dealing with the treatment of amalgam tattoo. All the articles are case reports with very short-term follow-ups from 2 to 21 months. The longest case report follow-up reported in the literature regarding the surgical treatment of an amalgam tattoo is by Pini-Prato and co-workers with a follow-up of 24 years, describing an optimal aesthetic result maintained over time (4). In the same case report (4), a two-stage approach is illustrated for treating an amalgam tattoo between maxillary incisors with a free gingival graft in the first stage and subsequent apically positioned flap for the final prosthetic restoration artifact. In contrast, Aguirre-Zorzano et al. (10) published a one-stage surgical procedure for treating amalgam tattoo using an association of muco-abrasion and free connective tissue graft; the outcomes seemed promising, and no signs of recurrence during 4-year and 5 month follow-up period. The bilaminar technique can be considered a "gold standard" procedure for the treatment of gingival recessions, with average root coverage (RC) up to 97.3% and complete RC up to 86.7% (19, 20).

All these aspects should be considered during the diagnostic process and treatment plan. In this clinical case, a one-stage approach was selected utilizing a tension-free partial-thickness pedicle flap. The primary goal was to remove the amalgam tattoo, and muco-abrasion with a diamond bur was performed. In addition, connective tissue graft was harvested from the palate to achieve an extremely favourable long-term aesthetic result while creating an adequate band of keratinized tissue around the prosthetic restorations. Furthermore, a pedicle laterally sliding flap was implemented from the canine and positioned distally to cover the mild recession on the first premolar and the connective tissue with a bilaminar approach.

CONCLUSION

Within the limits of this 8-year follow-up case report, a one-stage mucogingival reconstructive procedure with a sub-epithelial connective tissue graft should be considered an effective treatment option in case of amalgam tattoo providing stable morphologic and cosmetic outcomes.

REFERENCES

1. Pini Prato G. Mucogingival deformities. *Annals of Periodontology*. 1999;4(1):98-101. doi:10.1902/annals.1999.4.1.98
2. Chapple ILC, Mealey BL, Van Dyke TE, et al. Periodontal health and gingival diseases and conditions on an intact and a reduced periodontium: Consensus report of workgroup 1 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. *Journal of Periodontology*. 2018;89(Suppl 1):74-84. doi:10.1002/jper.17-0719
3. Mathews DP. Treatment of the amalgam tattoo in the esthetic zone. *Journal of Esthetic and Restorative Dentistry*. 2020;32(8):770-775. doi:10.1111/jerd.12647
4. Pini Prato G, Selvaggi F, Magnani N, Franceschi D. Long-Term Results (24 Years) of the Treatment of Amalgam Tattoo in the Anterior Maxillary Region: A Histologic and Clinical Case Report. *The International Journal of Periodontics & Restorative Dentistry*. 2020;40(6):891-896. doi:10.11607/prd.4905
5. Hassona Y, Sawair F, Al-karadsheh O, Scully C. Prevalence and clinical features of pigmented oral lesions. *International Journal of Dermatology*. 2016;55(9):1005-1013. doi:10.1111/ijd.13133
6. Owens BM, Johnson WW, Schuman NJ. Oral amalgam pigmentations (tattoos): a retrospective study. *Quintessence International (Berlin)*. 1992;23(12):805-810.
7. Forsell M, Larsson B, Ljungqvist A, Carlmark B, Johansson O. Mercury content in amalgam tattoos of humanoral mucosa and its relation to local tissue reactions. *European Journal of Oral Sciences*. 1998;106(1):582-587. doi:10.1046/j.0909-8836.1998.eos106108.x
8. Buchner A, Hansen LS. Amalgam pigmentation (amalgam tattoo) of the oral mucosa. A clinicopathologic study of 268 cases. *Oral Surgery, Oral Medicine, Oral Pathology*. 1980;49(2):139-147. doi:10.1016/0030-4220(80)90306-0
9. McCullough MJ, Tyas MJ. Local adverse effects of amalgam restorations. *International Dental Journal*. 2008;58(1):3-9. doi:10.1111/j.1875-595x.2008.tb00170.x
10. Aguirre-Zorzano LA, García-De-La-Fuente AM, Estefanía-Fresco R. Treatment of Amalgam Tattoo With a New Technique: Mucoabrasion and Free Connective Tissue Graft. *Clinical Advances in Periodontics*. 2019;9(3):120-124. doi:10.1002/cap.10058
11. Thumbigere-Math V, Johnson DK. Treatment of amalgam tattoo with a subepithelial connective tissue graft and acellular dermal matrix. *Journal of International Academy of Periodontology*. 2014;16(2):50-54.
12. Mikami R, Mizutani K, Nagai S, Pavlic V, Iwata T, Aoki A. A novel minimally-invasive approach for metal tattoo removal with Er:YAG laser. *Journal of Esthetic and Restorative Dentistry*. 2021;33(4):550-559. doi:10.1111/jerd.12721
13. Yilmaz HG, Bayindir H, Kusakci-Seker B, Tasar S, Kurtulmus-Yilmaz S. Treatment of amalgam tattoo with an Er,Cr:YSGG laser. *Journal of Investigative and Clinical Dentistry*. 2010;1(1):50-54. doi:10.1111/j.2041-1626.2010.00011.x
14. Campbell CM, Deas DE. Removal of an Amalgam Tattoo Using a Subepithelial Connective Tissue Graft and Laser Deepithelialization. *Journal of Periodontology*. 2009;80(5):860-864. doi:10.1902/jop.2009.080613
15. Mizutani K, Mikami R, Tsukui A, et al. Novel flapless esthetic procedure for the elimination of extended gingival metal tattoos adjacent to prosthetic teeth: Er:YAG laser micro-keyhole surgery. *Journal of Prosthodontic Research*. 2022;66(2):346-352. doi:10.2186/jpr.JPR_D_21_00045
16. Ishikawa I, Aoki A, Takasaki AA. Potential applications of Erbium:YAG laser in periodontics. *Journal of Periodontal Research*. 2004;39(4):275-285. doi:10.1111/j.1600-0765.2004.00738.x
17. Gojkov-Vukelic M, Hadzic S, Pasic E. Laser Treatment of Oral Mucosa Tattoo. *Acta Informatica Medica*. 2011;19(4):244-246. doi:10.5455/aim.2011.19.244-246
18. Tinti C, Parma Benfenati S. *Terapia Mucogengivale: Tecniche Di Prelievo.*; 1999.
19. Chambrone L, Sukekava F, Araújo MG, Pustiglioni FE, Chambrone LA, Lima LA. Root-Coverage Procedures for the Treatment of Localized Recession-Type Defects: A Cochrane Systematic Review. *Journal of Periodontology*. 2010;81(4):452-478. doi:10.1902/jop.2010.090540
20. Chambrone L, Salinas Ortega MA, Sukekava F, et al. Root coverage procedures for treating localised and multiple recession-type defects. *The Cochrane database of systematic reviews*. 2018;10(10):CD007161. doi:10.1002/14651858.CD007161.pub3

European Journal of Musculoskeletal Diseases
ISSN 2038-4106/2022

Case report

MANAGEMENT OF RECURRENT APHTHOUS STOMATITIS IN A YOUNG MAN WITH FOOD ALLERGIES: A CASE REPORT

M. Contaldo

Multidisciplinary Department of Medical-Surgical and Dental Specialties, University of Campania Luigi Vanvitelli, Naples, Italy

Correnspondence to:
Maria Contaldo, DDS
Multidisciplinary Department of Medical-Surgical and Dental Specialties,
University of Campania Luigi Vanvitelli, Naples, Italy
e-mail: maria.contaldo@unicampania.it

ABSTRACT

Recurrent aphthous stomatitis (RAS) is the most frequent oral condition, estimated to affect over 20% of the worldwide population, with a higher prevalence in females and young. Despite the benignity of aphthae ulcerations, their recurrence may invalidate the quality of life of the subjects, and ongoing treatments based on the use of corticosteroids -both topical or systemic- are needed. Nevertheless, a proper pre-treatment investigation of the elements triggering RAS may be beneficial in reducing the vicious circle related to them. The present paper reports a case of RAS to describe diagnostic procedures and treatment.

KEYWORDS: *stomatitis, inflammation, pain, relief, steroid*

INTRODUCTION

Recurrent aphthous stomatitis (RAS) is the most frequent oral condition (1), estimated to affect over 20% of the worldwide population, with a higher prevalence in females and young (2).

The RAS etiology is still debated, but its onset seems associated with various triggering factors, such as local traumatism, stopping smoking, nutritional deficiencies, hormonal changes, food allergies, and stress, all acting on genetic-immunological predisposed subjects (3).

Clinically, aphthae appear as single or multiple roundish, not bleeding ulcerations of the oral lining mucosa, covered by fibrin, and surrounded by a thin inflammatory halo (4). RAS may be characterized by minor, major, or herpetiform ulcerations according to size (5, 6) and is dichotomized into simple and complex forms according to the lack or presence of extra-oral involvement. The latter is associated with systemic diseases such as Behçet syndrome (7), PFAPA syndrome (periodic fever, aphthous stomatitis, pharyngitis, and cervical adenitis) (8), Sweet syndrome (9), or celiac disease (10).

Despite being benign, the recurrences impair the daily activities of the subjects affected (11). The treatments available do not eradicate the pathology but aim to reduce the symptomatology, mainly discomfort, pain, and recurrences. The

Received: 23 June 2022
Accepted: 28 July 2022

ISSN: 2038-4106

present work reports a case of RAS to describe diagnostic procedures and treatment.

CASE REPORT

A 35-year-old man came to the Unit of Oral Pathology of the University of Campania, "Luigi Vanvitelli", referring to a history of recurrent painful "vesicles" variable in size and affecting various sites of his mouth.

First, an anamnestic interview was conducted to establish any possible factors associated with its onset. The patient said he has never smoked and does not suffer or have suffered any particular disease in the past. He did not take any drugs and reported not having any digestive problems or changes in bowel habits, seeming otherwise healthy. At the intra-oral examination, various small roundish ulcerations were detected on the right lateral margin of the tongue and in the upper left vestibular fornix (Fig. 1).

The ulcerations did not bleed and clinically resembled aphthae. Once diagnosed based on the referred recurrences and clinical data (roundish, not bleeding ulcerations smaller than 1cm of the lining mucosae), a diagnosis of RAS with minor aphthae was defined.

Considering the patient referred the onset of the present lesions a week before and that minor aphtha spontaneously healed within approximately two weeks, the only treatment suggested was the use of adhesive gel formulations based on 0.2% hyaluronic acid. It must be applied to the ulcers, forming a physical barrier and quickly reducing pain, bacterial superinfections, and mechanical friction, thus promoting healing and relieving pain (12).

Blood tests were prescribed to investigate any triggering factor associated with RAS. In detail, glycemia, blood count, iron status through sideraemia, blood transferrin and ferritin amounts, vitamin B and folic acid amounts, celiac markers (to exclude any co-occurring silent celiac disease), and PRIST (Paper RadioImunoSorbent Test) to count the total IgE amount and consider any allergic diathesis, were prescribed.

Ten days later, the patient returned, reporting the healing of the sites previously affected by RAS and exhibiting the blood test results. They revealed no iron deficiencies, and the vitamin B group and folic acid were in the normal range, as well as glycemic status and blood count. The sole parameter that increased over the normal range was the PRIST, whose increase is a non-specific indicator of allergies. At this point, an allergic diathesis was hypothesized, and a fecal parasitological test was prescribed to exclude parasitic infections, which can justify the increase in PRIST in lack of allergies. On the same occasion, a RAST test was also requested to measure the IgE amount to the most common allergens (foods, drugs, pollen, mites, moulds, and latex) to consider some food and topical allergies responsible both for IgE increase and RAS.

The RAST reported moderated (2,500 U/ml) increase in IgE for peanuts and hazelnut and a very high (22,300 U/ml) increase in chocolate IgE. He then reported to work as a business consultant for a banking society, and in that period of the year (March-May), he felt overwhelmed by the workload and used to eat lots of chocolate bars and bread with chocolate and hazelnut cream. Meanwhile, new aphthae were discovered on the ventral tongue and the labial lower right mucosa.

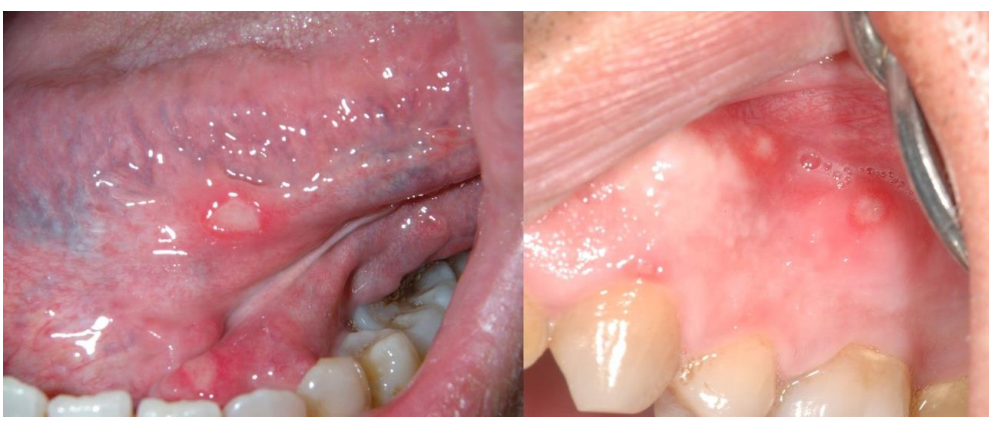

Fig. 1. *Various aphthous ulceration of the covering mucosa of tongue margin and upper fornix.*

Based on referred eating habits, the RAST, and the lack of any change in other blood findings, a diagnosis of RAS associated with food allergies to chocolate and hazelnuts was made. Hence, the patient was instructed to have a diet free of the allergens found to treat the recurrences, while a drug therapy was established to treat the actual aphthae.

Despite the use of local corticosteroids (clobetasol propionate in cream or betamethasone sodium phosphate effervescent tablets as a rinse) would have been indicated, it was opted for the following therapy, given the high tolerance and the rarity of undesirable effects, the allergic nature of the trigger, and to avoid antifungal coverings in association with the cortisone -as desired by the patient:

Sodium dichromoglycate, SDCG (500 mg/granules in dispersible sachets), three times a day per three weeks to mouthwash and then swallow. SDCG inhibits the IgE-mediated release of histamine and other substances in type-1 immune reactions, reducing mast cells' degranulation of proinflammatory cytokines (13).

Pentoxifylline (400 mg tablets) is ingested twice daily every three weeks. Pentoxifylline is used for its rheological properties on red blood cells (reducing blood viscosity) and fibrinolytic and inhibitory action of leukocyte activation (14).

The patient returned for follow-ups every three months for 1.5 years, referring to maintaining a diet free from the allergens indicated, and did not report any RAS on any occasion.

CONCLUSION

Despite the benignity of RAS, recurrence may invalidate the quality of life of the subjects, and continuous treatments based on the use of corticosteroids -both topical or systemic- are needed. However, a proper pre-treatment investigation of the factors triggering RAS (15) may be beneficial to reducing the vicious circle and can orient toward therapeutic alternatives with fewer adverse effects related to multiple steroid therapies (16).

REFERENCES

1. Baccaglini L, Lalla R, Bruce A, et al. Urban legends: recurrent aphthous stomatitis. *Oral Diseases*. 2011;17(8):755-770. doi:10.1111/j.1601-0825.2011.01840.x
2. Plewa MC, Chatterjee K. Aphthous Stomatitis. *StatPearls Publishing* 2022. https://pubmed.ncbi.nlm.nih.gov/28613713/
3. Jurge S, Kuffer R, Scully C, Porter S. Number VI Recurrent aphthous stomatitis. *Oral Diseases*. 2006;12(1):1-21. doi:10.1111/j.1601-0825.2005.01143.x
4. Edgar NR, Saleh D, Miller RA. Recurrent Aphthous Stomatitis: A Review. *The Journal of Clinical and Aesthetic Dermatology*. 2017;10(3):26-36.
5. Cooke BE. Recurrent oral ulceration. *The British Journal of Dermatology*. 1969;81(2):159-161.
6. Lehner T. Autoimmunity in oral diseases, with special reference to recurrent oral ulceration. *Proceedings of the Royal Society of Medicine*. 1968;61(5):515-524.
7. Turk MA, Hayworth JL, Nevskaya T, Pope JE. Ocular manifestations of Behçet's disease in children and adults: a systematic review and meta-analysis. *Clinical and Experimental Rheumatology*. 2021;39(5):94-101. doi:10.55563/clinexprheumatol/pt60bc
8. Wang A, Manthiram K, Dedeoglu F, Licameli GR. Periodic fever, aphthous stomatitis, pharyngitis, and adenitis (PFAPA) syndrome: A review. *World Journal of Otorhinolaryngology - Head and Neck Surgery*. 2021;7(3):166-173. doi:10.1016/j.wjorl.2021.05.004
9. Sleiman J, Hitawala AA, Cohen B, et al. Systematic Review: Sweet Syndrome Associated with Inflammatory Bowel Disease. *Journal of Crohn's and Colitis*. 2021;15(11):1864-1876. doi:10.1093/ecco-jcc/jjab079
10. Pastore L, Muzio LL, Serpico R. Atrophic Glossitis Leading to the Diagnosis of Celiac Disease. *New England Journal of Medicine*. 2007;356(24):2547-2547. doi:10.1056/nejmc070200
11. AL-Omiri MK, Karasneh J, Alhijawi MM, Zwiri AMA, Scully C, Lynch E. Recurrent aphthous stomatitis (RAS): a preliminary within-subject study of quality of life, oral health impacts and personality profiles. *Journal of Oral Pathology & Medicine*. 2014;44(4):278-283. doi:10.1111/jop.12232
12. Dalessandri D, Zotti F, Laffranchi L, et al. treatment of recurrent aphthous stomatitis (RAS; aphthae; canker sores) with a barrier forming mouth rinse or topical gel formulation containing hyaluronic acid: a retrospective clinical study. *BMC Oral Health*. 2019;19(1). doi:10.1186/s12903-019-0850-1

13. Walker DM, Dolby AE. Aphthous ulceration, cromoglycic acid, and cellular immune response. *The Lancet*. 1975;305(7921):1390. doi:10.1016/s0140-6736(75)92309-0
14. Altenburg A, El-Haj N, Micheli C, Puttkammer M, Abdel-Naser M, Zouboulis CC. The Treatment of Chronic Recurrent Oral Aphthous Ulcers. *Deutsches Aerzteblatt Online*. 2014;111(40). doi:10.3238/arztebl.2014.0665
15. Romano A, Santarelli A, Lajolo C, et al. Analysis of oral mucosa erosive-ulcerative lesions by reflectance confocal microscopy. *Journal of Biological Regulators and Homeostatic Agents*. 2019;33(3 Suppl. 1):11-17. DENTAL SUPPLEMENT.
16. Ghali H, Abdulhamed B. Treatment of Recurrent Minor Aphthous Stomatitis Using Diode Laser (940nm). *Journal of Population Therapeutics and Clinical Pharmacology*. 2021;28(2). doi:10.47750/jptcp.2022.864