UNIVERSIDADE FEDERAL DE UBERLÂNDIA FACULDADE DE ODONTOLOGIA TRABALHO DE CONCLUSÃO DE CURSO

LUCIANO LEITE DE CASTRO

EXTENSIVE ORAL MELANOMA ON THE HARD PALATE: CASE REPORT

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Trabalho de Conclusão de Curso apresentado a Faculdade de Odontologia da Universidade Federal de Uberlândia, como requisito parcial para obtenção do título de Graduado em Odontologia

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AGRADECIMENTOS

Conquista é um substantivo feminino que significa ‘’ o processo que leva alguém a obter alguma coisa’’. Além da definição, conquista significa retribuição pelo esforço empregado. Nesse caso, esforços, no plural. E por trás desse trabalho, existiram vários. Mesmo sabendo da possibilidade de esquecer alguém, não por ingratidão, mas por mera distração, espero trazer aqui meu carinho e respeito por todos aqueles que, de alguma maneira, me trouxeram até aqui. Carrego o afeto que cada um merece.

Primeiramente, àqueles que me trouxeram ao mundo. Que me fazem continuar e sentir vivo. Eu não poderia estar aqui sem eles. De todo o amor que sinto e aprendi a dar, o motivo são eles. Pai, Mãe, vocês sabem, mas obrigado. Amo vocês daqui até o fim, mesmo sabendo que o fim não existe com vocês.

Aos meus irmãos, que na maior parte do tempo estavam longe, mas sempre do lado, se fazendo presente em algum conselho ou ligação.

À minha família do Tocantins, que pelo seu amor caloroso, me aqueceu mesmo nos dias mais frios de Uberlândia.

À minha outra metade familiar, meu povo mineiro, que sempre me trata de um jeito especial, me fazendo sentir sempre feliz e aconchegado.

Bom, como não acredito em grau de importância, mas na singularidade que cada um representa, trarei aqui outras partes fundamentais dessa conquista. À minha orientadora, que teve que ressignificar, mais de uma vez, o significado de paciência. Que me ajudou, abriu meu horizonte da universidade e sempre exigiu mais porque sabia que eu poderia ir além. Meu muito obrigado.

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Enfim, sinceramente, eu poderia escrever mais um tanto inimaginável de palavras, todas elas com o apreço que cada pessoa merece. Mas, cada um que estava presente na minha vida sabe e sente. Eu pulso alegria por fazerem minha vida acontecer.

Por fim, homenageio um mineiro e, consequentemente, Minas Gerais que me acolheu tão bem. Guimarães Rosa diz que: ‘’ A vida é um eterno rasgar-se e remendar-se’’. E hoje eu remendo mais um capítulo da minha história**.**

Melanoma Oral extenso em palato duro: Relato de caso

O melanoma de mucosa oral (MMO) representa uma neoplasia maligna de caráter agressivo e incidência rara, correspondendo a menos de 1% das lesões orais malignas. Este trabalho apresenta um caso de MMO que se manifestou como pigmentação focal de grandes dimensões no palato duro. Paciente do sexo masculino, 54 anos de idade, foi encaminhado ao Programa de Cuidados Específicos às Doenças Estomatológicas (PROCEDE) da Universidade Federal de Uberlândia MG/Brasil para avaliação de lesão detectada pelo cirurgião-dentista generalista. À anamnese, paciente relatou prática de tabagismo por vinte anos, com abstenção do hábito há vinte anos. À oroscopia, observou-se pigmentação focal, enegrecida com áreas avermelhadas na região mediana do palato duro, estendendo-se da região de caninos a segundos molares superiores. A hipótese de diagnóstico foi de MMO. À biópsia incisional, o fragmento de tecido revelou mucosa revestida por tecido epitelial estratificado, parcialmente ulcerado, e presença de neoplasia contendo pigmentos de melanina, compatíveis com MMO. Após a confirmação do diagnóstico, o paciente foi encaminhado para o serviço de cirurgia de cabeça e pescoço do Hospital do Câncer, onde foram realizadas 27 sessões de radioterapia e 4 sessões de braquiterapia. A importância do exame clínico sistemático da cavidade bucal para a detecção de pigmentações assintomáticas e isoladas faz-se necessária, bem como a necessidade de um maior conhecimento por parte dos cirurgiões dentistas da natureza destas lesões, uma vez que o diagnóstico precoce é essencial para aumentar as chances de cura dessa neoplasia maligna agressiva.

Palavras-chave: Melanoma oral, palato duro e pigmentação focal.

SUMMARY

ABSTRACT

Oral mucosa melanoma (OMM) is a rare malignant neoplasm of aggressive character, and it accounts for fewer than 1% of malignant oral lesions. This paper presents a case of OMM manifesting as a large focal pigmentation on the hard palate. A 54-year-old male patient was referred by a general dentist for specific assessment of the detected lesion. During anamnesis, the patient reported smoking for twenty years and abstaining from the habit for twenty years. On oral examination, a focal black pigmentation with red areas was observed in the median region of the hard palate, extending from the canine to upper second molars region. The diagnostic hypothesis was OMM. Upon incisional biopsy, the tissue fragment revealed mucosa covered by stratified epithelial tissue and partially ulcerated, as well as the presence of neoplasia containing melanin pigments, compatible with OMM. After diagnostic confirmation, the patient was referred to the head and neck surgery service of the local cancer center, where 27 sessions of radiotherapy and 4 sessions of brachytherapy were performed. Systematic clinical examinations of the oral cavity for the detection of asymptomatic and isolated pigmentations are necessary, and it is important to improve dentists' knowledge of the nature of these lesions, since early diagnosis is essential to increase the chances of curing this aggressive malignancy.

KEY WORDS: Oral Neoplasms; Oral Cancers; Oral melanoma; Hard palate; Focal pigmentation; Head and Neck Neoplasms

INTRODUCTION

Pigmented lesions are common in the oral cavity, and the vast majority of these lesions are benign. Among them, oral mucosa melanoma (OMM) stands out as a malignant neoplastic lesion with aggressive behavior and rare incidence, accounting for fewer than 8% of other types of melanoma and less than 1% of malignant oral lesions.[1-4] Causal factors are not yet fully defined. Unlike skin melanoma, there is no relationship between sun exposure and its onset. However, there are reports in the literature that relate OMM to smoking or exposure to harmful chemical agents such as formaldehyde.[5-8]

OMM originates from the atypical proliferation of melanocytes present in the epithelial tissue. [2] In the skin, melanocytes are responsible for the production of melanin, but in mucous membranes, their function remains unknown.[9,10] Approximately 90% of melanomas occur on the skin, and only 1.3% on mucous membranes. Clinically, the lesion manifests itself as an asymmetric and irregularly shaped macula, predominantly in the mucosal region of the palate (32%), followed by the maxillary gingiva (16%). The lesion may have ulcerated areas, and, in cases of invasive behavior and vertical growth, nodular consistency. The color varies between black, brown and purple, depending on the amount of pigment present and vascularization of the affected region.[2,8-12]

Similar to cutaneous melanoma, primary mucosal melanoma of the head and neck has a higher incidence among white people.[10] The highest occurrence is reported among males and among people between 20 and 60 years of age, with a higher incidence at 50 years of age.[11-14] Most patients have no symptoms and seek care due to self-perceived changes in oral tissues. In the rare symptomatic cases, bleeding is the most common finding. In some situations, the initial presentation consists of multiple pigmented lesions, establishing a pattern suggestive of physiological pigmentation. Due to these factors, in most cases, there is a delay in diagnosis, resulting in a poor prognosis and low survival rate.[9,11,15]

There is no well-established consensus on the treatment of OMM, but it is believed that, whenever possible, complete surgical excision is the most effective approach. Surgical treatment is commonly associated with chemo- and radiotherapy, depending on the stage of the lesion's evolution.[16,17] There is a difficulty in classifying the OMM according to the criteria of its epithelial manifestation since the vast majority

of these lesions are diagnosed at very advanced stages that need a more complex classification.[8,11] The presence of lymphatic metastases at the time of diagnosis is one of the main factors that determine the treatment approach and prognosis.[18]

There is a shortage of concrete information about the etiology and epidemiology of OMM in the literature, in addition to a lack of consensus on the ideal treatment, thereby indicating the need of more research and reports on the subject. This study aims to report a case of an extensive OMM in the palate with late diagnosis.

CASE REPORT

A 54-year-old Caucasian man presented to the Program of Specific Care for Stomatological Diseases (PROCEDE) of the Federal University of Uberlândia, referred by a general dentist for evaluation of “lesion on the palate.” On history, the patient reported no symptoms, moderate alcohol consumption and history of smoking for 20 years and being smoke-free for another 20 years. He had good general health but high blood pressure (180/90 mmHg), which was reasonable due to the considerable anxiety caused by the consultation.

In intraoral physical examination, a black lesion with red areas could be seen in the median region of the hard palate, extending from the canine to upper second molars region, measuring approximately 3.5 x 3 cm (Figure 1). On cone beam computed tomography exam, which was requested by the dentist, the erosion of the hard palate could be seen in the midline region at the height of the upper molars in coronal (Figure 2) and sagittal (Figure 3) views, demonstrating bone resorption caused by the lesion, since this area corresponded to the affected region. To perform the incisional biopsy, 15 mg of midazolam was administered 45 minutes before the procedure to decrease the patient's blood pressure levels. Samples were collected from three regions: the right and left lateral borders and one in the posterior region of the lesion. It was prescribed amoxicillin 500 mg, trometamol ketorolac (Toragesic®) 10 mg and mouthwash with 0.12% chlorhexidine digluconate for 7 days.

The patient returned after 1 week to remove the sutures and receive the histopathological report. Microscopic examination revealed a mucosa covered by stratified epithelial tissue, partially ulcerated, and the presence of malignant neoplasm deeply invading the underlying connective tissue consisting of cells with a

shape ranging from fusiform, ovoid to epithelioid, sometimes diffusely dispersed, sometimes forming small nests. Individually, these cells exhibited an intense polymorphism, nuclear hyperchromatism, with some cells resembling a vesicular nucleus, anisocytosis, anisokaryosis and nucleoli evident in most of them, and cytoplasm ranging from vesicular to eosinophilic, with many of them containing melanin pigments. Small necrotic areas were observed in the interior of the tumor as well as leukocyte infiltration, which was preferably located on the periphery. Figures of typical and atypical mitoses were frequently observed. Of note, it was possible to notice tumor cells permeating blood vessel walls; however, tumor emboli were not observed. In some analyzed fragments, if they were obtained from a more marginal region of the lesion, there was a proliferation of melanocytes at the epithelial-conjunctive junction, with some of them located in the upper layers of the epithelial tissue (Figure 4). Immunohistochemical analysis detected positive staining for vimentin, S-100, HMB45 and Ki67 (30% of neoplastic cells), while epithelial, lymphoid and smooth muscle markers were negative. A conclusive diagnosis of primary OMM was established. Upon diagnosis, the patient was referred to the local cancer center for consultation with the head and neck surgery area (Figure 5).

For cancer taging, a positron emission computed tomography (PET-CT) was performed. The images were acquired in a multislice computed tomography device after an intravenous injection of 8.98 mCi of fluorodeoxyglucose-18F. There was uptake of the radiopharmaceutical in a mild thickening of the soft tissues adjacent to the hard palate associated with an apparent irregularity in the palatal bone cortex, suggesting erosion in the bone adjacent to the lesion. Thus, the presence of a neoplastic process was identified only in the palatal region, without other areas of increased uptake.

In view of the findings, the treatment plan defined for the patient was a combination of radiotherapy and brachytherapy sessions. To start treatment, the patient underwent a pre-radiotherapy dental consultation in which the need for endodontic treatment of maxillary left central incisor was indicated. It was carried out in two weeks, thereby allowing the patient to start radiotherapy. The patient's treatment started and consisted of approximately 60 Gy divided into 27 sessions of radiotherapy and 30 Gray divided into 4 sessions of brachytherapy. At the end of the sessions, the patient was reassessed by the physicians responsible for the case and its conclusion was defined.

Upon reevaluation of the patient after 8 months, there was a slight decrease in the size of the lesion and there was a necrotic area of approximately 3 mm in diameter in the most posterior portion of the lesion, close to the midline. After careful inspection, bone exposure was noted in this region and was diagnosed as osteoradionecrosis. For treatment, he was prescribed chlorhexidine mouthwash three times a day and topical irrigation with propolis once a week. The patient was followed up and reported improvement in the discomfort caused by the osteoradionecrosis and better clinical aspect could be observed (Figure 6).

DISCUSSION

OMM represents a malignant neoplasm with aggressive behavior and rare incidence, corresponding to 0.2 to 8% of the total cases considering all body locations and fewer than 0.5% of all malignant oral lesions.[1,12] It peaks in the sixth decade of life, with a higher occurrence in males.[11-14] The 5-year survival rate is approximately 15 to 38%.[14] Such variability can be explained by the different clinical conditions possible at the time of the examination.

The neoplastic transformation of melanocytes in the basal layer of the epithelium represents the process of formation of this neoplasm. These cells proliferate in a disorderly manner, producing melanin without proper regulation mechanisms.[12] The color varies in the amount of pigment and may be gray, black, red or purple, or rarely, amelanotic.[1] The etiology of OMM is not yet fully established. However, studies have shown possible participation of agents such as microtrauma and smoking, specifically due to the action of formaldehyde.[5-8] The patient reported being a smoker for twenty years. However, there is not enough evidence to support the association between smoking and the appearance of the tumor.[4] In addition, the habit had been suspended for more than twenty years, which makes this relationship even more improbable.

The epidemiological profile of the present case agrees with most of the reports found in the literature. For sex and age, it corroborates recent systematic studies, revealing prevalence among men aged between the fifth and eighth decades of life.[11-14] The location of the lesion is also compatible with most findings, confirming the palate as the most affected site (32%).[2,8,12]

The patient reported here is Caucasian, which is consistent with studies that report a higher prevalence of head and neck OMM in Caucasian patients.[10,19] However, a previous study reported that Japanese individuals are more predisposed to primary malignant melanoma of the oral cavity.[20] As the data are contradictory, future epidemiological and genetic studies will be needed to provide more robust evidence about possible ethnic predisposition for malignant melanoma.

Oral melanoma can present as five types according to clinical aspects: pigmented nodular, nonpigmented nodular, pigmented macular, pigmented mixed, and nonpigmented mixed type.[21] The reported case includes the proposed clinical classification, presenting a pigmented nodular type, with red areas, rounded spots, following the melanoma manifestation pattern.

Histopathological analysis of the material obtained by incisional biopsy was sufficient to establish, unequivocally, the diagnosis of malignant melanoma. Usually, melanocytic forms of melanoma, which correspond to 90% of cases, can be safely diagnosed by conventional histopathology, with no need for immunohistochemistry.[17,22] However, even so, in this case, this test was performed, showing positive results for vimentin, S100 protein, human melanoma and ki67. The immunohistochemical panel confirmed the diagnosis of OMM.

Therapeutic alternatives to OMM include surgery, radiotherapy, chemotherapy and immunotherapy, alone or in combination.[3,17] Although there is no universally established protocol, surgery is considered the main form of treatment, sometimes combined with other therapies.[23,24] However, due to the extent and site of the injury reported here, surgery was not considered viable by the medical team. Surgical treatment, with a safety margin, would cause great tissue loss and consequent morbidity and difficulty in aesthetic-functional rehabilitation. Thus, the therapeutic option was radiotherapy combined with brachytherapy. Although there is information in the literature that melanoma is not radiosensitive, other studies have shown that radiotherapy is a valid modality for the management of melanomas, as an isolated therapy or associated with surgery.[1,3,17,23,24]

The case of malignant melanoma described, despite the growth and invasion of adjacent bone, did not present evidence of regional and distant metastatic involvement. A study classified head and neck melanoma in three stages: I – lesion confined to the oral cavity, II – lesion with local metastasis and III – lesion with distant metastasis.[19] The present case is classified as stage I. Regarding the prognosis, the

data are conflicting and confusing. Nevertheless, according to Patel et al. (2002), stage I has a five-year survival rate of 56.4%, while for stages II and III, the rate is 0%. According to these data, the case would have good prognosis. Nevertheless, other factors such as sex, age, ethnicity, thickness of the lesion and vascular invasion, can interfere in survival rates, making this estimate quite variable.[19]

Eight months after the initial consultation, with the end of the radiotherapy and brachytherapy sessions, there was an improvement in the clinical picture of the lesion. However, as an adverse effect of radiotherapy treatment, osteoradionecrosis arose. This complication is relatively common in patients undergoing radiation in head and neck regions and may be present in approximately 33% of patients.[26] The condition of osteoradionecrosis is being treated and monitored.

The moment of diagnosis directly influences the patient's future condition. It is known that injuries recognized in early stages have better prognosis than more advanced injuries.[1,27] The present study demonstrates the aggressive character of OMM, especially when diagnosed in advanced stages. Therefore, the recognition of these lesions at incipient levels becomes essential for survival. Biopsies in pigmented lesions with no cause or effect are mandatory to rule out OMM. The patient’s history, in conjunction with extra and intraoral physical examination, will be used to guide the treatment.

CONCLUSION

The present study reports a case of an extensive OMM with late diagnosis. It is a rare lesion in the oral cavity that has an extremely aggressive character. For this reason, it requires the attention of dentists in routine examinations, especially when there are focal pigmented lesions. Biopsies are mandatory in initial lesions in order to rule out the possibility of malignancy. It is known that the moment of diagnosis of OMM directly influences the effectiveness of the treatment and the patient's survival.

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FIGURES AND CAPTIONS

Fig 1 – Initial clinical aspect of the lesion.

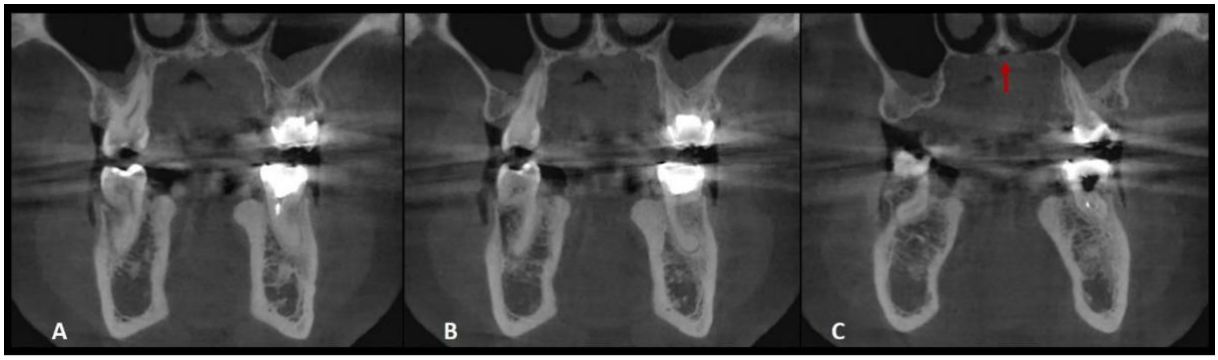


Fig 2 – Coronal view of tomographic image (A, B and C). The arrow in C indicates the region of bone resorption.

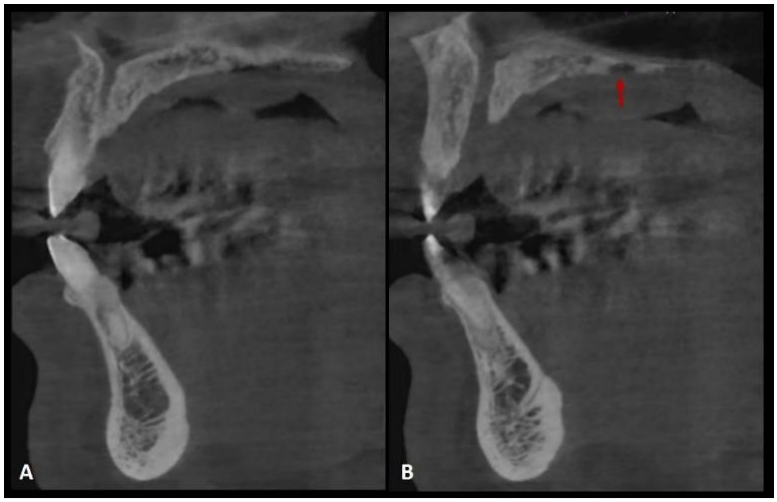


Fig 3 – Sagittal view of tomographic image (A and B). The arrow in B indicates the region of bone resorption.

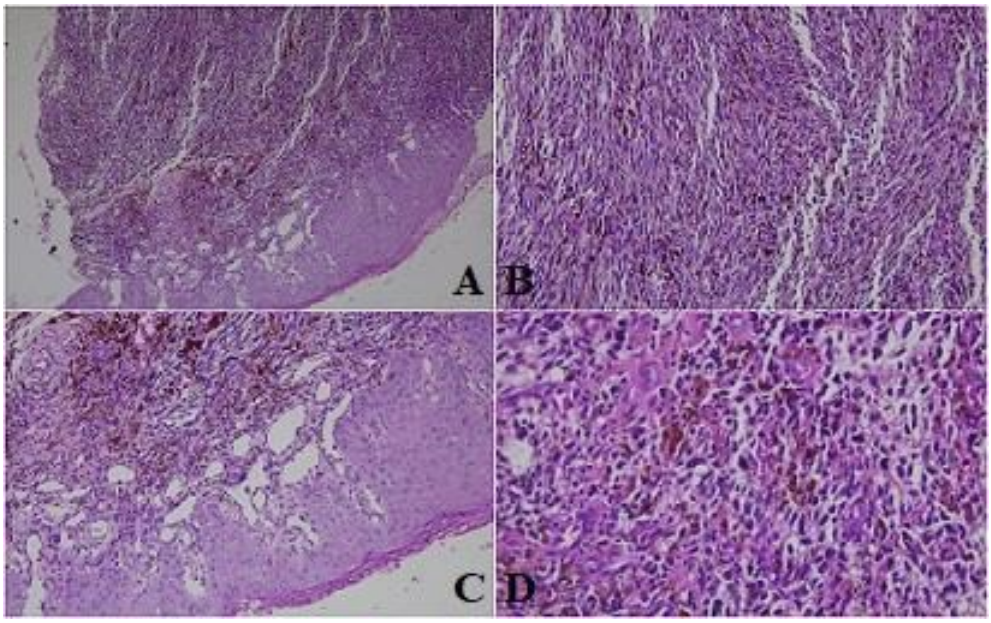
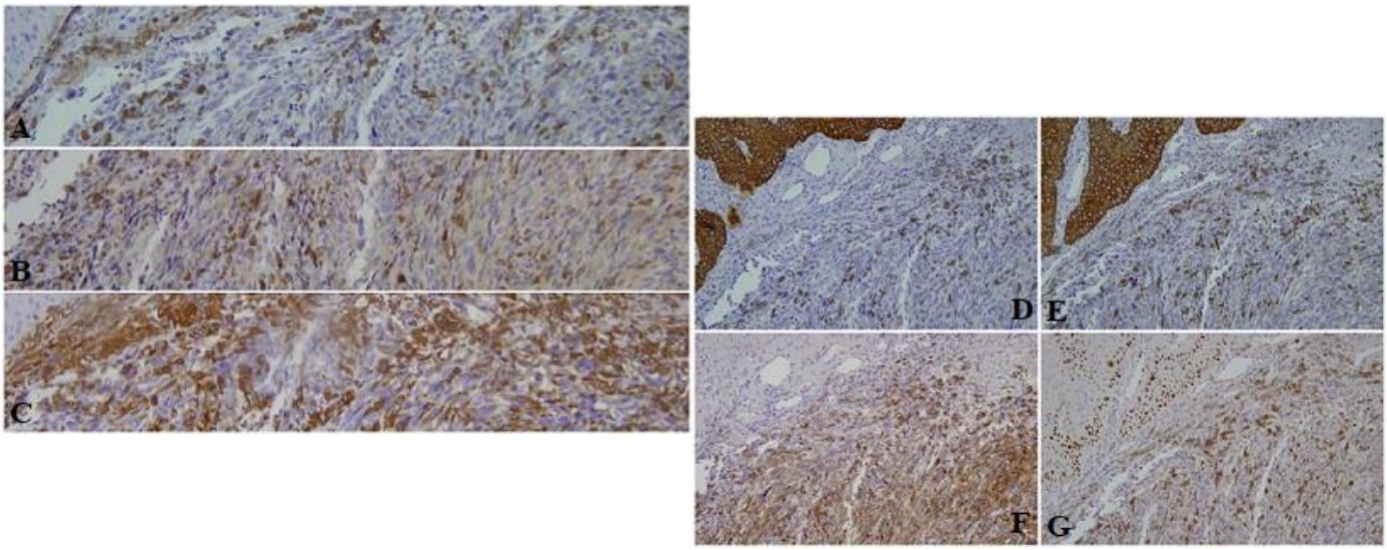


Fig 4 – Hematoxylin and eosin (H&E) stained histologic images of the lesion showing



an overall view, x10 (A), dermis aspect, x20 (B), transition dermis/epidermis, x20 (C) and the presence of melanocytes, x40 (D).

Fig 5 - Immunohistochemistry (IHC) images at ×200 magnification for CD45RB (A), S100 (B), vimentin (C), CK5 (D), AE1-AE3 (E), HMB-45 (F) and KI-67 (G).

Fig 6 – Clinical aspect of the region one year after radiotherapy / brachytherapy and treatment of the osteonecrosis.

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Experimentation involving human subjects will be published only if such research has been conducted in full accordance with ethical principles, including the World Medical Association Declaration of Helsinki and any additional requirements of the country in which the research was conducted. Manuscripts must include a statement that the experiments were undertaken with the understanding and written consent of each subject and according to the abovementioned principles. A statement regarding the fact that the study has been independently reviewed and approved by an ethical board should also be included. Editors reserve the right to reject papers if there is doubt as to whether appropriate procedures have been used.

Clinical Trials:
Report clinical trials using the CONSORT guidelines at www.consort-statement.org. A CONSORT checklist and a flowchart should also be included in the submission material.

Manuscript Format and Structure

Presentation:
The presentation must clearly convey clinical reports, research findings, or review objectives. Try to avoid using technical jargon, but clearly explain where its use is inevitable. Titles, abstracts, and main text should be written in language readily intelligible to any dentist.

Abbreviations/Acronyms:
Abbreviations should be kept to a minimum, particularly those that are not standard. Terms and names referred to as abbreviations or acronyms should be written out when first used with the abbreviation in parenthesis. Standard units of measurement need not be spelled out.

Names of Teeth:
The complete names of individual teeth must be given in the text. Only in tables and figures, individual teeth can be identified using the FDI 2-digit system if full tooth names are too unwieldy.

Structure:
Include a title page, Abstract, main text, References, Acknowledgments, and tables, figures, and legends as appropriate.

Title Page:
Include the title of the article and the full name, degrees, title, and professional affiliation of every author. If the paper was presented in a

conference or to an organized group; note the name of the conference or organization, location, and date. List up to 6 key words in alphabetical order. Provide the address, fax number, and email address of the corresponding author.

Tables and Figures:
Illustrations and tables should be numbered and cited in the text in order of appearance and grouped at the end of the text. When necessary, high-resolution images must be sent to the Managing Editor upon article acceptance: Elizabeth Ducker (elizabeth.ducker@googlemail.com).
Note that original artwork or slides may still be required after acceptance of the article and that article acceptance is pending receipt of acceptable art. Although low-quality images may be adequate for review purposes, print publication requires high-quality images. Submit EPS (line art) or TIFF/JPEG (photographs) files only. Photographs should have a resolution of 300 dpi and line drawings should have a resolution of 600 to 1200 dpi in relation to the reproduction size. EPS files should be saved with fonts embedded.

Figure Legends:
Figure legends should begin with a brief title for the whole figure and continue with a short description of each panel and the symbols used.

Reference List:
Literature references in the text should be cited using superscript numbers (after punctuation) in order of appearance, and correspond to the numbered reference list. All references cited in the text must be listed at the end of the paper. Do not include unpublished data or personal communications in the reference list.

Standard Scientific Journal:
Benoliel R, Eliav E. Neuropathic orofacial pain. Oral Maxillofac Surg Clin North Am 2008;20:237–254.

Journal Supplement:
Bartlett D, Ganss C, Lussi A. Basic Erosive Wear Examination (BEWE): A new scoring system for scientific and clinical needs. Clin Oral Investig 2008;12(Suppl 1):S65–S68.

Standard Text Book:
Kielbassa AM (ed). Radiotherapy of the Head and Neck. Implications for dentists, ear-nose-throat physicians, and radiologists [in German]. Hannover: Schlütersche; 2004:43.

Book Chapter:
Paul S. Nonmetal posts: How do they fare in daily dentistry? In: Sadan A (ed). Quintessence of Dental Technology 2008. Chicago: Quintessence, 2008:61–70.

Thesis:
Müller J. Penetration and sealing ability of different adhesives in subsurface lesions of enamel [in German]. Berlin: Doctoral Thesis; 2005:28.

Internet/URL:
The WHO Oral Health website. Available at: http://www.who.int/oral_health. Accessed 17 August 2013.

Manuscript Types

All articles should be clinically relevant to all dentistry-related disciplines and addressed to the general dentist.

Topic Review and Systematic Review Articles:
The review can be a topic review or systematic review. It should cover a topic of interest for the general practitioner and should address a clinical problem, diagnosis, or treatment. Reviews should offer a broad view of the field.

The review *Abstract* should have not more than 250 words and include: *Objectives*, *Data Sources*, and *Conclusion*.
The main text should be divided into *Introduction*, *Data Sources*, *Resources Selection*, *Review*, *Discussion*, and *Conclusion*. Search strategies must be described and the use of evidence-based systematic approaches is expected. The *Discussion* and *Conclusion* should address the relevance to the general practitioner and should be supported with clinically relevant photographs.

Original Scientific Articles:
Original scientific articles must reach the highest international standards in the field and should be relevant to dental practice. The articles should describe significant and original experimental observations and provide sufficient details so that the observations can be critically evaluated and, if necessary, repeated.

The article *Abstract* should be no more than 250 words giving details of what was done, using the following structure: *Objectives*: A clear statement of the main goal of the study and any tested hypotheses. *Method and Materials*: Describe the methods, study design, and data analysis. *Results*: Main results of the study, including the outcome of any statistical analysis. *Conclusion*: State the major conclusions of the study and their implications and relevance to the practice of dentistry.

The main text should include *Introduction*, *Method and Materials*, *Results*, *Discussion*, and *Conclusion* sections.

The *Introduction* should summarize the background of the research objectives and should emphasize the relevance of the study to the practice of dentistry.

The *Method and Materials* section must contain sufficient detail such that, in combination with the references cited, all clinical trials and experiments reported can be fully reproduced. Manufacturers of materials should be named, known methods should be referenced, and data analysis should be described.

The *Results* section should be presented in a logical sequence in the text, tables, and illustrations.

The *Discussion* section should include association to previous studies, and implications of the findings to the practice of dentistry should be included.

The *Conclusion* section should not summarize the findings. Instead, the conclusions should relate to the aims of the study and the relevance to dental practice. The conclusions should be supported by the data.

Case Reports and Short Case Presentation Articles:
Case reports should have importance and significance to the practitioner; repetition of well-known and extensively published conditions or methods will not be accepted. Case reports should include: *Abstract*, *Introduction*, *Case Presentation*, *Discussion*, and *Conclusion/Recommendation* when necessary. The *Abstract* should have not more than 250 words and summarize the case. The article should emphasize the new information provided and the relevance to general practitioners. Sufficient follow-up period is required, and high-quality images should be included.

Short Case Presentations: These should be used for interesting but simpler cases, which the authors would like to share with the readers. The abstract should include not more than 150 words and the main text is limited to 800 words. Only four illustrations and five references can be included.

Method Presentation Articles: The method presentation must offer significant improvements in clinical practice (a novel technique, technological breakthrough, or practical approaches to clinical challenges). The main text should be divided into an *Introduction*, *Report*, and *Discussion*. All parts should be well-illustrated with clinical images, radiographs, diagrams, and, where appropriate, supporting tables and graphs.