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Case report

Photodynamically dealing with bisphosphonate-related osteonecrosis of the jaw: Successful case reports

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1. Introduction

Bisphosphonate-related osteonecrosis of the jaw (BRONJ) comprises an area of exposed bone within the maxillofacial region that persists for more than 8 weeks in a patient exposed to bisphosphonates and who had not performed radiotherapy in the head and neck region [1]. There are no universally accepted treatment protocols for BRONJ. The approach strategies vary between conservative therapies (such as antibiotics prescription) and surgical interventions [2]. However, the increasing number of antibiotic resistant microorganisms requires the development of alternative therapies [3]. In that way, photodynamic therapy (PDT), which is known for its higher microbicidal activity reported in several in vitro and in vivo studies [3,4], may be promising to treat BRONJ. The purpose of this manuscript is to report 2 cases of BRONJ treated complementarily with PDT, followed by the placement of autologous membranes of platelet-rich fibrin (PRF) in the bone defects, which aimed for stimulation and acceleration of bone regeneration [5].

2. Case reports

2.1. Case 1

A 46-year-old feodermic female was referred to our Stomatology Clinic for the evaluation of an extraoral fistula in the submental region. During anamnesis, the patient reported the surgical extraction of the inferior teeth 2 years previously, which was followed by lower alveolar mucosa inflammation, along with drainage of purulent content and pain since then. She also mentioned to have osteoporosis, thus being medicated with Alendronate 70 mg (1 tablet per week) for 6 years, and systemic lupus erythematosus, taking Prednisone 20 mg (1 tablet per day) for such condition. The extraoral physical examination revealed an erythematous tumefaction of smooth and glossy surface, with a firm consistency and

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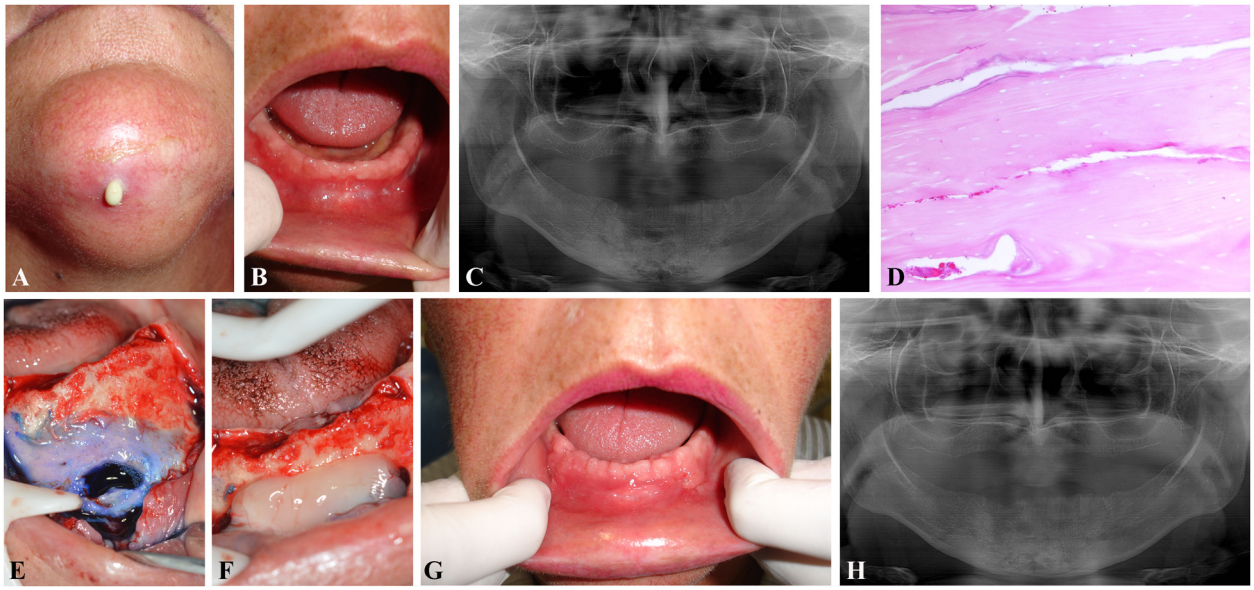

Fig. 1. (A) Extraoral fistula in the submental region; (B) Intraoral fistula located on the lingual surface of the lower alveolar ridge in the area of the lower incisors; (C) Initial radiograph: radiolucent lesion with irregular aspect and ill-defined margins, located in the anterior basilar portion of the jaw; (D) Microscopically, fragments of necrotic lamellar bone lacking osteocytes were observed (Hematoxylin and eosin staining HE – 400×); (E) PDT; (F) PRF; (G) 14 days of follow-up: absence of exposed bone and infection; (H) Final radiograph: 10 months of follow-up, observing bone neoformation.

considerable amount of purulent content drainage, located in the submental region (Fig. 1A). The intraoral exam revealed a fistula, also presenting drainage of purulent content, although in lesser quantity, located on the lingual surface of the lower alveolar ridge in the area of the lower incisors (Fig. 1B). A panoramic radiography and cone beam computed tomography showed a radiolucent lesion with irregular aspect and ill-defined margins, located in the anterior basilar portion of the jaw, more accentuated on the lingual surface (Fig. 1C). Microscopic evaluation of an incisional biopsy revealed fragments of necrotic lamellar osseous tissue and thus the diagnostic hypothesis was defined as BRONJ, stage 3 (Fig. 1D). Initially we prescribed Amoxicillin 875 mg + Potassium Clavulanate 125 mg and Metronidazole 400 mg (3 times a day for 15 days), which led to a significant clinical improvement. However, there was still the need for surgical debridement once the signs had not suffered complete resolution even after antibiotic therapy. Accordingly, the surgical debridement of the necrotic bone was performed under local anesthesia, and PDT was employed during the transoperative (Fig. 1E). The PDT protocol adopted consisted of topically placing toluidine blue dye (TBO) at 37.5 mg/L in the surgically exposed bone for 5 min, which was followed by vigorous washing (bacterial photoinactivation with several photosensitizers (PS) including TBO is better after a wash, leading to better rates of bacteria killing [6]) with saline solution and then continuous low-level laser (InGaAlP – Twin Flex, MMO®, São Carlos, SP, Brazil) 660 nm irradiation, punctually and in contact mode, delivering 100 J/cm^2 with 40 mW, and during 100 s per point. The total energy was 4 J per point and a total of 8 points, spaced 1 cm from each other, was employed. Thus, the total energy applied on the affected tissue was 32 J per total treatment.

Several previous studies have shown interesting results concerning a significant bacterial inactivation followed by TBO placement with varying concentrations such as 15 mg/L [7]; 25 or 100 mg/L [8] along with light irradiation that usually falls into red wavelengths. In that way, the present study was based on these previous reports, utilizing a TBO concentration (37.5 mg/L) that was in between those previously referenced, and also very analogous irradiation procedures 660 nm and 40 mW of power delivered by a 0.04 cm^2 spot size [7]; the laser parameters utilized herein actually comprise very similar energy densities often utilized in the literature, such as a recent report on PDT after chemotherapy-induced oral lesions (120 J/cm^2 at 660 nm and 40 mW of power; spot size of 0.04 cm^2) [9]. In that way, although this is the first study to successfully report TBO-mediated PDT to treat BRONJ, the current methodology is in accordance with similar antimicrobial photodynamic inactivation studies performed previously.

The bone defect was filled with PRF (Fig. 1F) and the suture was performed with Vicryl®. The same antibiotic therapy initially prescribed was then recommended postoperatively. 14 days of follow-up showed full coverage of bone tissue by mucosa and absence of infection (Fig. 1G), and 10 months later a complete healing of the operated area, with the presence of bone neoformation and absence of symptoms was detected (Fig. 1H).

2.2. Case 2

A 51-year-old feodermic female was referred to our Stomatology Clinic for the extraction of the lower right lateral incisor and lower right canine. During anamnesis, the patient reported to have performed endodontic treatment in these teeth about 1 year ago, and at the present moment we detected intraoral drainage of purulent content and painful symptomatology. She also said to present diabetes mellitus and osteoporosis, currently taking Alendronate 70 mg (1 tablet per week). The extraoral physical examination did not reveal significant alterations. Intraoral exam indicated exposed necrotic bone, located in the vestibular region of the jaw, and apically to the lower right canine (Fig. 2A). The exposure of the root of the lower right lateral incisor and lower right canine was also observed (Fig. 2A). A panoramic radiography showed a radiolucent lesion with irregular aspect in the region of the cited teeth and a slight radiopacity at the site of the exposed bone; radiopacity of the alveolar crest located between the lower right lateral incisor and lower right canine was also observed (Fig. 2B). Microscopical examination of an incisional biopsy was later performed and revealed bone tissue lacking osteocytes along with peripheral resorption with bacterial colonization (Fig. 2C), fulfilling the criteria for BRONJ stage 2, along with the clinical appearance. The patient reported to be allergic to penicillin, so Clindamycin 300 mg (3 times a day