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Case report

A case report of bisphosphonate related osteonecrosis of the jaw treated by photodynamic therapy

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1. Introduction

Bisphosphonate Related Osteonecrosis of the Jaw (BRONJ) is defined as “necrotic bone exposed in maxillofacial region lasting for more than eight weeks in bisphosphonate treated patients who have not undergone head and neck radiation therapy” [1]. This complication of bisphosphonate therapy was first described in 2003 by Marx among multiple myeloma patients [2]. The accumulation of these drugs in bone mineral matrix over a period of time combined with their anti-angiogenic properties result in non-healing lesions after dental extractions (> 70% cases), implant surgeries and periodontal surgeries involving osseous injury [3,4].

Photodynamic therapy (PDT) is being increasingly combined with other therapeutic options in the management of BRONJ [5,6]. Antimicrobial and anti-inflammatory properties of PDT stimulate proliferation and collagen synthesis of human periodontal ligament cells and gingival fibroblasts [7]. It has also exhibited no cytotoxicity to these cells in-vitro [7]. Hence, we employed photodynamic therapy in the treatment of stage 3 BRONJ as the mainstay of therapy.

2. Case report

A 73 year old female patient was referred to the outpatient department of Periodontics in January 2017 with complaint of “pain and pus discharge from below the left lower jaw region since past five years.” The patient history included monthly oral bisphosphonate dosage (Ibandronic acid 150 mg, duration: 3 years) for osteoporosis. The bisphosphonate was stopped in February 2011 after the extraction of mandibular left first molar, since the extraction led to onset of pain and intermittent episodes of swelling. Patient had no history of head and neck radiotherapy.

On intra-oral examination a sequestrum was seen with respect to the extraction site in left mandible along with bone exposure. Purulent exudation from the extra-facial fistula in left submandibular region and facial asymmetry were noted. The orthopantomogram (OPG) revealed osteolysis of the left mandible. The intra-oral site was debrided and sequestrum biopsied (4 cm x 2 cm x 0.8 cm). The biopsy revealed branching bony trabeculae, areas of necrosis and fragments of dead bone. According to the Position Paper by the American Association of Oral and Maxillofacial Surgeons (AAOMS), this case was diagnosed at Stage 3, which is defined as exposure of necrotic bone with pain, infection and extra-oral fistula [1] (Fig. 1).

The patient also reported taking oral Clindamycin (450 mg 8 hourly for 3 weeks) prior to reporting to us. Clindamycin was stopped on the advice of physician because the patient’s creatinine levels were raised. Pus culture was performed but no microbial growth was obtained probably due to prolonged antibiotic intake. Thereafter, treatment with photodynamic therapy was initiated in our department. Each session consisted of staining the intra-oral bone exposure and the extra-oral fistula with Thiazin-Derivat dye (HELBO® Blue Photosensitizer) for 60 s, followed by rinsing with saline in multifunction syringe to remove excess dye and any dye deposits. This was followed by the application of diode laser with a 3D pocket probe with exposure time of 1 min per cm^2 (HELBO® Theralite laser). The patient was treated with 2 sessions per week for first two weeks (4 sessions), followed by one session per week over next 6 weeks (6 sessions). The 11th and 12th sessions were provided after one month of their previous sessions. Since there is no standardized regimen or protocol for scheduling treatment sessions, the photodynamic therapy was provided in coherence with healing rate of the BRONJ lesion. The patient was also instructed in oral hygiene

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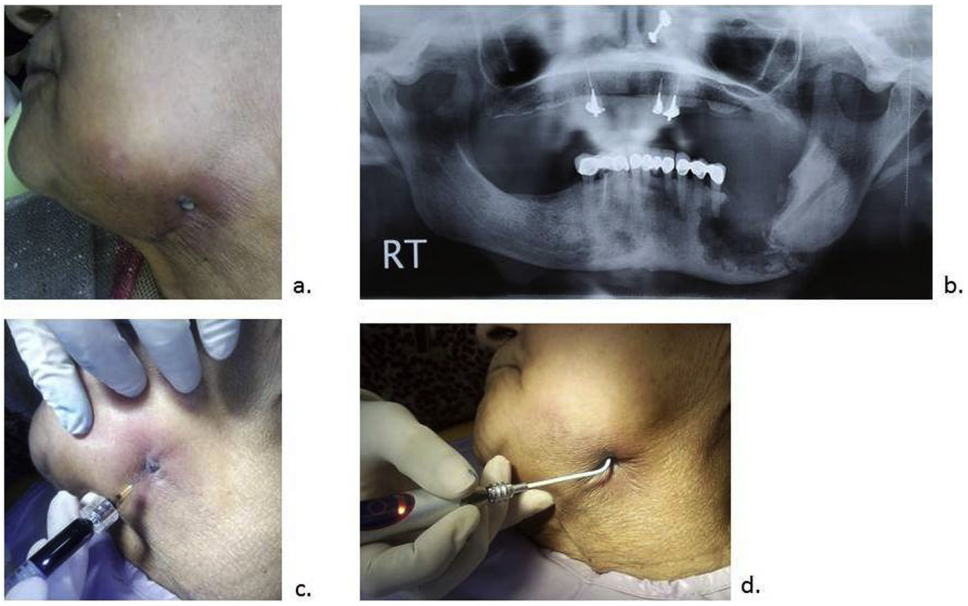

Fig. 1. Picture a. Initial Presentation of lesion in 2017. Picture b. Pre-treatment OPG depicting the lesion in left mandible. Picture c. Dye injected in the extra-oral fistula. Picture d. Laser application during 5th PDT session.

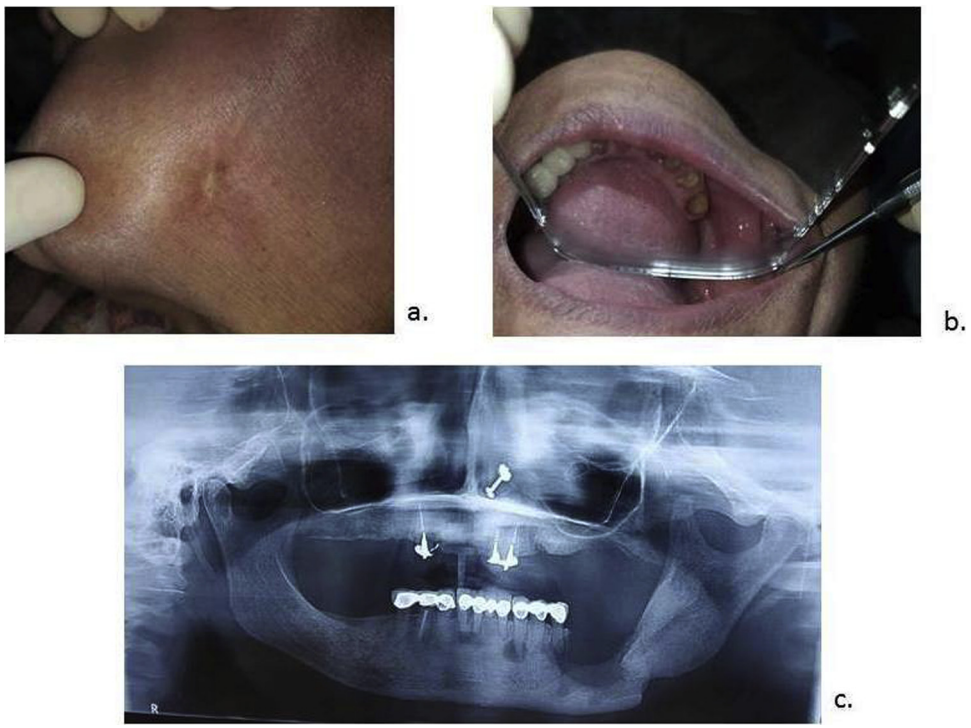

Fig. 2. Picture a. Post-treatment healed extra-facial fistula. Picture b. An indirect view of the healed intra-oral left posterior mandibular region. Picture c. 1 year post-treatment OPG.

measures and advised use of Povidone-Iodine mouth rinse in a 1:20 (ml) dilution every 3–4 h (7.5%w/v) during treatment.

3. Results

After the first 4 sessions scheduled twice per week, the lesion started to improve. There was no pus discharge with reduction in size of extra-oral fistula orifice. The patient was further treated by once a week session until the fistula showed complete healing externally. Complete healing of the extra-oral fistula was seen after 8 weeks in 10 treatment sessions. The intra-oral lesion was asymptomatic after 12 sessions, however complete soft tissue coverage of the exposed bone was achieved over a year. The patient compliance was high and she rigorously maintained oral hygiene. This included flushing the lesion with saline and regular rinsing with antimicrobial mouthwash during the treatment period. The patient was on regular follow-up appointments after last PDT session. During the follow up of 2 years there was no recurrence of the fistula, no bone necrosis or sequestration and no superimposed infection or suppuration. The patient was free of pain (Fig. 2).

4. Discussion

Treatment recommended by AAOMS for BRONJ stage 3 is symptomatic therapy with oral antibiotics and anti-bacterial mouth rinse combined with surgical debridement/resection for long term palliation of infection/pain. However, in this case, complete resolution of infection was achieved only using PDT.

The PDT treatment regimen of twice a week for first two weeks was followed in this report. It was also reported by Rugani P et al. in 2013 [5]. They reported use of the above regimen of PDT in 5 women with BRONJ stage 0 who showed complete healing after the first 4 sessions. They also reported employing the same regimen of photodynamic therapy in 7 surgically treated BRONJ stage 2 patients of whom 5 patients showed resolution of lesion [5]. However, they did not report recall of patients for further treatment sessions. A similar case report has been described by Minamisako MC et al. for treatment of BRONJ Stage 2. Their management comprised of conservative treatment with Clindamycin 600 mg/day and topical application of chlorhexidine gluconate (0.12%) [6]. They reported occasional bi-weekly and more frequent weekly sessions comprising of superficial bone debridement, PDT, and LLLT application for 12 months, until clinical healing of bone exposure, accounting a total of 37 sessions. They concluded that, while PDT controlled the infection, LLLT promoted total repair of oral mucosa [6]. The variation in the PDT regimen and the healing period in these case reports could be attributed to the difference in stage of BRONJ lesion and difference in adjunctive treatment that was selected.

In this case, when PDT was applied directly to bone and suppurating tissues, it was found have no harmful effects on the surrounding tissues corroborating its application in successful management of BRONJ. While PDT is established as an adjunct in non-surgical treatment of periodontal pockets and for intra-canal biofilm management in endodontics, sound evidence elucidating its role in BRONJ treatment is required [8].

5. Conclusion

To summarize, photodynamic therapy can be a viable treatment of advanced stages of BRONJ, which is otherwise considered difficult to treat and may even be recalcitrant to therapy. The excellent healing documented by case reports must encourage future clinical trials.

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Conflicts of interest

None of the authors have any conflict of interest to be disclosed.

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