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Xing-Ming Shi, Norman Chutkan, Mark W., Carlos M.. "Chapter 3 Mechanism of Glucocorticoid-Induced Osteoporosis: An Update", IntechOpen, 2012

Aesthetic consideration in patient management with severe periodontitis aggravated by oral dexamethasone ABSTRACT Background: The treatment of severe periodontitis must consider immune response, local condition, including aesthetic aspects. The tooth loss, especially in the anterior area, lead to psychological issue in some patient. Aesthetical aspects must consider as one goal in periodontal treatments. On another side, the daily use of dexamethasone gives a great contribution to the severity of the disease. Purpose: To report the aesthetic consideration in patient management of severe periodontitis aggravated by oral dexamethasone. Case: The 44- years old female patient was reported to have tooth mobility in many areas. Grade 3 mobility of Miller's index was found in the upper right and left central incisor, grade 2 was found in teeth 44, 43, 42, 41, 31, 32, and grade 1 was found in teeth 33, 34, 35. Due to the condition, the central anterior should be extracted. She also has seafood allergies. For 2 years, the patient has consumed oral dexamethasone periodically to prevent allergic reactions. Case Management: Initial periodontal therapy was designed prior to tooth extraction, socket preservation, and immediate denture on 11 and 21. Metal frame combined with acrylic denture were designed to support the tooth splint and replace the teeth on the mandible. To modulate the immune system, the patient was treated with sub-antimicrobial-dose Doxycycline 20 mg twice a day for three months and vitamin E was prescribed once a day. Since dexamethasone may contribute to immune response and osteoclastogenesis, a patient was referred to an internist to replace steroidal inflammatory drugs. Conclusion: Treating severe chronic periodontitis must consider immune response, local condition, including aesthetic aspects. In this case, the use of dexamethasone might worsen the periodontal breakdown. However, the periodontal treatment, the use of host modulation therapy and replace dexamethasone with cetirizine are expected to improve these conditions. Keywords: host modulation therapy; periodontitis; periodontal diseases; oral dexamethasone INTRODUCTION Periodontitis, is a common disease in the oral cavity consisting of slow irreversible damage of periodontal supporting tissue over a period of time.1 It has been shown that deep periodontal pockets as a result of alveolar bone destruction

have been associated with an increase in the number of tooth loss.2–4 The tooth loss, especially in the anterior area, lead to psychological issue in some patient.5 Aesthetical aspects must consider as one goal in periodontal treatment.6 Periodontitis is an inflammatory disease caused by microorganisms and characterized by progressive destruction of periodontal tissue.7 The pathogenesis of the destructive periodontal disease is currently understood as the response given by an individual to the bacterial challenge of subgingival dental biofilm.4 This response is modulated by different mechanisms, including environmental and acquired factors.8,9 The variety of environmental and acquired factors, including genetics, comorbid, local and dental factors, and medicine, modify the condition of periodontal disease patients.9–11 To the best of the authors' knowledge, there is no clear epidemiological data regarding the number of periodontitis patients using dexamethasone. However, several studies explained strong relationship between the effect of dexamethasone and tissue destruction in periodontitis. Previous studies analyzed the role of synthetic glucocorticoid, included dexamethasone, has direct effects on osteoblast, osteocyte and osteoblast function resulting in reduce remodeling and may cause diminished repair of microdamage to bone.11 Glucocorticoid induced inhibition of osteoblast differentiation via ERK signaling,12 and it also induced osteoporosis through Runx2 signaling pathway.13 Dexamethasone, steroidal inflammatory drugs, was clearly demonstrated has capability to modulate the inflammatory process in periodontal tissue.14 It was reported may decrease the bone mineral density and mineralized matrix.12,13,15 This study reports the esthetic consideration in patient management of severe periodontitis aggravated by oral dexamethasone. CASE The 44-year-old, systemically healthy, has seafood allergic, nonsmoker female patient was diagnosed generalized periodontitis Stage IV Grade C. For 2 years, patient has consumed oral dexamethasone periodically to prevent allergic reaction. The patient did not reveal any severe periodontal destruction or early tooth loss in her family history, and there were not external abnormalities found (Figure 1). The patient has not received any periodontal treatment in the past time. The patient expressed her concern about aesthetics. Extra oral and intra oral image with periodontal chart and radiographic of the patient were taken before periodontal treatment. The oral examination showed severe calculus and 2 teeth mobility in several area was measured by using Miller's tooth mobility index.16 Grade 3 of Miller's index were found in upper right and left central incisor, grade 2 were found in teeth 44, 43, 42, 41, 31, 32 and grade 1 were found in teeth 33, 34, 35. Gingival recession and periodontal pocket up to 9mm were found in most of the teeth (Figure 2 and 3). Radiograph examination revealed severe bone loss in upper right and left central incisor. Bone loss also occurs in other areas (Figure 4). Figure 1. Extra oral image of the patient. Figure 2. Periodontal chart (A) upper arch (B) lower arch. Figure 3. Intra oral image of the patient, before (A) and after scaling and root planning. Figure 4. (A) X-ray image teeth 17, 16, 15; (B) X-ray image teeth 11, 21; (C) X-ray image teeth 2. 2, 2. 3, 24; (D) X-ray image teeth 23, 24, 25; (E) X-ray image teeth 25, 26, 27; (F) X- ray image teeth 44, 43, 42; (G) X-ray image teeth 42, 41, 31, 32; (H) X-ray image teeth 33, 34, 35. Initial periodontal therapy was designed prior to tooth extraction, socket preservation and immediate denture on 11 and 21. Metal frame combined with acrylic denture were designed to support the tooth splint and replace the teeth on mandible.17 To modulate immune system, the patient was treated with host modulation therapy.18 Sub-antimicrobial-dose Doxycycline 20 mg were prescribing twice a day for three months and vitamin E was prescribing once a day.19–21 Periodontal flap surgery combined with bone graft augmentation was planned to regenerate periodontal tissues.22 In addition, patient referred to internist to replace steroidal inflammatory drugs. CASE MANAGEMENTS At the first visit, patient was treated by scaling, root planning and fiber splint on teeth 44, 43, 42, 41, 31, 32, 33, 34, 35 (Figure 3 and 5A). Imediate denture for maxilla and metal frame denture for mandible were designed (Figure 6). Patient was prescribing doxycycline 20 mg and vitamin E twice a day for three months for host modulation therapy19,21,23 and patient referred to internist for medical assessment. Laboratory assessment show the fasting glucose level was 89 mg/dl (normal: 70-115 mg/dl) and 2-hours glucose level was 135 mg/dl (normal: <200 mg/dl), HBA1C was 4,5 % 5 (normal: 5,7%; pre diabetes: 5,7-6,4%; diabetes:>/=6,5%). Dexamethasone was replaced with another anti-histamine, cetirizine dihydrochloride, to prevent allergic reaction. Figure 5. Fiber splint on tooth 34-45 (A), Periodontal abscess on tooth 34-45 (B), Abscess healing on tooth 34-45 (C). At the second visit, one week after periodontal splint treatment, patient came to control her condition and continued the treatment. There were abscess on 34, 33, 32, 31, 41, 42, 43, 44, 45. Plaque and debris found in oral cavity (Figure 5B). Amoxicillin 500 mg combined with metronidazole 500 mg were prescribing for 3 days, and oral hygiene instruction were given to the patient for abscess treatment. Metal frame was tried on mandible and occlusion was adjusted (Figure 6B). Figure 6. Lower arch metal frame design and immediate denture tooth 11 and 21 (A). Fitting the metal frame and searching the bite for denture (B). At the third visit, abscess was healing in 34, 33, 32, 31, 41, 42, 43, 44, 45 (Figure 5C). Surgical procedure for socket preservation on tooth 11 and 21 was perform. To replace the edentulous, immediate denture on maxilla and metal frame on mandible were inserted. Socket preservation 11, 21 followed by immediate denture carried out under local anesthetic drug and removable metal frame was inserted. Surgical steps were explained briefly in Figure 7. Under aseptic and anesthetic procedures, 11 dan 21 were extracted. Socket debridement were performed and bone graft mixed with PRF were applied. The socket was sutured by braided- non absorbable silk 4.0. Immediate denture was inserted on maxilla to replace 11 and 12, and metal frame was inserted on mandible to replace edentulous. Occlusal evaluation was performed to avoid trauma from occlusal. The patient was instructed to unreplaced the immediate denture for 24 hours. Paracetamol 500 mg and kalium diclofenac 25 mg three times a day were prescribing for three days. Two weeks after surgery, the wound healing was gain (Figure 11.L). Figure 7. Asepsis technique using povidone iodine to prevent infection and mepivacaine 2% with epinephrine 1:100.000 (Scandonest 2% Special) was administered for the surgery. (A) The extraction of 11; (B) The extraction of 21; (C) socket debridement of 11 and 21; (D) PRF was mixed with bone graft (Batan Research Tissue Bank); (E) bone graft application in socket 11 and 21; (F) The socket was sutured with braided non-absorbable silk 4.0 (Mersilk); (G) Buccal side of immediate denture 11 and 21; (H) Occlusal side of immediate denture 11 and 21; (I) and (J) Sagital view removable metal frame partial denture on mandible; (K) Occlusal view removable metal frame partial denture on mandible; (L) The wound healing after 2 weeks socket preservation surgery. DISCUSSION This case presents the aesthetic consideration in patient management with severe periodontitis. Prolong inflammatory process leads tissue destruction in periodontal tissue.24,25 Loss of anterior teeth particularly in adolescents increased demand for tissue maintenance and esthetic.26 The hopeless teeth substitution using denture in one visit could give solution for patient. Some previous studies reported the alternative treatment of single visit replacement of central maxillary were immediate denture27 and fiber-reinforced composite resin.26 Since the periodontitis cause the tissue destruction and tooth mobility, the treatment started with teeth splinting of 34, 33, 32, 31, 41, 42, 43, 44, 45 to maintain the stability of abutment.28 Previous study suggested variety of periodontal splinting, including removable partial denture were designed to stabilize the mobility tooth. They recommend some particular design of partial denture to enforce the abutment.28–30 Metal frame removable partial denture is the ideal prosthesis for patient with periodontal problem. They give better stability because of the rigidity. This prosthesis could prevent mesial and distal displacement of teeth, lateral pressure, and prevent dental extrusion. Furthermore, removable partial denture made from metal frame return the efficiency of overall mastication. They might divide masticatory load and give stabilization force with splint mechanism so that the natural teeth can function well.17 Socket preservation in tooth 11 and 21 was performed with demineralized freeze-dried bone xenograft (DFDBX) (Batan Research Tissue Bank) and platelet rich fibrin (PRF). Xenograft in socket preservation techniques delayed the socket healing. However, it will help conserving anatomy of the bone. Xenografts are considered the most used bone fillers in the socket preservation procedures due to their osteo-conductive matrix framework that enhances the growth of new bone around it.31 PRF consists of an autologous leukocyte-platelet-rich fibrin matrix, composed of a tetra molecular structure, with cytokines, platelets, and stem cells within it. PRF acts as a biodegradable scaffold that favors the development of micro vascularization and able to guide epithelial cell migration to its surface. PRF has great potential for bone and soft tissue regeneration without inflammatory reactions and may be used alone or in combination with bone grafts. The advantages of these techniques are promoting homeostasis, enhance the bone growth and maturation.32 The patient was referred to internist due to suspect of systemic problem that may cause severe bone and clinical attachment lose in many teeth. Dexamethasone was replaced by cetirizine dihydrochloride. Dexamethasose may cause impair wound healing and diminish bone mineralization. Experimental study in animal periodontal model revealed dexamethasone cause more attachment loss and made a bone more easily fractured as compared to controls. Anti-inflammatory effect from dexamethasone can minimize clinical signs of inflammation at first by reducing host response. Impaired host response could be responsible for more tissue breakdown.14 Through the inhibition of osteoblast differentiation via ERK pathway and Runx2 signaling, dexamethasone may cause osteoporosis, and decrease bone mineral density.12,13,15 Different result was shown by Metzger et all's study. Periapical lesion was induced in rat by occlusal exposure of their first molar. However, systemic dexamethasone downregulates the bone resorption in periapical inflammatory lesions.33 Cetirizine dihydrochloride is an antihistamine used to relieve allergy symptoms such as watery eyes, runny nose, itching eyes/nose, sneezing, hives, and itching. It works by blocking histamine that body makes during an allergic reaction. Adverse effect profile of cetirizine 9 generally being of mild to moderate intensity to be comparable with other antihistamine like astemizole, ebastine, fexofenadine, loratadine, mizolastine or terfenadine.34 Cetirizine is an antagonist of TLR2 and TLR4 receptor. The suppressive effect on TLR2 and TLR4 will decrease the production of IL-8 as pro-inflammatory cytokine and CCL20 as macrophage inflammatory protein. This experiment confirmed the addition of cetirizine one hour before stimulation in human gingival fibroblast by using TLR2 and TLR4 ligand and histamine downregulate the production of IL-8 and CCL20. Beside TLR2 and TLR4, cetirizine also blocks histamine link with histamine-1 receptor (H1R) in human gingival fibroblast.35 We assumed dexamethasone and cetirizine show different effect in periodontal tissue. The mechanism of action these steroidal anti-inflammatory drugs still remain unclear. Dexamethasone cause bone destruction in animal periodontal model. In other hands, cetirizine may regulate inflammatory process in human gingival cells. Further study will be needed to discuss the effect of steroidal anti-inflammatory drug in periodontal tissue. However, we suggest cetirizine dihydrochloride gives ideal treatment for allergic in patients with periodontal disease. Doxicycline 20 mg twice a day for three months is a subantimicrobial-dose doxycline. Doxycline was the most potent tetracycline in the inhibition of collagenolytic activities. Golub et al.36 in 1990 reported that this property of doxycycline provided the pharmacological rationale for the use of a low or subantimicrobial dose of doxycycline, which was shown to be efficient in inhibiting mammalian collagenase activity without developing antibiotic resistance. The aims of periodontal treatment are to prevent further disease progression, minimize tooth loss, restore periodontal tissue destruction, and maintaining the healthy periodontium. Previous studies explained no one periodontal treatment shown more important than others.37,38 The combination between non surgery38 and surgery periodontal therapy37 might relieve several unfavorable effects of theses severe periodontitis. The adequate periodontal therapy may decrease the risk on systemic condition, such as cardiovascular disease by continuous bacteremia.39 Furthermore, periodontal disease may cause the inflammatory cytokines production induced gram negative strictly anaerobic bacteria.40 However, the periodontal therapy might regulate these inflammatory cytokines.41,42 In conclusion, the treatment of severe chronic periodontitis must consider immune response, local condition, including esthetic aspects. In this case, the use of dexamethasone might worsen the periodontal breakdown. However, the adequate surgery and surgery non- therapy, such as the host modulation therapy and replace dexamethasone with cetirizine, are expected to improve these conditions. 10

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