PERIODONTAL MANAGEMENT OF A PATIENT WITH CHRONIC KIDNEY DISEASE: A CASE REPORT

Daniela Cia **Penoni**[1,2]*, Flávia **Sader**[3], Marcos Nunes **Silami**[4], Anna Thereza Thomé **Leão**[2], Sandra Regina **Torres**[5]

[1]Department of Preventive Dentistry, Odontoclínica Central da Marinha, Brazilian Navy, Rio de Janeiro, Brazil
[2]Department of Dental Clinic, Division of Periodontics, Dental School, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil
[3]Department of Dental Clinic, Division of Periodontics, Odontoclínica Central da Marinha, Brazilian Navy, Rio de Janeiro, Brazil Universidade Federal Fluminense, Dental School, Rio de Janeiro, Brazil
[4]Department of Dental Clinic Stomatology and Oral Pathology Clinic, Brazilian Navy, Odontoclínica Central da Marinha, Rio de Janeiro, Brazil
[5]Department of Oral Pathology and Diagnosis, Dental School, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil

Palavras-Chave: Doenças Periodontais. Nefropatia. Anlodipino. Crescimento excessivo da gengiva.

RESUMO

Introdução: A associação entre doença periodontal e doença renal crônica (DRC) tem sido reconhecida nos últimos anos. O crescimento gengival excessivo pode ser um efeito colateral de alguns medicamentos prescritos para pacientes com DRC. **Objetivos:** O objetivo deste estudo foi relatar o manejo odontológico de um paciente com DRC que apresentava periodontite e aumento gengival. **Relato do caso:** Um paciente do sexo masculino, 55 anos, procurou atendimento odontológico e foi diagnosticado com periodontite generalizada em estágio avançado e crescimento gengival associado ao uso de anlodipina, um bloqueador dos canais de cálcio de ação prolongada. O tratamento consistiu em interrupção da anlodipina, sessões de instruções de higiene bucal e terapia periodontal básica. Posteriormente, foi realizada terapia periodontal convencional, com raspagem e alisamento radicular dos quatro hemiarcos, seguida de cirurgia periodontal a retalho e gengivectomia. Considerando os sítios periodontais com profundidade de bolsa à sondagem (PBS) ≥ 4mm no início do tratamento, a média de PBS foi reduzida (início: 5,94 ± 1,80; final: 2,76 ± 1,38), bem como a média do nível clínico de inserção (início: 5,55 ± 1,51; final: 4,52 ± 1,47).A doença periodontal foi controlada e não houve recorrência do crescimento gengival após 18 meses de acompanhamento. **Conclusão:** O tratamento odontológico deste paciente com DRC e envolvimento periodontal incluiu a interrupção da anlodipina, terapia periodontal básica e avançada e gengivectomia. A higiene bucal adequada pode ajudar a prevenir a recorrência do crescimento gengival excessivo e a manutenção de um estado periodontal saudável.

Keywords: Periodontal Disease. Kidney Diseases. Amlodipine. Gingival Overgrowth.

ABSTRACT

Introduction: The association between periodontal disease and chronic kidney disease (CKD) has been recognized over the years. Gingival overgrowth may be a side effect of some of the drugs prescribed for patients with CKD. **Objective:** The objective of this manuscript was to report the dental management of a patient with chronic renal disease who presented periodontitis and gingival overgrowth. **Case report:** A 55 years old male patient sought dental treatment, and was diagnosed with generalized periodontitis in advanced stage and gingival overgrowth. The overgrowth was associated to the use of amlodipine, a long-acting calcium channel blocker. The treatment consisted of interruption of amlodipine, sessions of oral hygiene instruction and basic periodontal therapy. Thereafter, conventional periodontal therapy, with scaling and root planning of the four hemiarches, surgical periodontal therapy and gingivectomy of the overgrowth were performed. Considering periodontal sites with a probing depth (PD) ≥ 4mm at baseline, mean PD was reduced (baseline: 5.94 ± 1.80; follow-up: 2.76 ± 1.38), as well as mean clinical attachment loss (baseline: 5.55 ± 1.51; follow-up: 4.52 ± 1.47). Periodontal disease was controlled and there was no recurrence of gingival overgrowth after 18 months of follow-up. **Conclusion**: The management of the reported patient with CKD and periodontal involvement included discontinuation of amlodipine, basic and advanced periodontal therapy and gingivectomy. Proper oral hygiene may help to prevent recurrence of the gingival overgrowth and to maintain periodontal health.

Submitted: April 22, 2020
Modification: June 08, 2020
Accepted: June 22, 2020

***Correspondence to:**
Daniela Cia Penoni
Address: Praça Barão de Ladário, 1 - Centro, Rio de Janeiro, RJ, Brazil - Zip Code: 20091-000
Telephone number: +55 (21) 2104-6596
E-mail: ciapenoni@yahoo.com

INTRODUCTION

Chronic kidney disease (CKD) is an abnormality of the kidney structure or function for more than three months, being considered a risk factor for premature death. There is an increasing prevalence of CKD due to the growth of the elderly population and the increasing rates of diabetes mellitus and hypertension.[1] Patients with chronic renal failure may require special dental care, since oral involvement of patients with CKD include oral manifestations of the disease itself, or side effects of its treatment. The most frequent oral manifestations of patients with CKD are pale mucosa, low salivary flow rates, altered salivary composition, dysgeusia, halitosis, increased dental calculus formation, uremic stomatitis, and osteodystrophia.[2,3]

CKD and periodontitis have common risk factors, such as smoking and diabetes mellitus.[4,5] The association between both diseases has been increasingly recognized over the last decades.[5-7] The influence of periodontitis on CKD may be explained by the burden of systemic inflammatory mediators resulting from periodontal infection, which exacerbates the existing metabolic disorder. Then, it could be expected that non-surgical periodontal therapy might decrease the pro-inflammatory state.[8,9] However, there is insufficient evidence to assume a potential benefit of periodontal treatment on renal function in CKD patients with periodontitis.[5,7] Although inconclusive, the opposite direction has also been investigated: CKD influencing the onset and/or progression of periodontal disease, possibly mediated by diabetes and hypertension.[6,10]

Gingival overgrowth may be a side effect of drugs used in patients with CKD, including calcium channel blockers, like amlodipine, to treat hypertension, and cyclosporine, an immunosuppressant commonly used in kidney transplantation recipients. The gingival overgrowth may hamper satisfactory oral hygiene, which complicates the periodontal condition [(11)].

Dentists need to know how to manage patients with kidney impairment during dental treatment.[12] The use of anticoagulant drugs and increased risk of bleeding should be investigated prior to oral invasive procedures. Prescription of drugs with renal metabolism may require adjustment of the dosage, mainly for patients under hemodialysis.[4]

The aim of this manuscript was to report the periodontal treatment approach of a patient with chronic renal disease, who presented generalized periodontitis and localized gingival enlargement associated to amlodipine.

CASE REPORT

A 55-year-old male with a history of CKD and severe hypertension was referred for dental treatment at the Periodontology Division of the Naval Dental Center (*Odontoclínica Central da Marinha/OCM*), Rio de Janeiro, Brazil, from the Nephrologist Division of the Hospital Naval Marcílio Dias, in October 2017. Patient complained of tooth mobility, changes in teeth position and gingival pain and bleeding. Anamnesis has revealed that the patient was not under dialysis, at that moment. Laboratory test results showed creatinine levels varying from 5.0 to 6.0 mg/dL, in the last four years. Intake of medications included losartan, furosemide, calcium carbonate, simvastatin, allopurinol, vitamin D and amlodipine. He had no history of smoking or alcohol use. He reported that kidney impairment was a result of 20 years with hypertension and no adherence to treatment.

During oral exam, an extensive mass was observed in the region of the inferior labial gingiva, measuring nearly 8 cm in diameter, presenting pinkish to reddish color, of soft consistency, with few superficial ulcerations on the surface, and bleeding on touch (Figure 1A). Biofilm accumulation was observed in the area, since the gingival overgrowth represented a challenge for oral hygiene. There were deep periodontal pockets in the region. The mass appeared to be a benign soft tissue lesion, with clinical aspect aggravated by biofilm accumulation. The differential diagnoses were gingival overgrowth attributed to the amlodipine, pyogenic granuloma, giant cell granuloma, and brown tumor of hyperparathyroidism. On radiographic evaluation, signs of bone involvement were observed (Figure 1B).

Periodontal parameters such as probing depth (PD) and clinical attachment level (CAL) were measured at six sites (mesial, distal, and middle sites of the buccal and lingual sides) on each tooth, using a North Caroline periodontal probe (Hu-Friedy®, USA). Additional assessment of periodontal status included the presence of bleeding on probing (BOP). Out of 138 evaluated periodontal sites at baseline, PD and CAL equal or higher than 4mm were observed in 49 (35.5%) and 51(36.9%) sites, respectively, and BOP was present in 61% of the sites. Periodontal exam revealed periodontitis stage IV, which is the most severe stage of periodontitis.

The evaluation of the panoramic radiography revealed the absence of teeth 26, 36 and 46; tooth 16 endodontically treated; and, multiple teeth with restorations. Vertical bone loss, extending to the apical third, compatible with advanced stage periodontal disease was also observed. The region adjacent to teeth 18, 17, 28 and 45, which presented clinically high level of mobility, showed imaging suggesting periapical lesions, therefore were referred to surgical extractions. Loss of lamina dura was identified

around some of the roots. No root resorption and cortical or medullary bone resorption were observed.

The objective of the treatment was to improve oral health by removing the gingival overgrowth, controlling periodontal disease. and enhancing oral selfcare. This way, treatment planning included oral hygiene instruction, periodontal therapy and gingivectomy. Discontinuation of causative medication was discussed with nephrologist, and amlodipine was interrupted in October 2017.

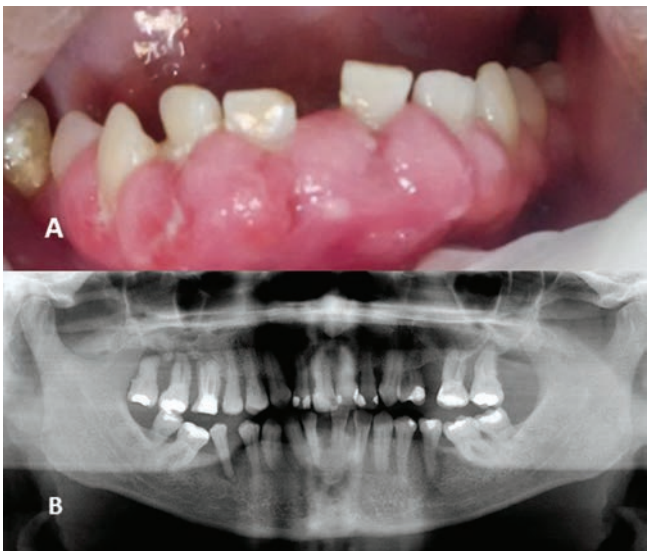


***Figure 1**: (A) Clinical aspect of gingival overgrowth; and (B) Panoramic image showing severe and generalized alveolar bone loss at baseline (October 2017).*

Two sessions of oral hygiene instruction and basic periodontal therapy were conducted by an oral hygienist. The need of an accurate self-oral hygiene was stressed, including the use of interdental brushes. Scaling and root planing, were performed by a periodontist, in four sessions of conventional therapy. Mouthwashes with 0.12% chlorhexidine were recommended every 12 hours for 15 days. At follow up examination, patient presented adequate oral hygiene, and periodontal therapy was completed in April 2018.

Although notably reduced, the gingival overgrowth was not completely eliminated after periodontal scaling. Patient was then scheduled for surgical periodontal treatment and gingivectomy (Figure 2). Before surgery, a complete hemogram, glicosis and creatinine levels were checked. His nephrologist was contacted, to confirm that the patient was able to receive an invasive oral procedure at that moment.

Surgical removal of the gingival overgrowth was planned not only for cosmetic, but also for functional reasons, as the lesion formed niches for the retention of bacterial biofilm and hampered patient's mastication. The surgical removal was performed on the lower anterior teeth region, through an internal bevel incision (Figure 2). A full-thickness flap was lifted and the flap was thinned with scissors. During surgical procedure, scaling and root planning were performed for removal of subgingival biofilm and calculus. Simple interrupted sutures were performed with 5.0 nylon thread.



***Figure 2**: Gingivectomy procedure (April 2018).*

Amoxicilin 500 mg was prescribed every 8 hours, for the seven days after surgery. Additionally, dipiron 500mg was prescribed for pain relief, every 6 hours, for the first three days, if necessary. Patient was also instructed to rinse with 0.12% chlorhexidine twice a day, for 15 days. Excised gingiva tissue was sent for histopathological analysis, and diagnosed as inflammatory gingival hyperplasia. The postoperative clinical aspect at 15-day showed a satisfactory result (Figure 3).



***Figure 3:** Fifteen days postoperative (May 2018).*

Patient did not attend the next scheduled follow-up dental visits. He came back to the clinic only one and a half year later, when he presented an acceptable oral hygiene pattern. There was BOP in 25% of the teeth and the periodontal disease was controlled (Figure 4). Data from mean PD and CAL comparing baseline with follow-up are shown in Table 1.

In the meanwhile, he was been treated by an orthodontist, and he was wearing an orthodontic appliance, since he complained about the changes in teeth position, due to advanced periodontal disease. His systemic condition had worsened, and presented 11.2 mg/dL serum creatinine. The medications in use were losartan, furosemide, calcium carbonate, simvastatin, allopurinol and vitamin D, and erythropoietin. Amlodipine was suspended. He was now on hemodialysis and referred to kidney transplantation by the nephrologist.

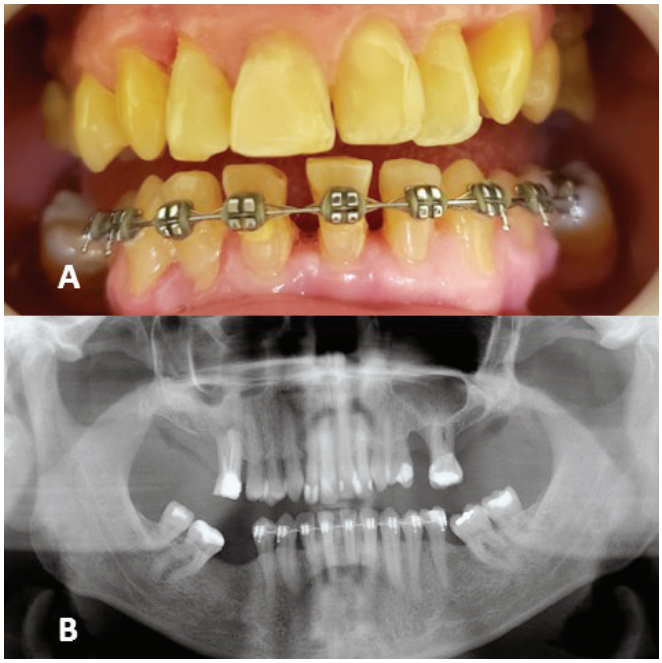


***Figure 4**: Clinical aspect at 18 months from periodontal therapy and gingivectomy (A); and follow-up panoramic image (B), (November 2019).*

***Table 1:** Data on probing depth and clinical attachment loss at baseline and follow-up.*

Periodontal parameter	PD		CAL	
	baseline	follow-up	baseline	follow-up
All sites (n=138)	3.38 (2.25)	2.13 (1.16)	3.43 (1.93)	3.09 (1.16)
sites ≥ 4mm *	5.94 (1.80)	2.76 (1.38)	5.55 (1.51)	4.52 (1.47)

*Notes: * sites ≥ 4mm: n= 49 for PD and n=52 for CAL. CAL: clinical attachment loss; PD: probing depth. Data presented by mean (standard deviation).*

DISCUSSION

It is estimated that 90% of patients with chronic kidney disease will have oral symptoms, either related to the disease or to its treatment. Periodontal disease is prevalent, severe, and under-recognized in patients with renal failure. Patients should be followed by a multiprofessional healthcare team and early oral exams should be reinforced.[13] This case report showed a successful periodontal approach of a male patient with CKD who presented periodontitis and amlodipine-induced gingival overgrowth. Males were considered three times as more than females to develop clinically significant overgrowth.[14]

Proposed mechanism connecting periodontitis with chronic kidney disease (CKD) involves systemic inflammation.[10] It is possible that CKD may influence the onset or progression of periodontal disease, possibly mediated by diabetes and hypertension. On the other direction, inflammatory cytokines involved in periodontitis may lead to the progression of CKD. Another theory suggests that periodontal bacteria enter the systemic circulation and exert their effects beyond the periodontium.[8,9] Reducing inflammation and bacterial load by periodontal treatment seem to improve kidney function, but further studies are necessary to determine whether prevention or treatment of periodontitis reduces the incidence or the severity of CKD.[5,7]

This case report study presented a patient with periodontitis stage IV grade C. At this advanced stage, periodontitis causes considerable damage to the periodontal support and may cause significant tooth loss, which implies in loss of masticatory function. Lack of control of the periodontitis and adequate rehabilitation, may lead to tooth loss. In fact, four teeth were lost in the beginning of periodontal treatment in the reported case.[15,16] There was a notable shift in periodontal parameters after non-surgical periodontal therapy, as shown by the reduction in means of PD and CAL. Other authors have stated that non-surgical periodontal therapy can effectively improve periodontal status in patients on end-stage renal disease. It is a relatively simple intervention, which has showed improved systemic effects in this population.[8] However, the improvement of the periodontal condition of the reported patient did not present a positive impact on the progression of CKD.

The patient of this case report presented a 20 years

history of hypertension, with no adherence to treatment. Hypertension and dyslipidemia may account to poor periodontal condition. In hypertension, changes in microcirculation can cause ischemia in the periodontium, which favors periodontal disease[17]. There might also be an interaction between periodontitis and hypertension, with the underlying inflammatory process interfering with the endothelial function. This could have implications for blood pressure control and the development of lesions in target organs.[17] Simvastatin intake, used to control dyslipidemia, was also reported by the patient. Periodontitis may be associated with dyslipidemia via systemic inflammation.[18] In the other direction, many cytokines released in periodontitis may stimulate hepatic free fatty acid synthesis, resulting in increased synthesis of very low-density lipoprotein and hypertriglyceridemia.[18]

Studies have reported that the use of calcium channel blockers, like amlodipine, may contribute to gingival overgrowth. Large deposit of gingival biofilm and calculus were observed in the reported patient at baseline, which may have led not only to the gingival overgrowth, but to periodontitis progression. Proper oral hygiene can help to prevent progression of medication induced gingival overgrowth, but does not resolve the condition in many cases.[19] The presence of gingival inflammation is an important cofactor for the expression of this effect.[14]

Individuals and healthcare professionals play important roles for the long-term success of periodontal treatment.[20] The reported patient presented 21% of BOP when he returned one and a half year later, comparing to 61% at baseline. Bleeding on probing should be the primary parameter to set thresholds for gingivitis. This emphasizes the need for a more comprehensive maintenance and surveillance of the successfully treated patient with periodontitis. A patient with gingivitis can revert to a state of health, but a patient with periodontitis requires life long supportive care to prevent recurrence of disease.[16]

Improved patient self-care leading to reduction of dental biofilm is one of the main aims for maintaining periodontal health. Although the patient did not attend the scheduled dental visits for one and a half year, the long-term success of the periodontal therapy relied on the patient, who was able to adequately perform oral hygiene. Therefore, it is emphasized that the contribution of the patient to the control of periodontal disease through improved oral self-care on a daily basis, is of paramount importance.[20]

It is worthy to mention that the management of the nephropathic patient requires cooperation amongst the heathcare team. Communication with the nephrologist, as reported, is advisable specially in cases when an invasive oral procedure needs to be performed.

In conclusion, the present case report highlights the importance of individualized oral care for patients with CKD. Health care professionals need to be aware of the oral features related to CKD, and patients should always be referred to dentists for oral evaluation.

ACKNOWLEDGEMENTS

The authors are grateful to all the colleagues of the Odontoclínica Central da Marinha for the collaboration on gathering data, and to Professor Fábio Ramôa Pires, from the Oral Pathology Laboratory of State University of Rio de Janeiro, who contributed with the histopathological diagnoses.

REFERENCES

1. Stevens PE, Levin A. Evaluation and management of chronic kidney disease: synopsis of the kidney disease: improving global outcomes 2012 clinical practice guideline. Ann Intern Med. 2013; 158 (11): 825-830.

2. Martins C, Siqueira WL, Oliveira E, Nicolau J, Primo LG, Dental calculus formation in children and adolescents undergoing hemodialysis. Pediatr Nephrol. 2012; 27 (10): 1961-1966.

3. Marinoski J, Bokor-Bratic M, Mitic I, Cankovic M. Oral mucosa and salivary findings in non-diabetic patients with chronic kidney disease. Arch Oral Biol. 2019; 102: 205-211.

4. Costantinides F, Castronovo G, Vettori E, Frattini C, Artero ML, Bevilacqua L et al. Dental Care for Patients with End-Stage Renal Disease and Undergoing Hemodialysis. Int J Dent. 2018; 2018, 9610892.

5. Deschamps-Lenhardt S, Martin-Cabezas R, Hannedouche T, Huck O. Association between periodontitis and chronic kidney disease: Systematic review and meta-analysis. Oral Dis 2019; *25* (2): 385-402.

6. Zhao D, Khawaja AT, Jin L, Li KY, Tonetti M, Pelekos G. The directional and non-directional associations of periodontitis with chronic kidney disease: A systematic review and meta-analysis of observational studies. J Periodontal Res. 2018; 53 (5): 682-704.

7. Zhao D, Khawaja AT, Jin L, Chan K W, Tonetti M, Tang SCW, Pelekos G. Effect of non-surgical periodontal therapy on renal function in chronic kidney disease patients with periodontitis: a systematic review and meta-analysis of interventional studies. Clin Oral Investig. 2020; 24 (4): 1607-1618.

8. Fang F, Wu B, Qu Q, Gao J, Yan W, Huang X, et al. The clinical response and systemic effects of non-surgical periodontal therapy in end-stage renal disease patients: a 6-month randomized controlled clinical trial. J Clin Periodontol. 2015; 42 (6): 537-46.

9. Chen LP, Hsu SP, Peng YS, Chiang CK, Hung KY. Periodontal disease is associated with etabolic syndrome in hemodialysis patients. Nephrol Dial Transplant 2011; *26* (12): 4068-73.

10. Kapellas K, Singh A, Bertotti M, Nascimento GG, Jamieson LM. Periodontal and chronic kidney disease association: A systematic review and meta-analysis. Nephrology (Carlton). 2019; 24 (2): 202-212.

11. Kendall P, Pugashetti JV, Aronowitz P. Drug-induced gingival overgrowth after renal transplantation. J Gen Intern Med. 2017; 32 (12): 1406.

12. Castro DS, Herculano ABS, Gaetti-Jardim EC, Costa DC. Alterações bucais e o manejo odontológico dos pacientes com doença renal crônica. Arch Health Invest. 2017; 6(7):308-315.

13. Borawski J, Wilczynska-Borawska M, Stokowska W, Mysliwiec M. The periodontal status of pre-dialysis chronic kidney disease and maintenance dialysis patients. Nephrol Dial Transplant. 2007; 22 (2): 457-64.

14. Ellis JS, Seymour RA, Steele JG, Robertson P, Butler TJ, Thomason JM. Prevalence of gingival overgrowth induced by calcium channel blockers: a community-based study. J Periodontol. 1999; 70 (1): 63-67.

15. Tonetti MS, Greenwell H, Kornman KS. Staging and grading of periodontitis: Framework and proposal of a new classification and case definition. J Clin Periodontol. 2018; 45 Suppl 2:, S149-s161.

16. Caton JG, Armitage G, Berglundh T, Chapple ILC, Jepsen S, Komman KS et al. A new classification scheme for periodontal and peri-implant diseases and conditions - Introduction and key changes from the 1999 classification. J Clin Periodontol. 2018; 45 Suppl 20: S1-s8.

17. Macedo PML, Vilela-Martin JF. Is there an association between periodontitis and hypertension? Curr Cardiol Rev 2014; *10* (4): 355-61.

18. Zhou X, Zhang W, Liu X, Li Y. Interrelationship between diabetes and periodontitis: role of hyperlipidemia. Arch Oral Biol 2015; *60* (4): 667-74.

19. Gopal S, Joseph R, Santhosh VC, Kumar VV, Joseph S, Shete AR. Prevalence of gingival overgrowth induced by antihypertensive drugs: A hospital-based study. J Indian Soc Periodontol. 2015; 19 (3): 308-311.

20. Slots J. Low-cost periodontal therapy. Periodontol 2000. 2012; 60 (1): 110-37.