CASE REPORT

Severe tertiary hyperparathyroidism with severe mandibular injury: case report

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Article received on March 11, 2020. Article accepted on December 2, 2020.

DOI: 10.5935/2525-5711.20200024



Abstract:

Objective: The Hyperparathyroidism is a disease characterized by the increased secretion of a Parathyroid hormone (PTH) in the organism, such as generalized osteoporotic processes and systemic calcifications. In addition to the skeleton in general, the jaws are also affected by the effects of Hyperparathyroidism. The aim of this study is to present a case of a patient with hyperparathyroidism and mandible lesion. **Summary Report:** Patient L. F, female gender, 32 years old, asymptomatic, chronic renal disease. Suffering from chronic glomerulonephritis for 4 years, she was referred to a university stomatology ambulatory by her nephrologist, due swelling evaluation on the left side of the face. High level of Parathyroid hormone (PTH) associated to mandibular injury incisional biopsy points at hyperparathyroidism diagnosis. If even after the parathyroidectomy been conducted High level of PTH were still present, it is the case tertiary hyperparathyroidism. **Conclusion:** It is crucial that dental surgeon examine for hyperparathyroidism whenever there are chronic renal patients affected by osteoporotic mandibular changes

Keywords: Hyperparathyroidism, Chronic Renal Insufficiency, Osteitis Fibrosa Cystica, Giant cells.

INTRODUCTION

The parathyroid is usually constituted by four glands located in the cervical region, posterior to the thyroid gland, responsible for the secretion of the parathyroid hormone (PTH), a hormone which function is to regulate levels of calcemic in the blood. The increase in parathyroid hormone secretion represents an endocrine disorder called hyperparathyroidism. The hyperparathyroidism can be divided into three types: primary, secondary and tertiary "^{1,2}.

Primary hyperparathyroidism usually occurs due to a hyperplasia or neoplasia that affects parathyroid gland. Secondary hyperparathyroidism normally represents the disease resulting from a process of chronic renal failure, which determines difficulty in the elimination of phosphorus from the organism generating hyperphosphatemia, decrease in the active form of vitamin D causing lower retention of calcium in the intestine and consequently, hypocalcemia with feed-back increase in the production of the parathyroid hormone by the glands parathyroid. And the called, tertiary hyperparathyroidism, represents severe cases of secondary hyperparathyroidism that are not responsive to any treatment, remaining only the parathyroidectomy^{3,4,5}.

Particularly related to the secondary and tertiary hyperparathyroidism, chronic renal failure is a worldwide public health problem, defined as progressive deterioration of the renal structure. The kidney is an organ that plays an important role in the metabolism of vitamin D, acting in regulating levels of calcemic and phosphorus⁶. without vitamin D, only 10%-15% of the calcium and 60% phosphorus from the diet are absorbed. Low serum levels of calcium and phosphate in high concentration cause a gradual loss of the bone, with calcium been released from the bone, increasing the osteoclastic activity, causing skeletal alterations⁷.

Thus, a series of bone losses become visible throughout the skeleton. This set of modifications osteoporotic of the skeleton is called renal osteodystrophy. Notoriously, the middle phalanges of the fingers, especially index and long fingers, corresponding the first spot of bone loss arising from the disease⁸. In more advanced stages of the secondary hyperparathyroidism, especially related to hemodialysis patients in stage V, the worsening of the renal osteodystrophy may occur, this scenario is called Cystic fibrosis, also known as "Brown Tumor", Denomination that arises from the hemorrhage and large deposition of hemosiderin inside the lesion. Radiographically, we have osteocytes areas which histopathology demonstrates the presence of giant multinucleated cells⁷.

Particularly considering the gnathic bones, several perceptible alterations are noticeable through radiographic examinations, for example, the panoramic radiograph. Among these findings, we must highlight the thinning of the basal cortical of the mandible, the widespread loss of the hard lamina with the dental elements, the alteration of the trabecular pattern of the spongy bone by acquiring the characteristic of ground glass aspect. Researches show that greater the severity of the hyperparathyroidism, higher the bone losses are observed⁹.

The type of hyperparathyroidism must be determined to orient the appropriate method of treatment. In primary hyperparathyroidism, medical therapy is surgical and aims to remove the affected gland, while in secondary, the treatment aims at solving renal failure.⁹ In the tertiary, the possible treatment is often almost solely by removing the parathyroid associated with renal transplant¹¹.

The objective of this present paper is to report the case of a patient affected by severe hyperparathyroidism due to chronic renal failure, which can be currently reclassified as a tertiary variant of the illness. The author expects to contribute to a better knowledge of this relevant illness that affects thousands of people worldwide, as well as their most common jaw manifestations.

CASE REPORT

Patient L. F, female, 32 years old, black, asymptomatic, presenting chronic renal disease arising from glomerulopathy chronic, in hemodialysis treatment, three days a week for 4 years, was referred by her nephrologist to the stomatology ambulatory of a university, due swelling evaluation on the left side of the face. In her medical history, it was noted that she suffered from hypertension, using several daily medications, among them: allopurinol 100mg, renal vit plus, omeprazole 20 mg, amlodipine 5 mg, apresoline 50 mg, atensina 0.2 mg, calcitriol 0.25, potassium chloride 5 ml, losartan 50 mg, selozok 100 mg, enalapril 20 mg, furosemide 40mg, in addition to erythropoietin 3000 ui by subcutaneous injection.

Extraoral physical examination revealed extensive swelling on the left side of the face, of slow growth, hard consistency, and non-identifiable mobility. By intraoral examination, a vestibular growth was perceived in the lower left side of the molars region (Figure 1a, 1b, 1c).



Figure 1. profile view of the volumetric increase, intraoral view of the lesion site, frontal view of the volumetric increase.

The patient already had a panoramic radiograph that showed a predominantly radiolucent lesion, with imprecise delimitation, extending partially from the middle of the ascending ramus to the tooth 35. Radiopaque formations adjacent to the periapical of the tooth 36 and 35 and "ground glass" aspect associated with widespread losses of lamina dura were also observed (Figure 2). A cone beam computed tomography of the jaw was required and revealed the expansive nature of the lesion, with thinning and destruction of the mandibular cortical (Figure 3). Also, upon the hypothesis of the secondary case of hyperparathyroidism and its manifestations of renal osteodystrophy, it was performed radiographs of the middle phalanges of the index and long fingers, with radiographic films periapical number 2, with the objective of analyzing the phalangeal cortical index that classifies bone losses in (P1), moderate (P2) and severe (P3). It was observed evident cortical reabsorption of the analyzed phalanges (classification P3), increasing the hypothesis of correlation with the increase of parathyroid hormonal levels (Figure 4).



Figure 2. Part of the panoramic radiograph showing the expansive radiolucent lesion in the mandible.

With the clinical findings and suggestive imaging, the patient was requested to ask her nephrologist to bring the next appointment some relevant laboratories examinations: Parathyroid plasmatic,



Figure 3. Axial section showing hypodense lesion with extensive lingual vestibular enlargement, discrete internal trabeculae, and rupture of basal cortical.



Figure 4. Carpal and phalanges radiograph showing an extensive osteoporotic picture.

alkaline phosphatase, calcium, and phosphorus. Among these, two examinations were altered, the alkaline phosphatase -1802 U/L (40-150 u/L) and the PTH-2545.0 pg/ml (12-65 pg/ml). At microscopic evaluation of hematoxilin-eosyn stained slides, the lesion was predominantly composed of dense irregular connective tissue. Cellularity was usually inconspicuous, except in some areas permeated by foci of curvilinear osteoid trabeculae. Yellowish-brown pigment suggestive of hemosiderin was evident throughout the sample. No giant multinucleated cells were identified (Figure 5). The microscopic picture was considered compatible with mandibular manifestation of severe hyperparathyroidism, suggesting renal osteodystrophy. Thus, it was concluded the diagnosis of secondary hyperparathyroidism (SHPT) and the mandibular expansion was compatible with a commonly called "Brown Tumor" lesion. The hypothesis for the radiopaque formations in the dental radiography was off Florida's cement-bone dysplasia.

Considering the patient's great biochemical imbalance, especially the HPT levels, the stomatologists requested the patient's hormonal control from the nephrologist's team before surgery to remove the mandibular lesion.

The nephrologist responsible, promptly answered to the request and provided the parathyroidectomy

of 2 of the 4 glands. After 1-month, hormonal levels remained very high (1800 pg/DL) and the patient's facial clinical aspect of was not altered (Figure 6), motivating the planning of removal of more 1.5 parathyroid glands in order to control the reabsorptive action of HPT, allowing the patient to undergo the surgical procedure of the mandible afterward.

Unfortunately, two months after the second intervention to remove the parathyroid glands, the patient had cardiovascular complications associated with chronic renal failure which caused her early death at 32 years old.

DISCUSSION

Progressive renal failure determines a lack of activation of D vitamin in the organism and predisposes a smaller calcemic gastrointestinal retention with consequent hypocalcemia. The biochemical imbalance of this mineral ultimately determines positive feedback



Figure 5. Microscopic image of the lesion - Bone tissue remodeling, hypercellularity foci with fusiform cells, moderately cellularized and vascularized region with hemosiderin deposition



Figure 6. Clinical aspect of the patient after the first parathyroidectomy, showing the persistence of the great left facial swelling.

for the increase of the parathyroid hormone unleashing a series of consequences to the individual, such as the renal osteodystrophy and the metastatic calcification^{3,12}

About 20 years ago, the clear majority of chronic renal patients had secondary hyperparathyroidism, a scenario that has been positively altered according to the improvement in renal therapies in hemodialysis centers. On the other hand, the greatest longevity of these patients determined the onset of many harmful consequences for the health of these patients, for instance, the bone lesions^{13,14}.

Brown tumors, especially, have becoming progressively decreased due to adequate monitoring of patients in nephrological centers. Although the patient was in permanent monitoring in a hemodialysis center and with relatively short hemodialysis time, she presented extensive mandibular brown tumor associated with extremely high level of the parathyroid hormone, which apparently was not being well monitored. In addition, as occurred in the exposed case report, surgical removal of a lesion should not occur until parathyroid hormone levels are minimally controlled. Calcium, phosphorus and alkaline phosphatase are essential laboratory tests to be ordered for patiens with suspected hyperparathyroidism. And is also important to emphasize that any patient with a mandibular swelling should be investigated about eventual hyperparathyroidism.^{14,15?}

Usually, brown tumors have multinucleated giant cells, a fact that did not occur in the present case report. Perhaps, this fact can be explained due to the biopsied site and the small size of the removed fragment. The clinical and imaging findings associated with the systemic disease of the patient made the dentists involved to request the nephrology team to dosage the parathyroid hormone, thereby emphasizing the importance of the dental surgeon in the knowledge of the oral manifestations systemic diseases^{16,17}.

It is important to note the importance of jaws imaging findings in the diagnosis of SHPT since the ground glass appearance and general loss of lamina dura were easily identified in the panoramic radiograph performed. It is also crucial to highlight the radiopaque formations, especially in the periapical regions of mandibular teeth, suggesting association with fibro osseous lesions, probably a florid cemento-osseous dysplasia. The radiographic examinations performed on the medium phalanges of the patient's fingers also showed intense osteoporotic condition, classifying her as phalangeal cortical index level 3 (P3), fact that correlates with high levels of parathyroid hormone, confirming the primary findings of this aggressive disease^{18,19}

Parathyroidectomies that do not effectively reduce satisfactorily the levels of the PTH, allows a reclassification of the secondary HPT as a tertiary variant since the gland would enter into an autonomous functioning cycle not respond anymore to the calcemic variations¹⁸. In the present study, the patient even after been removed 2 glands continued with very high levels of the hormone showing the aggression of the disease and contributing to an unfavorable prognosis of the patient, culminating with her death at 32 years old, before the removal of more parathyroid glands remaining.

Chronic renal disease affects the life quality of thousands of people around the world, since in most of the cases the individuals become dependent of hemodialysis machines or in the waiting list awaiting the compatibility of a kidney transplant. A progressive improvement of technology in nephrology has allowed the greatest longevity of the individuals with such kidney conditions, yet the best action remains the early intervention to avoid severe conditions, sometimes even irreversible, like the presented case report. The dentists have a relevant goal to be attentive to information's in the medical history of patients, correlating the systemic findings with local ones, contributing to the diagnosis and proper treatment the earliest possible in the sense that these individuals have the best quality of life.

CONCLUSION

Given the manifestations of the hyperparathyroidism in the gnathic bones, is crucial that the dentist surgeons know minimally the course of this disease and the probable clinical, imaging and laboratory signals of the disease to contribute to the diagnosis and treatment of this severe illness affecting thousands of people across the world.

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