Periodontal disease in Paget’s disease of bone

Niccolò Nuti
Marco Ferrari

Odontostomathologic Unit, Policlinico “Le Scotte” University of Siena, Siena, Italy

Address for correspondence:
Niccolò Nuti
Odontostomathologic Unit
Policlinico “Le Scotte” University of Siena
Siena, Italy
E-mail: niccolonuti14@gmail.com

Summary

A 59-year-old man suffering from Paget’s disease of bone and periodontal disease was examined in anticipation of bisphosphonate treatment. The previous therapy with clodronate resulted ineffective and markers of bone turnover were markedly elevated. Periodontal disease was correctly approached and treated with an excellent outcome. 5 mg zoledronate iv infusion induced a remarkable reduction of bone markers which persisted on time within the normal range. After zoledronate treatment no signs of osteonecrosis of the jaw (ONJ) were observed. A correct management of periodontal disease is mandatory in pagetic patients on bisphosphonate treatment.

KEY WORDS: periodontal disease; Paget’s disease of bone; ONJ (osteonecrosis of the jaws).

Introduction

Periodontal disease is a chronic infectious disease that affects teeth support tissues, including gum and alveolar bone. Symptoms include red and swollen gums, persistent bad breath, and receding gums and loose teeth. It is generally divided into two groups: gingivitis, which causes inflammatory abnormalities of the gums; and periodontitis, characterized by loss of connective tissue and alveolar bone which damages the bone and connective tissue that support the teeth (1, 2).

People usually don’t show signs of gum disease until they are in their 30s or 40s. Men are more likely to have gum disease than women. Epidemiological data have shown that the most frequent findings among the elderly are the accumulation of bacterial plaque with consequent gingivitis and mild or moderate alveolar bone loss (1.8% had no signs of periodontal disease and 3.3% showed severe periodontal lesions) (3). Risk factors are smoking, diabetes, medications that can reduce the flow of saliva, which has a protective effect on the mouth, genetic susceptibility (4, 5). Chronic periodontitis is the most common type of periodontal disease: it can begin in adolescence but the disease usually does not become clinically significant until people reach their mid-30s. The other forms of the disease are aggressive periodontitis that can occur as early as childhood; disease-related periodontitis that can also be associated with systemic diseases, such as type 1 diabetes, Down syndrome, AIDS; and necrotizing periodontal disease, that is very uncommon acute infection of the gum tissue (6).

Paget’s disease of bone is a metabolic disease characterized by focal abnormalities of bone turnover (7). The normal skeletal architecture and structure are gradually substituted by lytic changes related to increased bone resorption, followed by the so-called mosaic pattern of woven bone. These abnormalities lead to the development of various complications including bone pain, skeletal deformity, pathological fracture, secondary osteoarthritis and in rare occasions osteosarcoma. There are large ethnic and geographical differences in prevalence of the Paget’s disease. Italian data show a reduced clinical severity of the bone abnormalities with respect to other populations, and confirm the familial aggregation of the disease in a consistent number of patients (8, 9). This observation provides further support for the importance of genetic and environmental factors in the pathogenesis of the disorder (10). Common sites of involvement include the pelvis (70% of cases), femur (55%), lumbar spine (53%) and skull (42%) (7).

Aim of pharmacological therapy in Paget’s disease is the decrease of the abnormal bone turnover. Even though different compounds have been used over the years, bisphosphonates are currently considered the treatment of choice. The efficacy of these drugs is demonstrated by a reduction in plasma alkaline phosphatase activity and an improvement in radiological and scintigraphic appearance (7). In a comparative study, a single course of intravenous infusion of zoledronate or neridronate resulted to be safe and effective, with a similar remission rates after 9 months from infusion (11).

Case report

In December 2013, a 59-year-old man was examined at the Odontostomathologic Unit of the University of Siena, Policlinico “Le Scotte” for suspected ONJ. His family history was indicative for cardiovascular risk (mother suffering from hypertension, uncle suffering from CAD). He is smoker until 1999, and suffering from hypertension since 2002. In 2010 he was hospitalized for acute cerebral ischemia. He is on treatment with antihypertensive and antiplatelet agents, and statin. Paget’s disease of bone was firstly identified in 1999 for the appearance of bone pain at dorsal spine, and increase of serum alkaline phosphatase: Paget’s disease involved vertebral bodies T8 and T9. In 1999 he underwent subtotal somatetomy of T8 and arthrodesis between T6 and T10; and a treatment with oral clodronate at the dosage of 400 mg daily.
was started. The clodronate therapy was continued until three months before the examination at the Odontostomatologic Unit. He was afebrile; his blood pressure was 140/85 mmHg. Normal clinical findings were collected at the examination of chest, heart and abdomen. His electrocardiogram showed sinus rhythm, physiological atrio-ventricular conduction velocity, normal phase of ventricular repolarization. The evaluation of metabolic bone markers showed normal calcium and phosphate levels (9.6 mg/dl and 3.0 mg/dl, respectively), serum total alkaline phosphatase and serum bone alkaline phosphatase were increased. 415 IU (30-120 IU normal range) and 216 μg/l (6-30 μg/l normal range). Increased values were observed also for serum cross laps, 0.910 ng/ml (0.142-0.522 normal range). Urinary calcium and phosphate excretion, and serum parathyroid hormone were within the normal range, while a condition of vitamin D insufficiency was detected (25OHD: 21.1 ng/ml). No modifications were observed as regards CBC, CRP and renal function. Orthopantomography (OPG) indicated multiple radicular residuals, deep caries on tooth 1.1, partial edentulism, atrophy of bone crest (Figure 1). Patient was underwent to bone scan using Tc99m that showed a marked increase of the uptake of radiotracer between T5 and T11, without blood flow and uptake of radiotracer modifications as concerns jaw (Figure 2). Oral examination of the gum area showed redness, puffiness, and bleeding on probing indicated inflammation and possible periodontal disease, together partial edentulism and the presence of destructive caries on tooth 1.1. Using a periodontal probe pocket depth were measured. The presence of several pocket depths greater than 6 mm indicated periodontal disease (Figure 3).

A treatment plan was scheduled in following steps. Scaling and root planning was performed; radicular residuals were extracted under antibiotic coverage to prevent the risk of ONJ; deep caries on tooth 1.1 was treated and then reconstructed. A treatment with native vitamin D was started at the oral dosage of 6250 IU per week. In May 2014 the patient was again reassessed at the Odontostomatologic Unit: reduction of inflammation of periodontal tissues was appreciated; furthermore the areas that were underwent to extraction surgery showed an excellent healing, excluding the presence of ONJ. Subsequently treatment for Paget’s disease of bone was carried out: zoledronic acid was i.v. administered at the dosage of 5 mg. No adverse effects and particularly acute phase reaction were reported. A new evaluation of bone remodeling markers performed at July 2014 indicated a dramatic decrease of bone turnover: serum calcium 9.63 mg/dl, serum phosphate 3.8 mg/dl, serum total alkaline phosphatase 92 IU, serum bone alkaline phosphatase were 21 μg/l, serum cross laps 0.450 ng/ml. Values within the normal ranges were appreciated as regards urinary calcium and phosphate excretion, serum parathyroid hormone, 25OHD.

A subsequent evaluation at December 2014 confirmed a good balance between bone reabsorption and bone formation markers (serum cross laps 0.510 ng/ml; serum total alkaline phosphatase 78 IU, serum bone alkaline phosphatase 17 μg/l, respectively).

Discussion

Osteonecrosis of the jaw (ONJ) is considered a side effect of prolonged bisphosphonate treatment (12). ONJ is characterized by exposed necrotic bone that persists for more than eight weeks, which was seen primarily among intravenous bisphosphonate users. Main signs and symptoms are an irregular mucosal ulceration with exposed bone in the mandible or maxilla, pain or swelling in the affected jaw, infection, possibly with purulence, and altered sensation. While rare among people with osteoporosis treated with oral...
Periodontal disease in Paget’s disease of bone

Figure 2 - Clinical shots showing the presence of multiple radicular residuals and deep caries on tooth 1.1 with destruction of distal side, high plaque index, inflammation of periodontal tissues partial edentulism.

Figure 3 - Tc99m whole body bone scan. The image indicates increased radiotracer bone uptake at dorsal spine.

Bisphosphonates, ONJ has captured the public’s attention in patients treated for cancer-related bone metastases (13). The identification of ONJ in pagetic patients treated with bisphosphonates is rare and occasional. For healthcare providers, especially dentists who are responsible for operating in the jaws, often inducing surgical trauma while placing osteointegrated implants or exodontias, the risk-benefit equation becomes important for various reasons: it affects the decision-making process of dental treatment planning, the prognosis of the chosen therapy, the quantification of ONJ risk, and more (14).

As regards the case report of present paper, the long-term treatment with clodronate at the dosage of 400 mg per day per os resulted absolutely ineffective. Laboratory investigations clearly indicated a condition of elevated bone turnover: consequently, an effective treatment was required. Controlled studies with etidronate, tiludronate, alendronate, risedronate, pamidronate and zoledronic acid have all demonstrated the efficacy in suppressing the localized bone turnover abnormality and in improving many symptoms in patients with Paget’s disease (7). As regards clodronate treatment, its efficacy to
reduce fragility fractures was demonstrated in osteoporotic patients (15). No data are published concerning the use of clodronate in Paget’s disease of bone. Inspection of the gum area demonstrated from one hand the presence of periodontal disease and from the other hand the absence of ONJ. The need of an effective bisphosphonate treatment required to minimize the risk of ONJ. Considering this goal, scaling and root planning were firstly carried out to reduce periodontal pockets and infection. The subsequent reevaluation allowed to define the good outcome of the dental procedure and to start the anti-resorptive treatment of Paget’s disease. Together the success of zoledronate therapy in term for normalization of bone turnover markers, we believe that the non appearance of a side effect as ONJ may represent an important result.

In conclusion, in pagetic patients the presence of periodontal disease must be accurately excluded or, if present, specifically treated. This approach allows a better management of Paget’s disease of bone and may prevent the development of ONJ.

References

1. Armitage GC. Periodontal diagnoses and classification of periodontal diseases. Periodontol. 2004;34:9-21.
2. Pihlstrom BL, Michalowicz BS, Johnson NW. Periodontal diseases. Lancet 2005;366:1809-1820.
3. Kaur N, Gajendrareddy PK, Hart T. Periodontal disease for the primary care physician. Dis Mon. 2011;57:174-183.
4. Lamster IB, Lalla E, Borgnakke WS, Taylor GW. The relationship between oral health and diabetes mellitus. J Am Dent Assoc. 2008 Oct;139 Suppl:195-245.
5. Kaur S, White S, Bartold PM. Periodontal disease and rheumatoid arthritis: a systematic review. J Dent Res. 2013;92:399-408.
6. LindenHYPERLINK “http://www.ncbi.nlm.nih.gov/pubmed/?term=Linden%20GJ%5BAuthor%5D&cauthor=true&cauthor_uid=23627336” GJ, LyonsHYPERLINK “http://www.ncbi.nlm.nih.gov/pubmed/?term= Lyons%20A%5BAuthor%5D&cauthor=true&cauthor_uid=23627336” A, ScannapiecoHYPERLINK “http://www.ncbi.nlm.nih.gov/pubmed/?term= Scannapieco%20FA%5BAuthor%5D&cauthor=true&cauthor_uid=23627336” FA. Periodontal systemic associations: review of the evidence. J Clin Periodontol. 2013;40 Suppl 14:S8-19.
7. Siris ES, Roodman GD. Paget’s Disease of Bone. In: Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism Eighth Edition. A John Wiley & Sons, Inc., Publication. 2013:659-668.
8. Gennari L, Merloti D, Martini G, Nuti R. Paget’s disease of bone in Italy. J Bone Miner Res. 2006;21:14-21.
9. Merloti D, Gennari L, Galli B, Martini G, Calabro A, De Paola V, Ceccharelli E, Nardi P, Avanzati A, Nuti R. Characteristics and Familial Aggregation of Paget’s Disease of Bone in Italy. J Bone Miner Res. 2005;20:1356-1364.
10. Kurihara N, Hiruma Y, Yamana K, Michou L, Rousseau C, Morissette J, Galson DL, Teramachi J, Zhou H, Dempster DW, Windle JJ, Brown JP, Roodman GD. Contributions of the measles virus nucleocapsid gene and the SQSTM1/p62(P392L) mutation to Paget’s disease. Cell Metab. 2011;15: 23-34.
11. Merloti D, Gennari L, Martini G, Valleggi F, De Paola V, Avanzati A, Nuti R. Comparison of Different Intravenous Bisphosphonate Regimens for Paget’s Disease of Bone. J Bone Miner Res. 2007;22:1510-1517.
12. Khosla S, Burr D, Cauley J, Dempster DW, Ebeling PR, Felsenberg D, Gagel RF, Gilsanz V, Guise T, Koka S, McCasley LK, McGowan J, McKee MD, Mohla S, Pendrys DG, Raisz LG, Ruggiero SL, Shafter DM, Shum L, Silverman SL, Van Poznak CH, Watts N, Woo SB, Shane E. Bisphosphonate-associated osteonecrosis of the jaw: Report of a task force of the American Society for Bone and Mineral Research. J Bone Miner Res. 2007;22:1479-91.
13. Hansen PJ, Knitschke M, Draenert FG, Irle S, Neff A. Incidence of bisphosphonate-related osteonecrosis of the jaws (BRONJ) in patients taking bisphosphonates for osteoporosis treatment - a grossly underestimated risk? Clin Oral Investig. 2013;17:1829-37.
14. Assael LA. Oral Bisphosphonates as a Cause of Bisphosphonate-Related Osteonecrosis of the Jaws: Clinical Findings, Assessment of Risks, and Preventive Strategies. J Oral Maxillofac Surg. 2009;67:35-43.
15. McCloskey E, Selby P, Davies M, Robinson J, Francis RM, Adams J, Kayan K, Beneton M, Jalava T, Pylkkänen L, Kenvaali J, Aropuu S, Karis JA. Clodronate reduces vertebral fracture risk in women with post-menopausal or secondary osteoporosis: Results of a double-blind, placebo-controlled 3-year study. J Bone Miner Res. 2004;19:728-736.