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Letter to the Editor

CLEIDOCRANIAL DYSPLASIA AND DENTAL IMPLANTS

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INTRODUCTION

Cleidocranial dysplasia (CCD) is a rare genetic disorder that primarily affects the generation of bones and teeth. CCD is caused by mutations in the RUNX2 gene, which is essential for bone and cartilage formation and tooth development (1). The disease can disrupt normal bone remodeling and repair mechanisms. This abnormal biological reaction not only alters bone formation, but also involves an immune reaction with inflammatory responses. CCD affects both skeletal and dental structures, with severe disruption of calcium metabolism. Various dysfunctions may occur such as supernumerary teeth and delayed formation of permanent teeth. In addition, the patient may have an underdeveloped upper jaw and a protruding lower jaw (prognathic). CCD may also present hypoplasia of the jaw bones with an impact on the placement of dental implants and delayed formation of permanent teeth complicates standard orthodontic or prosthetic treatments.

DISCUSSION

Implants require osseointegration, a process which can generate an *in-situ* immune reaction and acute inflammation that can progress to chronic inflammation. CCD is a rare genetic disorder caused by mutations in the RUNX2 gene. This gene is essential for bone and cartilage formation and the development of teeth, and CCD primarily affects the generation of bones and teeth. CCD patients with chronic inflammation or impaired wound healing have limited osseointegration between bone and the titanium surface of implants (2).

The RUNX2 genetic mutation can alter the activity of osteoclasts and osteoblasts, affecting the balance between bone formation and resorption (3). In CCD, the supernumerary teeth can be a vulnerable site for bacterial infections that affect the entire oral cavity; this increases the risk of infections surrounding dental implants (4). Moreover, the lack of bone in this disease can increase the inflammatory effect, with destruction of the tissues around the implant, inducing peri-implantitis.

The increased vulnerability to the inflammatory process that occurs in CCD influences the production of cytokines with alteration of the RANK-ligand (RANK-L)-Osteoprotegerin (OPG) axis. RANK-L is a protein of the tumor necrosis factor (TNF) family that is produced by osteoblasts after various stimuli, which can include that by cytokines, growth factors, and/or hormones. The RANK-L ligand is produced by stimulated osteoblasts and binds to its specific RANK

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receptor expressed on osteoblasts and osteoclasts. This effect is necessary for the maturation and survival of osteoclasts that carry out the activity of bone resorption.

OPG is structurally similar to RANK and acts as a decoy receptor by binding RANK-L and blocking its biological activities. The life and activity of osteoclasts depends on the ratio between RANK-L and OPG. In fact, when there is an excess of RANK-L, bone resorption prevails. However, when OPG levels are higher than those of RANK-L, bone resorption is slowed down. Therefore, bone remodeling is characterized by a balance between resorption and neoformation of the mineralized bone matrix.

In CCD, inflammation and the abnormal immune response can alter the activation of nuclear factor-kappa B (NF-κB), with dysregulated production of cytokines and growth factors. Macrophages and T cells are amongst the immune cells involved in this inflammatory process, and their activity could delay healing after implant surgery and hinder the successful outcome of the implant. CCD requires surgical extraction of supernumerary teeth and orthodontic alignment, with grafts and bone volume augmentation in case of abnormal maxillary bone density. Implants may need customization depending on the bone alteration. The use of modified implants could be useful for improving osseointegration and reducing inflammation. The use of anti-inflammatories or immune response modulators could be useful to prevent implant rejection (5). Additionally, the role that RUNKX2 plays in the immune process needs to be further investigated. Using implants with biological coatings and antibiotic treatments could improve the outcome of implants in patients with CCD. Therapies aimed at RUNX2 dysregulation could give better results both at the inflammatory and immunological level.

CONCLUSIONS

Future studies will help to further elucidate the mechanisms that occur in CCD. These may improve the results that are achieved in dental implantology. A combined study involving orthodontics, surgery, and immune system and inflammatory inhibition may significantly improve the available therapy for patients affected by CCD.

Conflict of interest

The author declares that they have no conflict of interest.

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