Immunopathological response in external dental resorption

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ABSTRACT

The study of root resorption and its immunopathogenesis is extremely important for preserving teeth within the oral cavity. Resorption may be inflammatory or by substitution and it can be triggered by traumatism, induced movement of teeth, periapical disease, periodontal treatment and whitening of non-vital teeth. During odontogenesis, dentin is protected from the immune system and later this protection is provided externally by the cementum, cementoblasts and enamel and internally by the odontoblastic layer. After the process of deciduous root resorption, dentin proteins that have not been yet been presented to the immune system become sequestered antigens that can induce autoimmune responses and play a role in etiopathogenesis of dental resorption. When their protective barriers are missing, hormones and cells that are present during inflammatory processes induce activation of clasts which, when unbalanced, no longer perform physiological bone remodeling and begin to provoke an immunopathological response that causes dental resorption. The main objective of this paper is to present the results of a review of the literature, discussing and elucidating important aspects of external root resorption and conducting an in-depth study of the role of immunopathological response in resorption.

Keywords: Resorption; Osteoclasts; Immunology.

Resposta imunopatológica das reabsorções dentárias externas: revisão da literatura

RESUMO

O estudo das reabsorções radiculares e a sua imunopatogenia são de suma importância para a manutenção dos órgãos dentários na cavidade bucal. As reabsorções são de caráter inflamatório ou por substituição, sua ocorrência pode ser conseqüência de traumatismos, movimentação dentária induzida, periapicopatias, tratamento periodontal e clareamento de dentes sem vitalidade. Na odontogênese, a dentina fica protegida do sistema imunológico, posteriormente, essa proteção é dada, externamente: pelo cemento, cementoblastos e esmalte; internamente pela camada odontoblástica. Após o processo de rizólise, as proteínas da dentina, que não foram apresentadas ao sistema imunológico, tornam-se um antígeno seqüestrado, o qual pode induzir respostas auto-

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imunes e participar da etiopatogenia das reabsorções dentárias. Na ausência de suas barreiras de proteção os hormônios e células presentes no processo inflamatório induzem a ativação dos clastos que, em desequilíbrio, deixam de sofrer a remodelação óssea fisiológica para promover uma resposta imunopatológica produzindo as reabsorções dentárias. Diante isto, o objetivo principal deste trabalho é, por meio de uma revisão na literatura, discutir e esclarecer aspectos importantes acerca das reabsorções radiculares externas, bem como um estudo aprofundado sobre a resposta imunopatológica das reabsorções.
Palavras-chave: Reabsorção; Osteoclastos; Imunologia.

INTRODUCTION

Nowadays the populations of developing countries are maintaining their teeth for longer, as a result of greater concern for oral health and control of dental caries and periodontal disease, and so dental resorptions are now the principal cause of loss of mineralized dental tissues (1).

External dental resorption can be seen as a late posttraumatic reaction, and as a consequence of orthodontic movement, orthognathic surgery, periodontal treatment, or whitening of teeth without vital pulp, among other causes. Its exact pathogenesis is still not fully understood, but it may have systemic origins associated with debilitating infections, endocrine disorders, bone disease (Paget's disease) or radiotherapy, but it can also be idiopathic (2). The immunopathological response may also play a role in the etiopathogenesis of resorption.

One of the reasons that dental resorption is important in dental clinical practice is its high frequency of occurrence. In the West, resorption affects from 5 to 10% of the population, excluding cases linked to orthodontic movements (1).

Both diagnosis and treatment of dental resorption can be problematic, since the causes are very often difficult to identify and determine precisely and with confidence, which has a negative impact on prognosis. It is therefore of fundamental importance to study the immunopathological response in dental resorption, with the objective of improving understanding of resorption so it can be prevented.

LITERATURE REVIEW

General considerations on root resorption

Different forms of external root resorption are classified according to their clinical and histopathological characteristics as superficial external root resorption, inflammatory external root resorption and resorption by substitution. These categories are further subdivided into cervical or apical forms (2). Since resorption does not cause painful symptomology, observation is limited to percussion sensitivity and slight mobility. Radiographically, there will be a radiolucent area with irregular margins at varying positions along the length of the root. Resorption is usually diagnosed on the basis of X-ray findings (3).

Two different types of dental resorption are seen: physiological and pathological. In physiological resorption the dental pulp remains vital, but this is not the case when resorption is pathological. The mechanisms by which root resorption occurs in deciduous and permanent teeth and are similar, although the processes that lead to resorption may be distinct (4).

Root resorption is a non-continuous process that is interrupted by "rest" periods during which it is possible to observe specific gaps, in which multinucleate odontoclasts can be found. During the rest periods there is neoformation, allowing the structures surrounding the root to reorganize (5). Prognosis is poor. However, some authors claim that early detection is linked with better prognosis (6).

Resorption mechanisms

Brezniak & Wasserstein, apud Júnior (7), reported that resorption of mineralized dental tissues occurs when absorptive cells gain access to mineralized tissues, after partial removal of the cementoblast layer and the cementoid tissue.

Root resorption has been linked to damage or partial destruction of the layer covering the precementum. Damage to this layer, by a local physical agent, gives the odontoclasts access to the mineralized tissues of the tooth. This initiates the process of resorption by odontoclasts acting in conjunction with the macrophages, through formation of a bone remodeling unit, which is managed by osteoblasts (an osteoblast-osteocyte syncytium) that have receptors for resorption mediators. The initial attack on the root generally occurs at the closest site to a specific hyalinized area of the periodontal ligament (sterile necrotic zone). This area is believed to be the result of compression of the periodontal ligament and its components, with a consequent reduction of nutritional support and formation of a degenerated and acellular zone (hyalinized area) precedes the process of resorption during orthodontic treatment (7).

According to Rygh, apud Júnior (7), resorption could be associated with the extent and duration of existence of the hyalinized area. Three stages of these areas of hyalinization are described: degeneration, elimination of destroyed tissues and repair (8). The phase during which destroyed tissues are eliminated has a direct relationship with the process of root resorption, since the periodontal membrane is narrowed and there is osteoclast activity that removes bone tissue, with the objective of reducing pressure and allowing vascularization, and there is cellular activity in the area that eliminates the destroyed tissues and enables repair (7).

If the area of hyalinization persists or increases in size over time, odontoclastic activity will be activated with the objective of aiding decompression of the area, the first step in elimination of destroyed tissues from the hyalinization zone. If dentin proteins are exposed to the immunopathologic system, an immunopathological response may be triggered (8).

Kumar et al., apud Júnior (7) claim that the process of resorption of hard tissues is the result of interactions between clast cells with local regulatory factors, the cytokines, generally originating in inflammatory cells, and systemic factors, primarily represented by hormones, of which sexual steroids and parathormone play a fundamental role.

Remodeling of mineralized tissues

Bone remodeling is controlled by parathormone, calcitonin, vitamin D and sexual steroids. Dental tissues are not a source of calcium reserves from which calcium could be removed and physiologically they do not take part in the process of bone remodeling, even under conditions of extreme need, such as malnutrition, pregnancy or hyperparathyroidism (8).

Resorption occurs in response to mechanical or chemical stimulation of cells in the periodontal ligament and is characterized by synthesis of prostaglandin (E-1), together with an increase in cyclic adenosine monophosphate. This process is regulated by the parathyroid hormones and calcitonin, neurotransmitters and cytokines or monokines (interleukin-1 alpha, interleukin-1 beta, interleukin-2, tumor necrosis factor and interferon-gamma) (9).

Local factors synthesized by the cells include the insulin-like growth factors (IGF I and II), transforming growth factor beta (TGF-β), fibroblast growth factors, platelet derived growth factor, (PDGF), bone morphogenetic proteins, cytokines (interleukins IL-1 and IL-6) tumor necrosis factor (TNF), colony stimulating factors (CSF) and products of arachidonic acid such as the prostaglandins (8).

The immunopathological response

From odontogenesis onwards, the dentin proteins are isolated both internally and externally. The external surface of the dentin is protected by newly-formed enamel, external epithelium, stellate reticulum, stratum intermedium, ameloblasts, Hertwig's epithelial root sheath, intermediate cementum (the hyaline layer of Hopewell-Smith), cementum and cementoblasts. The internal surface of the tooth is protected by the odontoblast layer, which is an arrangement of juxtaposed cells (9).

The dentin of the root surface is covered by an epithelial network of cells from Hertwig's sheath and remains protected by these cells during tooth formation. As the root dentin and the hyaline layer are formed, Hertwig's epithelial sheath disintegrates by apoptosis and its fragments form a network that allows follicular cells to pass through it and undergo aposition on the neoformed root surface. Before fragmentation, the cells of Hertwig's epithelial root sheath intensely synthesize an enameloid known as the hyaline layer of Hopewell-Smith or the intermediate cementum (9).

However, our immune system is capable of recognizing the cells of its own body without an immunopathological response. However, an unrecognized cell mutant, originating from the same body, induces a humoral or cellular immunoresponse, reacting with sensitized antibodies or lymphocytes.

The greater the phylogenic distance between antigen and receptor, the greater the immunoresponse. This process occurs constantly in our bodies, eliminating antigens without causing tissue damage. This is an immunoresponse; if the response does damage tissues, it becomes known as an immunopathological response (8).

Dental resorption can be considered immunopathological process, a defense mechanism that is clinically detectable by its harmful effects on tissues and in which there are effects typical of autoimmunity. Another element is a class of antigens described as "sequestered," which, because of their special locations or late formation are not presented to the immune system during construction of immune memory. In external dental resorption, these autoantibodies possibly act as antigens until absorption of the roots of the deciduous teeth, when they would be exposed and sensitized to the immune system. This would then play an active role in the event of renewed exposure (8). Exposure of dentin proteins is not in itself sufficient to sustain the resorption process. It is also necessary that inflammatory mediators are released or cellular stress occurs for the resorption process to be maintained.

A study utilizing an in vivo model assessed antibody titers of dentin proteins and observed a reversible reduction in levels during the active phase of dental resorption, with levels returning to their previous values after removal or loss of the resorbed roots. These results prove the immunopathological character of dental resorption (8).

In another study, in which an unfractionated extract of human dentin was analyzed, serum IgG levels were higher among participants with root resorption (8,10). Specific IgG levels were higher in patients with root resorption by substitution than in patients with inflammatory root resorption. Patients with active apical inflammatory or substitution root resorption exhibited a lower mean lymphocyte proliferation index than healthy people free from resorption (8).

There is no evidence proving a genetic predisposition among people who have dental resorptions. The mediators that are synthesized and released, the cells that perform resorption and the enzymes released are all phenomena determined by genes that control cell functions, but they are not triggered by a specific gene for dental resorptions. There is also no individual or genetic predisposition (11).

CONCLUSIONS

Based on a review of literature on the factors that stimulate, regulate and control the immunopathological response in root resorption, it was observed that dentin has the capacity to provoke an immunopathological response to mechanical or chemical elimination of the cementoblast layer.

No studies have proven a relationship with systemic diseases that rupture the barrier formed by cementoblasts, stimulating an immunopathological response in dentin. There is therefore no evidence that root resorption is linked to systemic factors.

Can we consider external dental resorption to be a reaction of mineralized tissues to epigenetic factors? It is necessary to study resorption in greater depth to be able to state with precision what its etiopathogenesis is. In the future, additional studies will be needed to discover which factors inhibit this immunopathological response, without losses or changes to human oral physiology.

It is important to discover the participation of immunopathological responses in dental resorption, so that prevention, early diagnosis, the ability to control resorption without tooth loss and safe orthodontic movements can all be made possible.

REFERENCES

1. Consolaro A. Reabsorções dentárias nas especialidades clínicas. 3ª ed. São Paulo: Dental Press; 2012. p. 26-34.
2. Dumfahrt H, Moschen I. A new approach in restorative treatment of external root resorption: a case report. J Periodontol. 1998;69:941-7.
3. Neville BW, Damm DD, Allen CM, Bouquot JE, Moleri AB. Patologia oral e maxilofacial. Rio de Janeiro: Guanabara Koogan; 2000.
4. Ottolengui R. The physiological and pathological. Dent Items Interest (Philadelphia). 1914;36:332-62.
5. Kronfeld H. The resorption of the roots. Dent Cosmos. 1932;74:103-20.
6. Camargo SEA, Moraes MEL, Moraes LC, Camargo CHR. Principais características clínicas e radiográficas das reabsorções radiculares internas e externas. Rev Odontol Univ Cid Sao Paulo. 2008;20:195-203.
7. Júnior CP. Fatores etiológicos das reabsorções dentárias em ortodontia e sua conduta de tratamento [dissertação]. Ipatinga: Instituto de Ciências Saúde Funorte/Soebrás; 2009.
8. Hidalgo MM. Estudo sobre potencial imunogênico da dentina: contribuição para a etiopatogenia da reabsorção dentária [thesis]. Bauru: Faculdade de Odontologia de Bauru; 2001.
9. Luan X, Ito Y, Diekwisch, TG. Evolution and development of Hertwig's epithelial root sheath. Dev Dyn. 2006;235:1167-80.
10. Sanchez L. Perfil sérico de IgG e IgM em pacientes submetidos a tratamentos ortodônticos: contribuição para a etiopatogenia da reabsorção dentária. Rev Dent Press Ortodon Ortop Facial. 2003;8:63-71.
11. Consolaro A, Consolaro RB, Martins-Ortiz MF, Freitas PZ. Conceitos de genética e hereditariedade aplicados à compreensão das reabsorções dentárias durante a movimentação ortodôntica. Rev Dent Press Ortodon Ortop Facial. 2004;9:13-23.