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Review Article

Periapical Cysts: Diagnosis and Treatments

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Abstract

Jaw cysts are the most abundant and the most varied in comparison to those affecting any other part of the human body. Periodical cysts are the most common cysts of the jaw . The peak incidence of root cysts is observed in the 4th and 5th decade of life, with a slight predilection for males.

There are several ways to diagnose a periapical cyst: Conventional X-ray, cone beam computed tomography (CBCT), ultrasonography (USG), magnetic resonance imaging (MRI) and magnetic resonance imaging (MRI).

The therapeutic approach can be conservative (Decompression, apexum procedure), or surgical (Enucleation, marsupialization) with or without filling. The pathological examination allows a confrontation with the clinical and radiological data in order to establish a precise and definitive diagnosis.

Keywords: *Periapical Cyst; Jaw Cyst; True Cyst; Pseudocyst*

Abbreviations

PC: Periapical Cysts; CBCT: Cone Beam Computed Tomography; USG: Ultrasonography; MRI: Magnetic Resonance Imaging; PAI: Periapical Index; PRP: Platelet-Rich Plasma; PRF: Platelet-Rich Fibrin; aPDT: Antimicrobial Photodynamic Therapy; $Ca(OH)_2$: Calcium Hydroxide; ROS: Reactive Oxygen Samples; MSCs: Mesenchymal Stem Cells; hPCy-MSCs: Human Periapical Cyst Mesenchymal Stem Cells

Introduction

Jaw cysts are the most abundant and the most varied in comparison to those affecting any other part of the human body. At least 90% of these pathological formations are of odontogenic origin. Jaw cysts arise from the odontogenic apparatus of the epithelial components or its residues trapped in the bone or gingival tissue [1].

Chronic apical periodontitis is characterized by the presence of inflammatory cells responsible for the release of cytokines and growth factors, playing an important role in the formation of periapical cysts (PC) [2].

PCs are the most common cysts of the jaw [3]. The peak incidence of root cysts is observed in the 4th and 5th decade of life, with a slight predilection for males [4].

What is a cyst?

A cyst can be defined as a pathological cavity lined by epithelium with fluid or semi-fluid contents. The term encompasses a collection of benign fluid-filled lesions, with or without an epithelial lining (pseudocyst). Therefore, the definition of choice is: "a pathological cavity whose contents are fluid or semi-fluid and which has not been created by the accumulation of pus" [1,5].

A cyst has three components: a central cavity (lumen), an epithelial lining, and an outer wall (capsule) (Figure 1). The cystic cavity usually contains fluid or semi-solid material such as cellular debris, keratin or mucus. The epithelial lining depends on the cystic nature and may be keratinized or non-keratinized, stratified squamous, pseudostratified, columnar or cuboidal. The cystic wall is composed of connective tissue containing fibroblasts and blood vessels [1].

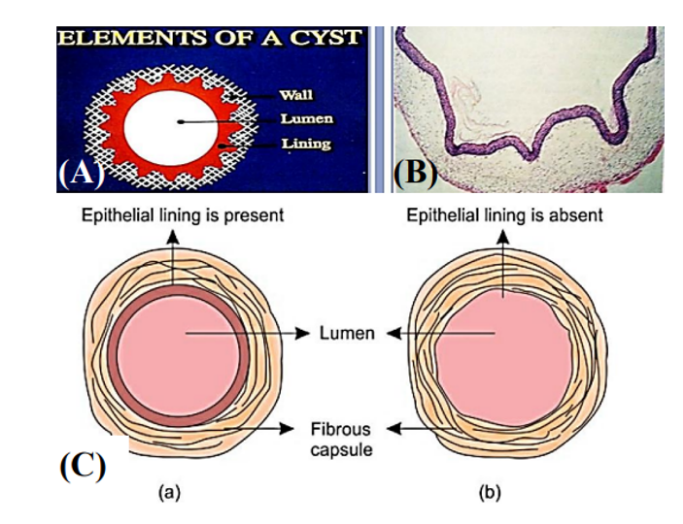

Figure 1: *(A) Cyst (B) Elements of a cyst. (C) True cyst (a) and pseudocyst (b) [1].*

Pathogenesis

Periapical cysts (PC) are the result of the resorption of the alveolar bone adjacent to the apical dental area. The carious or traumatic condition leads to the death of dental pulp tissue. The inflammatory stimulus from a pulpal region reaches a periapical region [3]. An immuno-inflammatory process modelled by the interaction between osteocytes, osteoblasts and osteoclasts as well as the RANK/RANKL/OPG system, the RANKL/RANK/OPG system is known to play a role in osteoclast maturation, bone modelling and remodelling [6].

During the episode of chronic apical periodontitis, several inflammatory cytokines and growth factors are released that can stimulate epithelial cell rests of Malassez, which are the remnants of the disintegrated Hertwig's epithelial sheath in the apical periodontal ligament, to proliferate and form a cyst [7].

The exact mechanism of cyst formation is still unclear [7].

Histopathology

Regardless of how apical cysts are formed, an apical cyst (pocket and true) is a pathologic cavity completely lined by non keratinized stratified squamous epithelium of variable thickness in a 3-dimensional structure [7,8].

In the presence of an active infection, the epithelial lining is thick and irregular, and infiltrated with inflammatory cells [7].

However, in the opposite case, the epithelial lining is thin and regular, and the infiltration of inflammatory cells is minimal, while cholesterol crystals may be contained in the cystic lumen. Histologically, a corresponding classification has been proposed, including pocket cysts (Figure 2) and true cysts (Figure 3). The cystic lumen is in communication with the root canal in the case of a pocket cyst, whereas the cyst cavity is completely closed by the epithelial wall in true cysts [7,8].

Diagnosis

Determination of the origin of the cystic lesion plays a crucial role in the therapeutic approach, since the conservative or surgical therapeutic approach must be adapted to the clinical context [5,9].

Conventional radiography

Panoramic radiography and periapical films are the backbones of diagnostic oral imaging studies [10].

PCs are radiologically characterized by a well-defined, well-circumscribed, unilocular radiolucency associated with the apex of the affected tooth with disappearance of the lamina dura. this radiolucency is surrounded by a radiopaque line (sclerotic border) [3,5].

Cases with large radiolucent areas can be seen when the lesion is aggressive or left untreated for a long time. PCs with high radiolucency often flatten when they reach the adjacent tooth; PCs rarely displace the adjacent tooth [3].

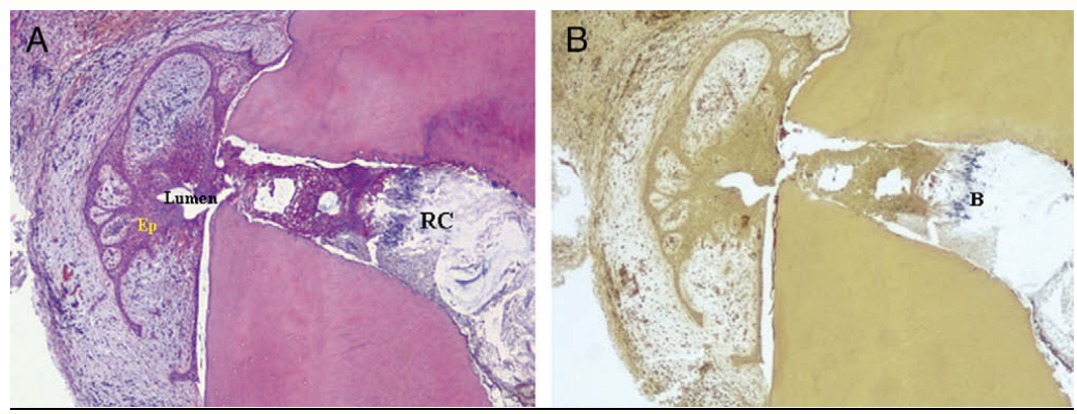

Figure 2: *Pocket cyst. (A) The cyst is attached to the root apex, and its lumen opens into the apical root canal space. Note several microcysts in the lining epithelium. Ep, epithelium; RC, root canal (hematoxylin-eosin; original magnification, (X25). (B) Bacterial colonies and necrotic tissue inside the apical root canal space in the section taken from the same specimen as in (A). B, bacteria (modified Brown and Brenn; original magnification, X25) [8].*

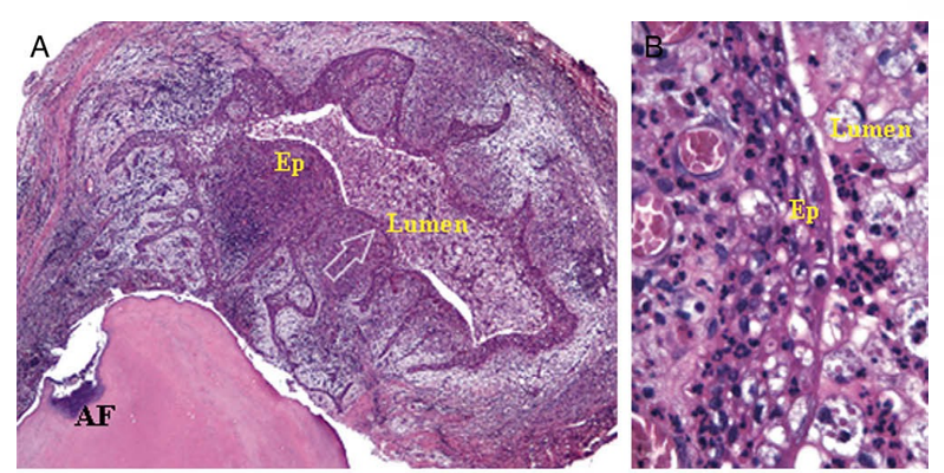

Figure 3: *True cyst. (A) The cyst is separated from the root apex, and its lumen is not continuous with the apical root canal space. Ep: Epithelium; AF: Apical Foramen (Hematoxylin-eosin; original magnification, X25). (B) Lining epithelium and fibrous connective tissue capsule indicated by open arrow in (A) are infiltrated with inflammatory cells, mainly polymorphonuclear leukocytes (hematoxylin-eosin; original magnification, X100) [8]. (AF: Apical Foramen/Ep: Epithelium) (Hematoxylin-eosin stain, original magnification x25) [5].*

When the lesions increase in size, it sometimes becomes difficult to determine the causative tooth, which involves testing the sensitivity of all the teeth in the area [5].

Even if the panoramic X-ray allows a general view of the jaws, it does not give information in the vestibulo-lingual direction [10].

Other limitations of panoramic radiography are: 1. inability to detect osteolytic lesions if bone loss is very low; 2. inability to visualize soft tissue abnormalities related to bone damage; and 3. artifacts especially near the midline [10].

Cone beam computed tomography (CBCT)

CBCT imaging offers a real-size dataset with multiplanar cross-sectional and 3D reconstructions which are based on a single scan, on using a low radiation dose [11].

The CBCT allows assessment of the size and proximity of the lesion to surrounding structures [12].

Sukegawa., *et al*. evaluated the morphologic characteristics of root cysts using computed tomography focusing on the location, size and condition of the surrounding bone in 60 men and 86 women. The results are as follows: the root cysts that occur in the maxilla are characterized by bone expansion, enlarging in the mesiodistal and buccolingual direction, while those that occur in the mandible progress in the mesiodistal direction without bone expansion. The clinical symptomatology correlates with the size of the lesion in the maxilla, however, it is noted that this correlation is not clear in the mandible, therefore the discovery of the mandibular lesion may be delayed [13].

Conventional radiography and cone-beam tomography have demonstrated a high ability to detect changes at the tissue level, but not at the cellular level. In this same context, neither of these techniques can reliably diagnose a root cyst from a granuloma clinically without histologic evidence [5,7,12].

Ultrasonography (USG)

Ultrasonography (USG) is a radiation-free, non-invasive and safe imaging method with many years of clinical experience [10,14].

Ultrasonography with color/power Doppler imaging of periapical lesions can provide specific information on the size of the lesion, its vascular supply, and internal content, with the ability to distinguish clear from mixed fluid, mucus, or purulent content [10].

Numerous studies have suggested that USG can be used for the differential diagnosis of periapical granulomas and cysts based on the characteristic differences of each lesion. The periapical cyst is a hypoechoic cavity surrounded by reinforced bone walls, filled with fluid and without evidence of internal vascularization on color and power Doppler examinations, however the granuloma is defined as a well circumscribed, hyperechoic/echogenic lesion with a rich vascular source [10,14].

Magnetic resonance imaging (MRI)

Magnetic resonance imaging (MRI) is a safe technique that provides important structural information about soft tissue due to the superior contrast and the high resolution provided by this technique, as well as its multiplanar capabilities. This technique has a range of clinical advantages in the diagnosis of cystic lesions, such as accuracy of lesion content whether solid or liquid and determination of the presence of an epithelial lining; in addition, vascular density can be detected on contrast-enhanced examinations [15-17].

MRI is superior to CBCT in the identification of fluid and fibrous tissue. Consequently, MRI has a greater sensitivity in the diagnosis of a periapical lesion than CBCT and has a greater precision in the evaluation of the real dimensions of a lesion. This examination makes it possible to estimate the proximity of the lesion to the noble anatomical structures [15,16].

MRI is a high-cost examination with long acquisition time which limits its applications in dentistry [15].

Therapeutic management

Decision-making management of periapical cysts

Since cystic lesions of the jaws are asymptomatic, diagnosis is incidental and often occurs on routine radiographic examination [5]. The evolution over time of these lesions is variable, with possible regression, static state or increase in size. For these reasons, cysts can be treated surgically (enucleation or marsupialization) or non-surgically. Nevertheless, whatever the choice, the principles of tissue economy must be scrupulously respected (Figure 4 and 5) [18].

The management of periapical cysts can be conducted according to the size of the lesion and the CBCT periapical index (PAI) [18].

Non-surgical management

Suction and irrigation technique

This technique is based on the use of two syringes, the first is an 18 gauge syringe attached to a 20 ml syringe that penetrates the oral mucosa and aspirates the cystic fluid. Another syringe cleans the lesion with its saline content. The next step is the creation of an evacuation path for the irrigant by inserting the new needle, which is brought out through the palatal tissue [18,19]. Aspiration of the cavity contents causes a decrease in internal pressure, thus slowing down osteoclastic activity and enlargement of the defect [18].

Clearing the cavity causes bleeding and subsequent clot formation, which plays a role in the healing mechanism. The disadvantage of this technique is the creation of buccal and palatal wounds that may cause discomfort to the patient [18].

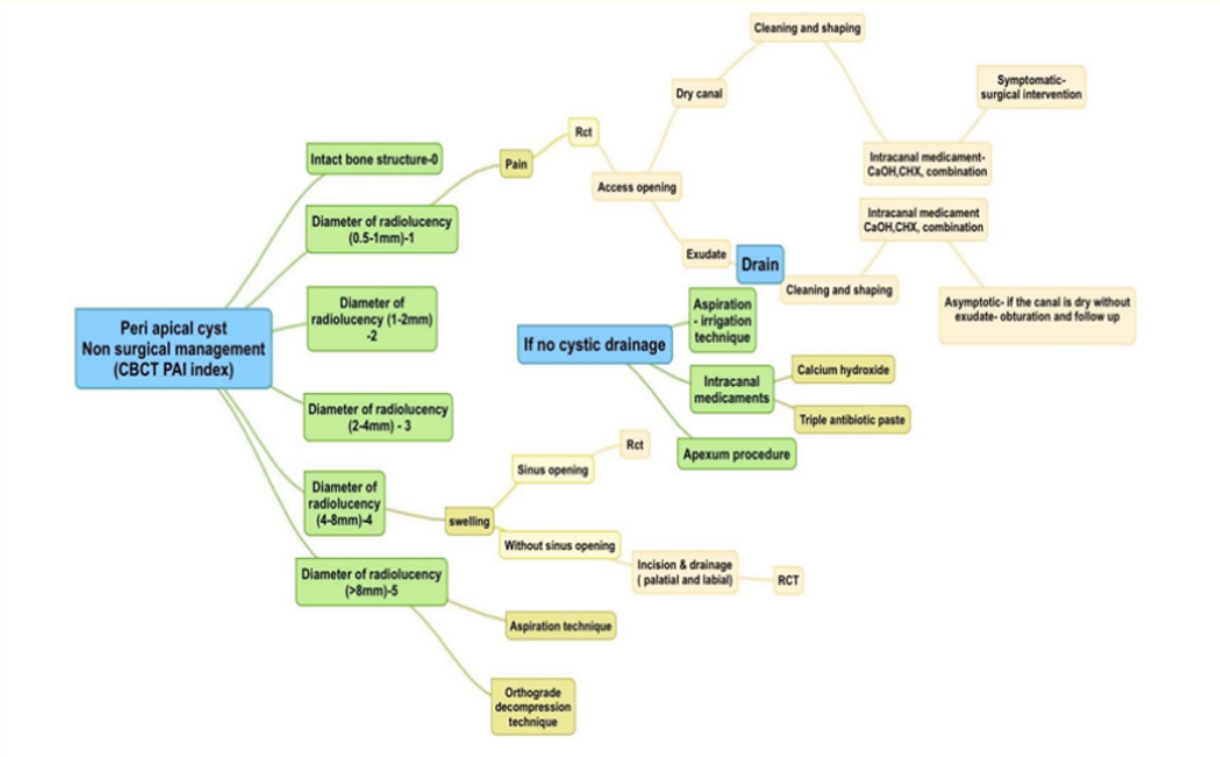

Figure 4: *Decision tree for periapical cyst - non surgical management. RCT: Root Canal Treatment [18].*

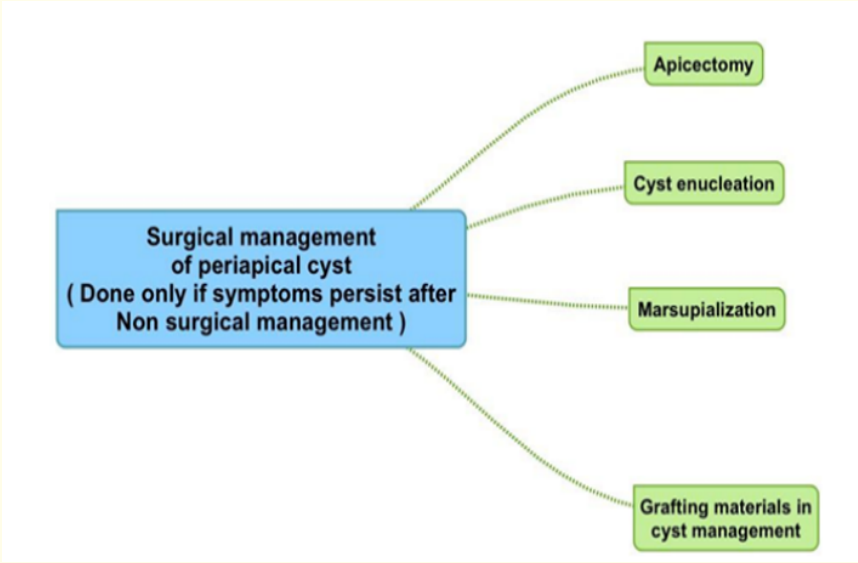

Figure 5: *Decision tree for periapical cyst - surgical management [18].*

Intracanal medication

The prevalence of true cysts remains below 10%. Thus 90% of chronic periapical lesions are likely to be healed by conventional root canal therapy, correct endodontic treatment should be carried out, followed by a temporization period (6, 9, 12 months, etc.), during which clinical and radiological monitoring of the case concerned in order to judge whether or not the periapical lesion has regressed [5].

Currently, the most used products are calcium hydroxide. Calcium hydroxide is an antibacterial agent that should not be used for more than 15 days, after which it is removed from the canal by means of sodium hypochlorite, followed by permanent root canal filling [18].

After one year, 89% of lesions likely to heal already show signs of repair (reduction in the size of the lesion) [5].

Apexum procedure

The apexum method is a minimally invasive technique compared to the open flap endodontic surgery. This technique is based on a device that directly accesses the lesion via the root canal (Figure 6 and 7) [20]. This procedure uses two sequential rotating devices, the Apexum NiTi Ablator and the Apexum PGA Ablator, designed to extend beyond the apex and fragment the periapical tissues by rotation in a low-speed handpiece, followed by washout of the fragmented tissue [18,20].

This technique results in significant less postoperative discomfort or pain than conventional root canal treatment or than reported for conventional apical surgery [20].

Decompression technique

The decompression technique is a simple technique and easily tolerated by the patient, since it relies on the placement of a drain in the lesion of different natures, including: the rubber dam in the shape of an "I", a polyethylene tube with a stent, hollow tubes, a polyvinyl tube, a suction catheter or a radiopaque latex tube. This method requires regular monitoring and periodic irrigation, as well as proper adjustment of the drain length [18,21].

Figure 6: *The Apexum procedure [20].*

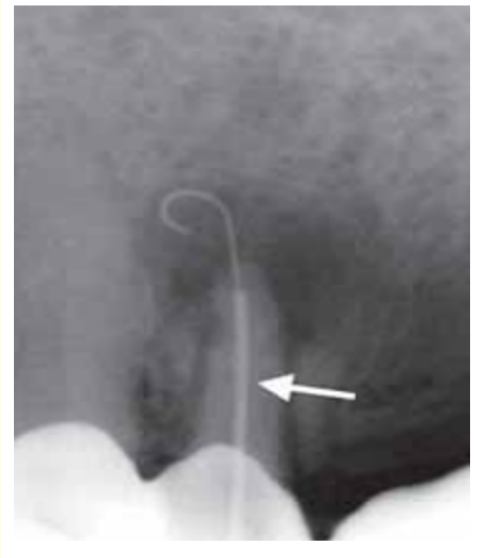

Figure 7: *The NiTi Apexum ablator in a periapical lesion. The NiTi Apexum ablator has been completely extruded from its sheath (arrow) and has penetrated the periapical lesion [20].*

This technique is a non-invasive means, minimizing the risk of damage to adjacent structures [18].

Surgical management

Enucleation and marsupialization of cysts

Marsupialization is a minimal surgical intervention of the odontogenic cysts with the objective of reducing the intracystic pressure by creating a window in the cystic wall in order to expose the internal surface of the lesion in the oral cavity, while preserving the cystic membrane and stitching around this opening resulting in a slow reduction of the cavity size [18,22]. The next step is the use of paraffin gauze to gently pack the cystic lesion until the line of junction between the cystic wall and the oral mucosa has healed, after a period of 3 to 6 months enucleation takes place [18].

Cystic enucleation and closure of the surgical site in one step is considered to be the gold-standard. This technique is recommended in the lesions of small size, or potentially aggressive lesions [18,22].

Enucleation is a technique of extirpation of an entire encapsulated lesion, allowing anatomo-pathological analysis of the totality of the lesion [22,23].

These techniques require a regular monitoring of the progression and the state of the defect. When faced with a cystic lesion, the practitioner must decide on the therapeutic approach, including: enucleation, marsupialization and decompression or a combination of these techniques [18,22,23].

Apicectomy

In the majority of large cystic lesions, marsupialization and enucleation are sufficient after endodontic treatment. However, apicectomy is only required if there is swelling. After cystic enucleation, a length of 2 - 3 mm of the apical root is resected and a retrograde obturation is performed with biocompatible materials such as glass ionomer, biodentine, MTA, etc. After apicectomy and retrograde obturation, graft placement can be recommended in function of the defect [18,23].

Grafting materials in cyst management

The placement of a bone substitute after periapical surgery is a means to achieve higher bone regeneration [24]. It must serve as a scaffold for bone formation and slowly resorb to allow replacement with new bone. For this purpose different types of bone grafts are available, namely autografts, allografts, xenografts and alloplasts [18,24].

To stimulate bone regeneration, the first-generation platelet-rich plasma (PRP) has been proposed as a method of introducing concentrated growth factors PDGF, TGF ß and IGF 1 into the surgical site, enriching the natural blood clot. PRP is a volume of autologous plasma with a 4- to 5-fold increase in platelet concentration [18]. The literature reports encouraging results with the use of platelet rich plasma (PRP) in conjunction with autologous bone grafts in bone defects [24].

Platelet-rich fibrin (PRF) is a rich concentrate of various growth factors that exhibit properties such as cell migration, attachment, proliferation, and differentiation [25].

However, studies have shown through two-dimensional (2-D) radiographic follow-up measurements (densitometry) after enucleation of an odontogenic cyst, an increase in bone density and comparable bone regeneration with and without filling with synthetic bone substitutes or autologous bone [26].

Bone regeneration was analyzed using 3D imaging software in a study of 26 patients who underwent cystectomy. The study showed no significant difference between healing with filling with autologous iliac crest and without filling material [27].

Enucleation of jaw cysts and primary closure without bone substitutes remains “state of the art” in most cases, even in large defects [28].

Antimicrobial photodynamic therapy (aPDT)

Given the inability to completely disinfect the entire root canal system and the many microorganisms that are known to be resistant to calcium hydroxide “$Ca(OH)_2$”, such as *F. nucleatum* ssp. *Vincentii, Enterococcus faecium* and *Enterococcus faecalis*, leading to possible failure of root canal treatment; aPDT as a complementary techniques is very effective [29].

The aPDT has demonstrated antimicrobial effects in various studies at different wavelengths with low-power laser or LED. In the presence of oxygen, the photochemical reaction and the production of reactive oxygen samples (ROS) occur, contributing to the disinfection of microorganisms. This procedure is a complementary technique to intracanal irrigation and medication, while being compatible and without thermal side effects on surrounding tissues [29,30].

However, in the case of a lesion related to a non-restorable or very mobile tooth, the treatment consists of the extraction of the causal tooth and the enucleation of the lesion [5,23].

Therapeutic innovations and scientific advances

Mesenchymal stem cells (MSCs) have a very significant regenerative potential. The main barrier to their clinical application is the complex way of obtaining them from healthy tissue [31,32].

In 2013, Marrelli., *et al*. demonstrated for the first time the presence of MSCs in human periapical cysts, called human periapical cyst mesenchymal stem cells (hPCy-MSCs) [31].

hPCy-MSCs could be considered an optimal cell source for tissue engineering applications. However, most of the studies conducted on the immunomodulatory properties of MSCs are *in vitro* studies, so additional research is needed to benefit from their regenerative potential in daily clinical practice [31].

Conclusion

Clinical examination is insufficient, various complementary examinations make it possible to diagnose a periapical cyst and to determine the type of intervention.

Periapical cysts are mostly tried to manage in conservative method, only in large infected cystic lesion cases the surgical management is to be considered.

The pathological examination allows a confrontation with the clinical and radiological data in order to establish a precise and definitive diagnosis.

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