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Treatment of large Periapical lesion with Platelet Rich Fibrin and Guided Tissue Regeneration with two year follow up- A Case Report.

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Abstract:
The endodontic system and the periodontium are closely interrelated and the infection of both leads to the appearance of endodontic-periodontal lesions. Along with the endodontic and periodontal classic treatment, in most cases, there is a need for regenerative periodontal therapy for the repair of the damaged tissue[1]. One material that stimulates bone healing is represented by platelet-rich fibrin (PRF)[1]. Platelet rich fibrin is widely used in stimulation and acceleration of soft tissue and bone healing because of local and continuous delivery of growth factors and proteins, mimicking the needs of the physiological wound healing and reparative tissue processes[2]. In this case report one case is presented in which large periapical cyst with respect to 21 22 was present. After through evaluation it was finalized that only conventional endodontic therapy was not enough to resolve the problem. So the treatment of choice was root canal treatment followed by periapical root‐end surgery and placement of PRF and GTR membrane. Results: At the end of six months, the defects showed complete bone regeneration. Conclusion: Production of a dense, cross‐linked, physically robust PRF made of intact platelets and fibrin by high‐speed centrifugation in the absence of exogenous thrombin,yields an ideal scaffold for use in tissue repair.

Key words: *Periapical surgery, platelet growth factor, platelet rich fibrin, GTR*

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I. Introduction

Periapical lesions can be either granulomas, abscesses or cysts and are primarily caused by root canal infection.The success of endodontic therapy depends on complete periapical repair and regeneration of soft tissue& bone. Most of the time teeth with periapical lesions heal satisfactorily after non‐ surgical endodontic intervention. Abramovitz et. al. had stated that not all large periapical lesions will heal with non-surgical treatment. He reported that about 24.5% of the cases required surgery to heal[3]. So apical surgery is the surgical management that is required for a tooth with periapical or periradicular lesions that can't heal with traditional endodontic approach.

Periapical surgery is aimed to remove periapical pathology followed by complete soft tissue & radiographic bone healing. This is evaluated clinically and radiographically. Since periapical surgery is the last resort of treatment before the tooth goes for extraction ,there is no room for failure. Careful evaluation of the case is a must before one proceeds with it[4]. Surgery is seen to provide better access to clean the root surfaces and apical lesions and to reshape the surrounding bone/root apex.

Therefore in surgical cases, success is achieved by proper root-end resection, root-end cavity preparation, and an adequate and tight root end retrograde filling. Bone & soft tissue regenerationcan be achieved by local application of hormones, growthfactors & plasma derivatives as advocated by studies[5].Bone morphogenic proteins, parathyroid hormone, platelet derived growth factor, platelet rich plasma, & enamel matrixproteins have been applied to promote healing of surgical wounds /defects. Platelet rich fibrin a biologic revolution constituted byfibrin network of platelets, leukocytes, cytokines, stemcells, & three dimensional

architectures, which favours wound healing & immunity. Platelets in PRF are capable of releasing platelet derived growth factor (PDGF)transforming growth factor1 (TGF1), insulin like growthfactor (IGF) & exhibit varied potent local properties likecell migration, cell attachment, cell proliferation & celldifferentiation even up to one week.

Armamentarium and technique

PRF preparation requires an adequate table centrifuge and collection kit including: A 18 gauge needle and 10 ml blood collection tubes.

Protocol for PRF preparation

10 ml of venous blood was drawn from the patient (fig-1). Whole blood was drawn into the tubes without anticoagulant and immediately centrifuged at 3,000 rpm for 10 minutes (fig-2).Within a few minutes, the absence of anticoagulant allows activation of the majority of platelets contained in the sample to trigger a coagulation cascade. The result is a fibrin clot containing the platelets located in the middle of the tube, just between the red blood cell layer at the bottom and acellular plasma at the top (fig-3).This clot was removed from the tube and the attached red blood cells scraped off and discarded.

II. Case Report

A 32 year old female patient came to the Department of Conservative Dentistry and Endodontics in North Bengal Dental College & Hospital with the discoloured teeth (#21,#22) since five years with attempted incomplete endodontic treatment from outside. She had pus discharging sinus since 6 months. On investigation periapical radiolucency involving 21, 22 and 23 was seen on IOPA (fig-4) and CBCT (fig-5) imaging revealed a radiolucency area measuring approximately 8.35 mm X 14.31mm in labiopalatal and mesiodistal diameter. Superior-inferiorly the radiolucent lesion extends from the crest of the alveolar bone wrt 22, 23 to approximately 5.75 mm below the nasal floor measuring approximately 16.01 mm. Discontinuity of the labial and palatal cortex can be appreciated wrt 22, 23 region. Partial radioopacity can be seen in the crown and root canals wrt 21, 22 region which can be suggestive of previous endodontic intervention. 21, 22 were found to be mobile beyond physiologic limits. Vitality of 23 was checked by electronic pulp tester (Parkell Pulp tester) and found to be non-vital. Non-surgical endodontic therapy (fig-6) was instituted in 21, 22 and 23and intracanal calcium hydroxide (ApexCal) was placed for 2 weeks. 23 was obturated as canal was dry, however 21, 22 showed frank exudation. 21, 22 were now given calcium hydroxide with iodoform (Metapex) for 4-6 weeks as intracanal medicament. This too proved ineffective with persistence of exudation as well as pus discharge from sinus. Hence surgery was planned in this case where apicoectomy of 21, 22 along with root end filling, curettage of periapical lesion and placement of PRF into the cavity that was decided to cover it by GTR membrane (HealiGuide).

Rectangular flap under LA was retracted and there was found bony perforation releasing cystic fluid (fig-7). The bony perforation was enlarged enough to see the root end of 21 & 22 with the help of surgical straight round carbide bur. Cystic lining was removed. The length of 3 mm of root end of 21, 22 was removed and root end cavity was prepared by ultrasonics retro tip (fig-8). The prepared cavity and bony defect was rinsed with normal saline. The root end seal was done by MTA (fig-8). The bony defect was filled up by freshly prepared PRF (fig-9) and the GTR membrane was placed over it (fig-10). Suturing was done by 3-0 black silk (fig-11). Post operative analgesics, antibiotics and instructions were given to patient. Sutures were removed on seventh post-operative day.

III. Results

The patient did not complain of any unusual or severe pain. There were no signs of infection, untoward reaction,wound dehiscence or extrusion of material (fig-12). Radiographically patient showed complete bone regeneration at the end of 24 months (fig-13,14,15).

IV. Discussion

Wound healing after periapical surgery includes osseous and dentoalveolar healing[6]. Under ideal circumstances, dento-alveolar healing will be presented with complete regeneration of periradicular tissues surrounding the previously affected roots[6].

Mineral trioxide aggregate (MTA) is found to have ideal properties as a root end filling material during apical surgery. Various authors have reported in their studies that MTA prevented leakage of dye, bacteria and endotoxins . Along with this MTA was also found to be a biocompatible material[7]. A complete apical cementogenesis over MTA was noted histologically along with complete regeneration of periradicular tissues[8].

The tissue regeneration techniques include cell differentiation, cell proliferation, and induction and/or conduction of tissue formation. These effects are obtained with various protocols: the use of bone substitutes, barrier membranes, growth factors, or a combination of such agents and materials.

Regenerative procedures frequently include the use of barrier membranes to encourage the growth of key surrounding tissues, while excluding unwanted cell types such as epithelial cells[9].

To help promote bone regeneration, local application of growth factors/cytokines and host modulating agents have been used to maximize the body's healing potential. Growth factors like platelet-rich plasma (PRP), bone morphogenic proteins (BMPs), platelet-derived growth factor (PDGF), parathyroid hormone (PTH), and enamel matrix proteins (EMD) have shown promising results in enhancing tissue regeneration[9].

Platelet rich fibrin(PRF) is used in the stimulation and acceleration of soft tissue and bony healing in peri-apical surgery because of the local and continuous delivery of growth factors and proteins, mimicking the needs of the physiological wound healing and reparative tissue processes. PRF is easy to obtain and inexpensive which makes it an ideal scaffold for use in tissue repair[2].

PRF is a biological revolution that consists of a fibrin network containing platelets, leukocytes, cytokines, stem cells. This architectural framework enhances tissue repair, wound healing and immunity.

PRF represents a new level in the platelet gel therapeutic concept which has a simplified processing without the artificial biochemical modification. Unlike other platelet concentrates, manufacturing of PRF does not need anticoagulants or bovine thrombin or any other gelling agents. Thus PRF is simply just centrifuged natural blood without any additional additives. Developed in France by Choukroun *et al*. in 2001 ; PRF is generated from a natural and progressive polymerization occurring during centrifugation. The fibrin network hence formed thus shows a homogeneous 3-dimensional organization which is much more coherent than natural fibrin clots[2].

PRF contains nearly 97% of platelets and more than 50% of leukocytes in the blood. Therefore PRF is a fibrin matrix polymerized in a tetra molecular structure, with additions of cytokines, platelet, leucocytes and circulating stem cells[10]. PRF is capable of releasing platelet derived growth factor (PDGF) , Transforming growth Factor 1(TGF 1) , Insulin like growth factor (IGF) and exhibit different potential properties like cell migration, cell attachment , cell proliferation and cell differentiation .Studies have confirmed that there is the gradual release of PDGF and TGF for 28 days from PRF .The platelets that are activated along with the released growth factors are trapped in the fibrin polymer[11].

There is presence of abundant fibronectin in PRF which enhances cell adhesion. Studies have shown that human osteoblasts have a higher degree of adhesion to fibronectin than to other extracellular matrix proteins. When the fibrin matrix of PRF undergoes remodeling, there is gradual release of cytokines. This ensured continuous release of growth factors that might, enhance cell proliferation during bone formation[12].

In PRF ; platelets and cytokines play an important part in the biology of this biomaterial; but the fibrin matrix supporting them certainly constitutes the determining element responsible for the real therapeutic potential of PRF.Choukroun et al (2006) had postulated in their study that fibrin matrix guides the healing processes. PRF contains platelet and growth factors , but they have a secondary role in the bioactivity of PRF. Therefore, PRF was stated not to enhance long term cellular proliferation, but it might play an important role in the revascularization of the graft by supporting angiogenesis[13].

Since every case is different, treatment modality also changes as per the situation. It has been noticed that an endodontic infection influences the progression of marginal bone loss in periodontitis[14]. Clinical studies showed that a persisting endodontic infection may be regarded as a contributing risk factor for aggravating marginal attachment loss[15].

An endodontic infection has been reported to stimulate the epithelial down growth along denuded dentin surfaces with marginal communication[16]. Exposed dentin surfaces are also seen to have significantly larger areas of resorption in infected roots compared to noninfected roots.

Nyman et al first reported the use of a membrane for regeneration of tooth-supporting structure in 1982[14]. A membrane will ensure a predictable new attachment formation by preventing gingival epithelium and connective tissue from contacting the root surface. The same principle works for endodontic surgery, where the ultimate objective is also regeneration of periradicular tissues including cementum, periodontal ligament, and alveolar bone.Therefore , the use of a membrane technique in guided tissue regeneration (GTR) has been seen to be successfully used in endodontic surgery which has already become a standard in periodontology .

As stated in studies the objectives of membrane application in endodontic surgery are similar to periodontics. It is to facilitate tissue regeneration by creating an optimum environment and *to* exclude nondesired fast-proliferating cells that interfere with desired tissue regeneration. Clinically we can classify peri-radicular lesions into 1) Ones limited to the periapical area , 2) Lesions that has eroded the lingual and buccal cortex, resulting in a through-and-through (tunnel) defect & 3) An apico-marginal with complete denudation of the buccal root surface[17].

Therefore we must categorize the type of lesion, to select the appropriate treatment.

For lesions that are limited to a periapical bone defect without marginal lesion; GTR membrane is the regeneration of periapical tissues, including the reestablishment of an apical attachment apparatus[14]. But in peri-apical lesions with concomitant marginal lesions ; also known as combined endodontic-periodontal lesions the membrane is employed to regenerate periapical and marginal tissues at the same time[18].

Only a few clinical studies have recommended the use of GTR in surgery where only periapical bone defect is present without marginal lesion. But GTR principle is found to contribute more favorably in the treatment of transosseous (through-and-through) lesions, even when marginal lesion is absent[14].

Whereas numerous studies have demonstrated good to excellent tissue regeneration following membrane application for treatment of combined endodontic-periodontal defects[19]. So-called hopeless teeth were saved by employing the GTR membrane following degranulation and endodontic surgery. Radiographically most of the cases demonstrated healing with dense and hard tissue[20].

Although challenging ; saving hopeless teeth with large peri apical lesions with or without communicating apico-marginal defects, or with cortical bone perforations ; a GTR technique with PRF as the graft material might prove to be clinically successful and so is presented in this case report.

Conflict of interest –There is no conflict of interest.

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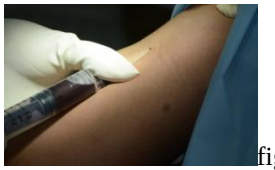
Figures- (fig-1 to 15)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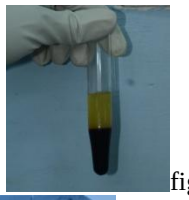
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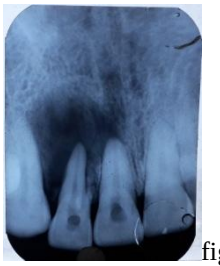
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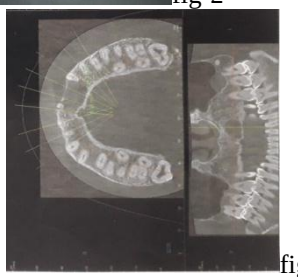
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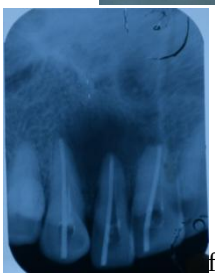
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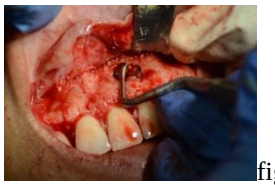
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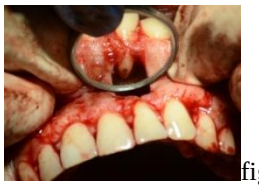
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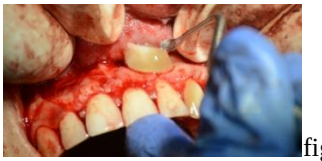
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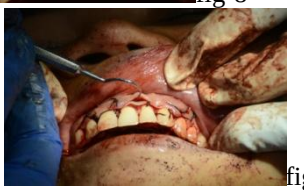
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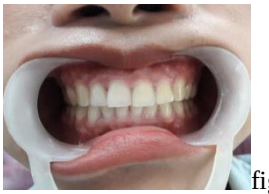
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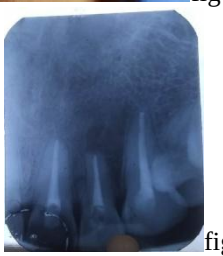
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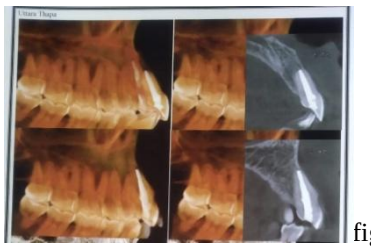
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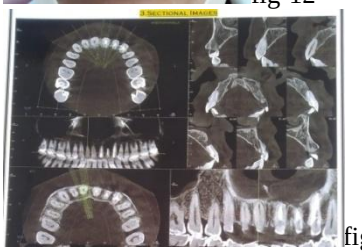
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