

Editorial

LIVE THE LIFE OF YOUR DREAMS:

Setting goals allows you to paint a vision of what you wish your future to be, make your vision so clear that all your fears become irrelevant. Vision without action is merely a dream, action without vision just passes the time, vision with action can change the world. It's not what you look at that matters, it's what you see that really matters. Your life's vision defines who you want to be, what you want to be known for and the set of experiences and accomplishments you aim for. Your vision helps define the goals by giving you a framework to evaluate those goals. Be brave enough to live the life of your dreams according to your vision and purpose instead of the expectations and opinion of others.

"When I dare to be powerful, to use my strength in the service of my vision, then it becomes less and less important whether I am afraid". Dream high up to the sky, so that you can atleast reach the tree top. Change the way you look at things and the things you look at will change. Change is painful, but nothing is as painful as staying stuck where you don't belong. Those who cannot change their minds

cannot change anything. All things are difficult before they are easy, make up your minds to set your goals right, work towards them and conquer your dreams.

Changes, no matter whether they seem good or bad at the time, will teach you something new. External change makes you more flexible, more understanding and prepares you for the future, internal change will encourage you to progress, external change will give you the experience and drive to push forward. So my dear students, the only thing worse than being blind is having sight but no vision. Vision is the art of seeing what is invisible to others. Do your best, your level best & do it with a will.

Best wishes

Dr Manoj Kumar KP

Editor

TABLE OF CONTENTS

1. Bone substitutes in Implant Dentistry – A Review pg 6
Dr.Swapna C, Dr.Priyanka K, Dr.Sheejith.M, Dr.Niveditha Prasad
2. Virtual treatment planning in bimaxillary orthognathic surgery - A Case Report pg 18
Dr Manoj Kumar K P, Dr Aparna S Nair, Dr Parvathy R, Dr Deepti Krishnankutty, Dr Sunu V S
3. Recent advances in ceramics -Literature Review pg 24
Dr.Noopura S, Dr.Ramesh Kumar, Dr.Elsy P Simon, Dr Ravi SV
4. Desmoplastic ameloblastoma -Literature review pg 33
Dr. Ahna Ali Akbar, Dr. Anu, Dr. Rajeesh Muhammed, Dr. Mayeesh Radhakrishna
5. Calcifying odontogenic cyst (COC) - Literature review pg 42
Dr.Anu.PV, Dr.Ahna Ali Akbar, Dr.Rajeesh Mohammed, Dr.Usha Balan

Literature Review

BONE SUBSTITUTES IN IMPLANT DENTISTRY – A REVIEW

* Dr.Swapna C, ** Dr.Priyanka K, * Dr.Sheejith M, *** Dr.Niveditha Prasad

Abstract

Bone substitute are often defined as “an inorganic, synthetic or biologically organic combination that can be inserted for the treatment of a bone defect instead of autogenous or allogeneous bone”. Bone substitutes are divided into bone grafts (autograft, allograft, xenograft), ceramics (hydroxyapatite, TCP, calcium sulphate) and growth factors (DBM, PRP, BMP’S). These substitutes aren’t suitable for every clinical use, and they need to be chosen selectively based on their purpose. This paper explores several articles from 1980 to 2021 in Medline, Google scholar and internet including systematic reviews and clinical trials regarding bone substitute materials used in implant dentistry, as in clinical application, for ridge augmentation, sinus lift and guided bone regeneration.

Corresponding Author: Dr.Priyanka K

Professor, **Post Graduate Student, *Senior Lecturer, Department of Prosthodontics, Crown and Bridge, KMCT Dental College, Manassery, Kozhikode 673602, Kerala*

Introduction

Dental implants is an established treatment for rehabilitating missing teeth. Success of dental implants depends on the quality and quantity of available bone in the recipient site. This however may be compromised due to periodontal disease, surgery, tumor and trauma which in turn necessitates the need for additional bone augmentation.¹ Various studies have shown

that bone resorption after tooth removal can be approximately 1.5–2 mm vertically and 3.8 mm in the horizontal plane within six months.²

Restoring this loss of bone volume is important for establishing an ideal site for implant placement. This is effectively achieved with the use of bone substitutes. In order to comprehend the concept of bone regeneration and to select the ideal bone

substitute material, the implant clinician should have a strong understanding about this. This review outlines about bone regeneration and various bone substitutes used in implant dentistry.

BONE REGENERATION

Bone is a dynamic organ with remarkable regenerative potential. Bone formation and resorption is carried out by osteoblasts, osteocytes, and osteoclasts. In certain situations, bone repair is inadequate and hence requires the assistance of biomimetic biomaterial.³ Bone density plays a very crucial role in the successful placement of an implant. In general, as per the guidelines, at least 1 mm of bone is required around a dental implant.⁴

Bone regeneration is commonly done by bone grafting. The unhealthy bones which can't be healed by itself in the human body are repaired and re-build using bone graft, which is placed on a recipient site by a surgical procedure.⁵ Rationale for bone grafting includes osseointegration, osseointegration, osseointegration and osteogenesis.^{4, 6}

Ideal requirements of bone substitutes used for bone regeneration in implant dentistry include⁵

1. Promote, interactivity of cell biomaterial, extra-cellular matrix deposition and adhesion of cells.
2. Allow adequate transportation of nutrients, gases and regulative elements to permit propagation survival of cells and differentiation.
3. The amount of tissue regeneration is approximated at controllable rate based on biodegradation.
4. Incite a minimal level of inflammation.

They offer wide range of growth factors that can induce mesenchymal stem cells to differentiate into osteogenic progenitor cells⁷ and helps in the osteoconduction by acting as a scaffold on which further apposition may occur.⁸ Autograft material is osteogenic and fulfils all three components of the regeneration triad [Osteogenetic, Osteoinductive, Osteoconductive property]. Iliac crest, Fibula, Tibia, bone removed from osteoplasty and ostectomy, cranium, radius are the extraoral sites and maxillary tuberosity, retromolar pad, palate, anterior Nasal spine, ascending ramus, coronoid

process, torus, mandibular symphysis are the intraoral sites.⁹ It was in the mid-1970s, Branemark began using autograft with dental implants in the treatment of the atrophic edentulous jaws.

However, the use of machined implants often placed simultaneously with the graft led to poor implant survival rates. Over the years, the use of intraoral donor sites has been preferred because it helps to decrease the complexity and risks of bone grafting.¹⁰ It offers minimal immunological reaction. The disadvantages include higher morbidity rate, increased inpatient stay, less revascularization and requires additional surgery.

ALLOGRAFTS

These are the grafts transferred between genetically dissimilar members of the same species.¹¹ Allografts can be⁹ FDBA and DFDBA (Decalcified FDBA)

Table 1: - Differences between FDBA AND DFDBA

S No.	Freeze-Dried Bone Allograft	Demineralized Freeze-Dried Bone Allograft
1.	More radio-opaque	More radiolucent
2	Only osteoconductive	Both osteoconductive, osteoinductive
3	Primary Indication: Bone augmentation associated with Implant treatment	Primary Indication: Periodontal disease associated with natural tooth such as attachment level gain, probing depth reduction, and osseous regeneration.

Allografts used for bone repair requires sterilization and deactivation of proteins.⁶ The form and size of allograft material contribute to the predictability of bone regeneration. Allografts are available in three particle forms: cortical, cancellous and cortico/cancellous. Cortical forms are associated with an increased density and greater space maintenance properties, which allow for slower resorption. Cancellous

chips are advantageous because they allow for osteoconductive scaffolding and deposition of osteoblasts while also providing faster resorption. The cortico/cancellous mixture allows for the benefits of both cancellous and cortical bone.¹² The particle size of the allograft material is another very important factor in the bone regeneration process. Particle size that is too small (less than 125 microns) leads to fast resorption with inconsistent bone formation.

A larger particle size (greater than 1,000 microns) restricts resorption and may be sequestered or result in delayed healing. Studies have shown an ideal particle size for predictable bone regeneration to be approximately 250–1,000 microns.¹²

Allografts are available in different shapes from granules to complete bone segments. Granules can be used in socket preservation for future implant placement, ridge reconstruction for prosthetic therapy, filling osseous defects and maxillary sinus floor elevation. Allogenic bone blocks can also be used for shell technique as a substitute for autogenous bone. This avoids the time required for harvesting and splitting of the autogenous bone blocks.¹³ According to Vieira et al fresh frozen allografts promote

satisfactory vertical bone formation as well as low resorption rates, good density, and implant stability.¹⁴ Allograft placement does not require additional surgery, hence reduces hospital stay. But the disadvantage is the possibility of disease transmission and immunogenicity.

XENOGRAFT

Xenografts are a type of bone graft in which the donor tissue is obtained from a genetically dissimilar organism which is basically osteoconductive, mainly bovine. Bovine bone is heated to facilitate deproteinization to eliminate the risk of disease transmission as well as the occurrence of allergic reactions. Deproteinization transforms it into a biologically derived HA ceramic.⁴ Histological studies have claimed that infiltration of bovine xenograft particles with newly formed bone could fill the interparticulate space.⁷ It has been shown to be very difficult to adequately screen xenografts for the possibility of viral presence.¹⁵

The Bovine Hydroxy Apatite (BHA) is considered a slow resorbing bone substitute that has osteoconductive properties and can be used as a space-filling material. The slow

resorption rate of the material has led to a successful and stable long-term stabilization around the implants.¹⁶ Recent studies demonstrated high primary stability of implants grafted with xenograft without any differences to natural healing. These results may be attributed to high bone fill of the defect (50%) 2 months after grafting.¹⁷ The advantages of xenograft include slow resorption, low cost and high availability. Immunogenicity is one of the main disadvantages.

SYNTHETIC VARIANTS

Platelet rich plasma (PRP)

Platelet-rich plasma (PRP) is generally used as a gel that is easily obtained from patient's blood. Centrifugation of blood through gradient density and the resulting blood platelets are mixed with thrombin and calcium chloride. Hence, PRP includes concentration of platelets and fibrinogen, as well as growth factors such as platelet derived growth factors (PDGF), vascular endothelial growth factor (VEGF), IGF, and TGF. It is not validated as a stand-alone bone substitute.^{18,19} Stahl et al in their study stated that PRP combined with grafting materials may transiently enhance bone

formation.²⁰ In recent studies, stability values in PRP-treated implants showed significant difference after 30 days. Initial burst of growth factors and their effect on healing and bone formation can be the cause for significant raise in stability values. It is safe due to its autologous origin as there is no risk of immunogenic reaction or transmission of diseases.²¹

PLATELET-RICH FIBRIN (PRF)

PRF is a natural fibrin matrix obtained by centrifugation process. It is prepared by centrifuging autologous whole blood without additives to form a platelet concentrate and without any anticoagulant in glass test tubes. Polymerization process is so natural and slow that it gives it a physiologic structural and architectural design that encourages the healing process.²² It consists of an autologous leukocyte-platelet-rich fibrin matrix with cytokines, platelets, and stem cells. It acts as a biodegradable scaffold, and favours in micro-vascularization and is able to guide epithelial cell migration to its surface and also has great potential for bone and soft tissue regeneration, without inflammatory reactions. It could be used alone or in combination with bone grafts, promoting

haemostasis, bone growth, and maturation.²³ You et al in their study concluded that PRF gel can induce more implant to bone contact than PRP in bony defect around the dental implant.²⁴ Biologic effects of PRP seems to start in the second week but PRF was detected during first week, showing that PRF expresses a stronger and more durable effect on the proliferation and differentiation of osteoblast than PRP. PRF placed during implant surgery enhanced the stability of implant.²⁵

GROWTH FACTORS

Growth factor refers to proteins capable of stimulating cell proliferation, cell differentiation and preventing apoptosis.²⁶ Among several growth factors, bone morphogenetic proteins (BMPs) which attract mesenchymal cells to the donor site by chemotaxis has received attention from the scientific community. Moreover, it provokes the differentiation of these cells to preosteoblastic cells which later transform to osteoblasts and cause bone formation.²⁷ Yeo et al, reported that BMP coated on an oxidized Ti surface induced more bone osseointegration, regeneration and volume.²⁸ Alveolar bone that is insufficient to support implant placement due to lack of

height or width may be augmented with bone morphogenic protein (BMP) which can be used alone or in concert with other bone graft materials as an alternative to invasive allograft bone-harvesting procedures.²⁹

TRICALCIUM PHOSPHATE (TCP)

Most widely used graft material in which calcium and phosphate are in ratio 1:1.5. These are beta-whitlockite crystals which are available in two forms as cement and ceramics.⁹ Bi hedral beta, monoclinic

alpha and hexagonal alpha/beta are the three recognized polymorphs of tricalcium phosphate.³⁰ The alpha forms are more soluble and biodegradable than the beta form. It may be used alone or in combination with other biodegradable agents, such as resorbable poly glycolic acid. Use of TCP immediately after tooth extraction was found to be very beneficial to keep the bone height and width, and to slow down the shrinkage associated with healings and will give us a better rate of osseointegration.^{30,31} Parel and Triplett showed in their studies that with the use of TCP allograft can be used to cover the bony defects around the immediate implant if the gap is >2.5 mm.³²

HYDROXYAPATITE

It is a main inorganic component of the structure of tooth which consists of calcium and phosphate but with a ratio of 1:1.67.⁹ HA, alone or combined with an auto/allo/xenograft, in the form of powders, porous blocks, or beads has been used to support alveolar bone regeneration.³⁰ HA is extremely biocompatible and does not promote any inflammatory response. HA

coated implant improves bone strength and initial osseointegration rate, but there is a chance of bacterial susceptibility of the HA coatings when compared with the titanium implants and coating-substrate interfacial fracture.³³

BIOACTIVE GLASS CERAMICS

They are made up of calcium oxide, sodium oxide, Silicon dioxide, potassium oxide and are referred to as 45S5 bioactive glass (Bioglass®).⁹ They have been widely used in dentistry for bone defects repair and reconstruction, because these glasses exhibit bone bonding. The use of bioactive glasses as alloplastic bone graft materials for alveolar ridge augmentation and maxillary sinus lift procedures has received increasing attention in implant dentistry. Besides Bioglass® other commercial types of

bioactive glass have been used for bone repair such as PerioGlas® and BioGran®.³⁴

CORAL

Corals have interconnected pores and a skeleton quite similar to cortical and spongy bones, Coral-based substitutes are mainly calcium carbonate that can be

transformed industrially into HA. Coralline HA are often used as growth factors carrier, such as BMP, TGF- β , or FGF. It can be found in different aspects like granules or blocks. It does not induce any inflammatory responses. Coralline HA is osteoconductive, can show an excellent bone-bonding capacity, avoids donor site morbidities, and is unlikely to promote disease transmissions or risks of deep infections.¹⁹

COMPOSITE POLYMER

Natural polymers such as collagen are slightly used alone rather than in combination with HA. They can be nonbiodegradable or fully biodegradable, thus allowing a total bone replacement in time without remaining of any foreign bodies. Polyesters like poly (ϵ -caprolactone) (PCL), can be synthesized by mimicking the collagenic matrix, which provide structural porosity and osteoconductive properties.

Most of the polymer-based bone substitutes are suitable to be used as bioactive molecules or growth factors carriers, potentially showing osteogenetic properties.¹⁹ Safak et al reported that the composite bone graft substitutes showed close integration with bone, when used in maxillary sinus floor augmentation.³⁵

RECENT ADVANCES

Bone tissue engineering

In recent years, new generations of bone substitutes have been developed in an attempt to obtain materials closer to the autograft standard by using biomaterials capable of inducing specific cellular responses at the molecular level, by incorporating the bioactivity and biodegradability of these materials.³⁶ Tissue engineering is based on three elements that must be in synergism: matrix (scaffolds), cells and signals (mechanical and/or molecules: proteins, peptides and cytokines). The absence or dysfunction of one element will halt or delay tissue regeneration.³⁴

CONCLUSION

Each bone substitute material developed thus far has its advantages and

disadvantages. Despite the rapid technological developments, there is no material manufactured that combines all the advantages of various materials. Since the introduction of dental implants, bone grafting has become an important procedure required for the treatment of patients with limited bone availability. Bone autograft, alone or together with other bone substitutes, has been the biomaterial of choice for clinicians. However different xenogenic, allogenic and synthetic biomaterials have shown promising results in many bone augmentation procedures. The actual process of maturation, which is the most fundamental part of clinical applications after each graft, has been studied by clinicians with different preferences when selecting the type of bone substitutes.

REFERENCES

1. Rodriguez R, Hartmann N, Weingart D. Current Concepts of Bone Regeneration in Implant Dentistry. Journal of Surgery [Jurnalul de chirurgie] 2015; 10(4): 263-265.
2. Van der Weijden F, Dell'Acqua F, Slot DE. Alveolar bone dimensional changes of post-extraction sockets in

- humans: a systematic review. *J Clin Periodontol* 2009; 36: 1048–1058.
3. Randolph R. Resnik. Bone Substitutes in Oral Implantology. *Chairside Magazine* 2018;12(3).
 4. S. Sangeetha, Ashish R. Jain. Current bone substitutes for implant dentistry. *Drug Invention Today* 2018; 10(8):1583-1589.
 5. K. Hemavarthini, Thamarai Selvan, V. Vidya Shree. Current bone substitutes in implant dentistry. *Int J Sci Res* 2020;9(12):16-18.
 6. Saima S, Jan SM, Shah AF, Yousuf A, Batra M. Bone grafts and bone substitutes in dentistry. *J Oral Res Rev* 2016; 8:36-8.
 7. Méndez-Ferrer, S., Michurina, T. V., Ferraro, F., Mazloom, A. R., MacArthur, B. D., Lira, S. A., Frenette, P. S. Mesenchymal and haematopoietic stem cells form a unique bone marrow niche. *Nature* 2010; 466(7308):829–834.
 8. Lichte, P., Pape, H. C., Pufe, T., Kobbe, P., & Fischer, H. Scaffolds for bone healing: Concepts, materials and evidence. *Injury* 2010; 42(6): 569–573.
 9. Patel Kishan Sanjay Kumar, and Sushma Kurella. Bone Grafting Materials in Dentistry: A Brief Review. *SVOA Dentistry* 2021:32-28.
 10. Misch CM. Autogenous bone: is it still the gold standard? *Implant Dent.* 2010 Oct; 19(5):361.
 11. Sharon Ann Jose, Sapna Bhaskaran, Sreepriya S S. Current trends in bone grafts for ridge preservation in prosthetic and implant dentistry. *Int J Sci Res* 2020;3(3):136-142.
 12. Shapoff CA, Bowers GM, Levy B, Mellonig JT, Yukna RA. The effect of particle size on the osteogenic activity of composite grafts of allogeneic freeze-dried bone and autogenous marrow. *J Periodontol.* 1980 Nov; 51(11):625-30.
 13. Fay Goldstep. Bone Grafts for Implant Dentistry. The Basics. *Oral Health* 2015
 14. Vieira, J.S, Brandão-Filho, E.M, Deliberador, F.R, Zielak, J.C, Giovanini, A.F, & Deliberador T.M. Dental Implant Placement with Simultaneous Anterior Maxillary Reconstruction with Block and Particulate Fresh Frozen Allograft

- Bone: A Case Report with 24-Month Follow-Up Data. *Case Reports in Surgery* 2017;1–4.
15. Jacobsen G, Easter D. Allograft vs. xenograft: Practical considerations for biologic scaffolds. *Musculoskeletal Transplant Foundation* 2008.
 16. Nasim Mahjoub Pour, Hugo De Bruyn. Bone Augmentation with Bovine Bone Xenograft: 5 Years Result of Retrospective Cohort Study. *Oral health and dental management* 2019;18(2)
 17. Yaniv Mayer, Ofir Ginesin, Hadar Zigdon-Giladi. Socket Preservation Using Xenograft Does Not Impair Implant Primary Stability in Sheep: Clinical, Histological, and Histomorphometric Study. *J Oral Implantol* 2020; 46 (6): 580–588.
 18. Albanese, A., Licata, M. E., Polizzi, B., & Campisi, G. Platelet-rich plasma (PRP) in dental and oral surgery from the wound healing to bone regeneration. *Immunity & Ageing* 2013; 10(1): 23.
 19. Fernandez de Grado, G, Keller, L, Idoux-Gillet, Y, Wagner, Q, Musset, A-M, Benkirane-Jessel, N, Offner, D. Bone substitutes: a review of their characteristics, clinical use, and perspectives for large bone defects management. *J Tissue Eng* 2018; 9:1-18
 20. Stahli, A., Strauss, F. J, & Gruber, R. The use of platelet-rich plasma to enhance the outcomes of implant therapy: A systematic review. *Clinical Oral Implants Research* 2018; 29: 20–36.
 21. Gopinath A, Ravikanth A, Kadiyala KK, Thota KM, Manne P, Babu MS. Effect of platelet rich plasma on stability of dental implants: A prospective comparative clinical study. *J NTR Univ Health Sci* 2017;6:107-13.
 22. Ersheidat, A, Al Banna, S, & Zafar, M.S. Platelet-rich plasma: a paradigm shift in implant treatment. *Dental Implants* 2020 :203–223.
 23. Cortese, A, Pantaleo, G, Amato, M, Howard, C.M, Pedicini, L, & Claudio, P. P. Platelet-rich fibrin (PRF) in implants dentistry in combination with new bone regenerative flapless technique: evolution of the technique and final

- results. *Open Medicine* 2017; 12: 24–32.
24. You, T, Choi, B, Zhu, S, Jung, J, Lee, S, Huh, J, Lee, H, Li, J. Platelet enriched fibrin glue and platelet-rich plasma in the repair of bone defects adjacent to titanium dental implants. *Int. J. Oral Maxillofac. Implants* 2007; 22 (3): 417–422.
 25. Oncu E, & Alaaddinoglu E. (2015). The Effect of Platelet-Rich Fibrin on Implant Stability. *Int. J. Oral Maxillofac. Implants* 2015; 30(3):578–582.
 26. Marco Cicciu. Growth Factor Applied to Oral and Regenerative Surgery. *Int. J. Mol. Sci.* 2020;21(20):7752.
 27. Lee K, Silva EA, Mooney DJ. Growth factor delivery-based tissue engineering: General approaches and a review of recent developments. *J R Soc Interface* 2011; 8:153-70.
 28. Yeo IS. Reality of dental implant surface modification: a short literature review. *Open Biomed Eng J.* 2014 Oct 31; 8: 114-9.
 29. Bowler D, & Dym H. Bone Morphogenic Protein. *Dental Clinics of North America* 2015 a; 59(2): 493–503.
 30. Iskaros M, Silver J, Blye JS, Cardenas MPR. Does B-Tricalcium Phosphate Work as a Bone Regenerative Material? *J Dent Oral Biol.* 2017; 2(18): 1106.
 31. Balakrishna Ramalingam, Vijay Ebenezer. Use of tricalcium phosphate and hydroxyapatite followed by dental implant - A systemic review. *Drug Invention Today* 2019;12(3):448-450.
 32. Parel SM, Triplett RG. Interactive imaging for implant planning, placement, and prosthesis construction. *J Oral Maxillofac Surg* 2004; 62:41-7.
 33. Joo L Ong, Daniel Chan. Hydroxyapatite and Their Use as Coatings in Dental Implants: A Review. *Critical Reviews in Biomedical Engineering* 2000;28(5-6):667-70.
 34. Saska S, Mendes L.S, Gaspar A.M.M, & de Oliveira Capote, T. S. Bone Substitute Materials in Implant Dentistry. *Current Concepts in Dental Implantology.* 2015; Chapter 2: 25-52.

35. Ahmet, Safak DDS; Alper Gultekin, Bahattin DDS, PhD; Karabuda, Zihni Cuneyt DDS, PhD; Olgac, Vakur DDS, PhD. Two Composite Bone Graft Substitutes for Maxillary Sinus Floor Augmentation. *Implant Dent* 2016 Jun;25(3):313-21.
36. Polo-Corrales L, Latorre-Esteves M, Ramirez-Vick JE. Scaffold design for bone regeneration. *J Nanosci Nanotechnol*. 2014 Jan; 14(1): 15–56.
37. Choi SH, Jang YS, Jang JH, Bae TS, Lee SJ, Lee MH. Enhanced antibacterial activity of titanium by surface modification with polydopamine and silver for dental implant application. *J Appl Biomater Funct Mater*. 2019;17(3).

Case Report

VIRTUAL TREATMENT PLANNING IN BIMAXILLARY ORTHOGNATHIC SURGERY - A CASE REPORT

*Dr Manoj Kumar K P, **Dr Aparna S Nair, **Dr Parvathy R, ***Dr Deepti Krishnankutty, ***Dr Sunu V S

Abstract

Orthognathic surgery is a technique sensitive procedure and virtual surgical planning aids in improving the accuracy and a preoperative insight into future intended orthognathic position. This case report depicts a patient with nasomaxillary deficiency and mandibular prognathism who had undergone Orthognathic surgery - Lefort I advancement and BSSO setback using virtual surgical planning.

Key words:

Orthognathic surgery, visual surgical planning, CASS, 3-D printing

Corresponding Author: Dr.Aparna S Nair

Professor and Head of the Department, **Post Graduate Student, *Senior Lecturer, Department of Oral and Maxillofacial Surgery, KMCT Dental College, Manassery, Kozhikode 673602, Kerala*

Introduction

Developmental dentofacial deformities primarily affect jaw bones and dentition with varied racial differences. The clinical presentation can be hyperplasia or hypoplasia of one or both the jaws. Bimaxillary deformities is quite common in

Asian and African ethnic population. Mild cases can be treated by camouflaged orthodontic treatment.¹ In moderate to severe cases causing aesthetic problems orthognathic surgical intervention may be deemed an essentiality.

The dentofacial anatomy is superimposed with the help of Digital Imaging and Communications in Medicine

(DICOM). Thereby establishing occlusal topography for fabrication of splints. Computer aided surgical simulation (CASS) aids in illustration of deformities and a preoperative insight into future intended orthognathic position.²

Orthognathic surgery is an accurate and complex procedure of repositioning maxillomandibular complex to balanced and aesthetically pleasing position. Virtual surgical planning (VSP) aid in visualizing dental arch relationship and bony structure into a virtual model. Compared to the conventional traditional methods 3D planning helps in reducing surgical time and improving accuracy

It provides better visualization of asymmetries and deformities.³ It gives options to stimulate various surgical procedures, detect complications in advance and helps in evaluating the temporomandibular joint. Pre-surgical prediction of jaw movements is necessary to accomplish better results.

Case Report

A 22-year-old male patient reported to our maxillofacial center with complaints of protruded lower jaw with difficulty in

speech and mastication. Clinical evaluation showed skeletal class III with a concave profile and increased facial angle, incompetent lips. On examination, mandibular prognathism with nasomaxillary deficiency was evident. Obliteration of labiomental sulcus and obtuse nasolabial fold was noted. Mild facial asymmetry was present with no TMJ disorder. On Intraoral evaluation dental compensation of lower anterior teeth was revealed. Patient had Class III molar relation and reverse overjet. Diagnosis was Angle's Class III malocclusion over Angle's Class III skeletal base. Further radiological evaluation using orthopantomogram and lateral cephalogram confirmed the diagnosis.

Treatment Plan

- Presurgical Orthodontic treatment - leveling of occlusion and alignment of arches
- Bimaxillary surgery- Lefort I osteotomy with repositioning and BSSO setback
- Post- surgical orthodontic follow-up - minor deformities in post-operative occlusion

9 months after bonding, alignment was almost complete and CBCT of jaws, facial

photographs, arch impressions and CBCT of dental models were taken. By overlapping computed images and facial photographs, 3-dimensional model was created. Using CAD-CAM technologies occlusal splint is generated for repositioning. After evaluation Lefort advancement of 4 mm, BSSO setback 5mm, midline shift towards right side by 4 mm was recommended with the fabrication of osteotomy guides for intraoperative guidance.

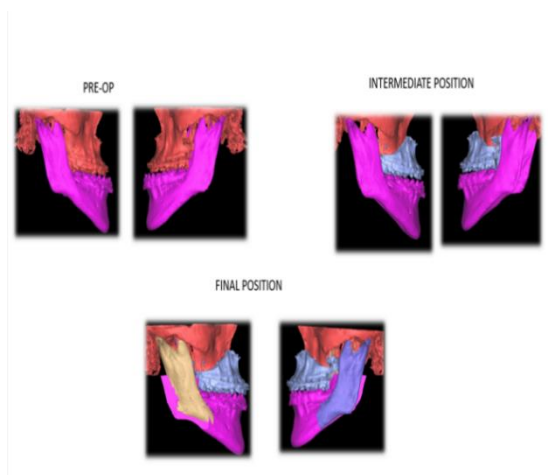


Fig1: Shows the preop evaluation, intermediate position and the final position of the jaw bones in accordance with Virtual surgical planning.

Surgical Procedure

Under nasotracheal intubation through vestibular incisions, Lefort 1 osteotomy performed. Advancement of osteotomized maxillary segment by 4 mm

was done using interim splint (fig 2) Fixation using L shaped Ti plate and screws at nasomaxillary and zygomaticomaxillary buttresses. After Bilateral Sagittal Split Osteotomy, mandible was setback by 5mm and rotation was done to correct midline shift using final splint. The osteotomized segments were fixed using titanium plates and screws. Post-operative Orthodontic treatment was continued for 6 months for alignment and minor corrections.



Fig 2 Advancement of osteotomized maxillary segment using interim splint.



Fig 3. Shows pre-operative and 1month post-operative pictures of the patient prior to post-operative orthodontic correction.

DISCUSSION

Orthognathic surgery is an evolving field which requires thorough knowledge of craniomaxillofacial relationships. An accurate diagnosis is important for achieving treatment goals. The craniomaxillofacial deformities require history, clinical examination and radiographical evaluation for diagnosis. Traditional method of clinical quantitative analysis, cephalometric and model analysis for production of guidance splints have been in use for the past decades.⁴ With the Virtual surgical planning (VSP) changed the paradigm of orthognathic

surgery with its accuracy, imaging dynamics, quantitative analysis, and predictability of aesthetic outcomes and functional movements. 3D printing in orthognathic surgery that include occlusal splints, osteotomy guides, spacers, patient specific implants, and printed models. The invent of 3D CAD-CAM technology into maxillofacial surgery has aided in reducing laboratory-based errors, time and cost required.

Development of laser sintering and biomedical printing has been promising in

development of CAD-CAM implants, spacers and splints.⁵ The 3-dimensional movements is advantageous in facilitating a real intra-operative experience to the surgeon. The overlapping of hard tissue and soft tissue elements by combining computed tomography images, digital photographs and dental cast models or intraoral scanning in DICOM software. This helps in the development of virtual model of the patient.

Lauren. et al. proposed first computerized design and fabrication of occlusal splints. Francisco. et al. proposed an approach with combination of 3D virtual dental casts and virtual pre-operative planning which has improved the accuracy

to a larger extent. Hernandez-Alfaro. et al. proposed the use of intra-oral scanner instead of impressions for better prediction and reduces pre-operative assessment time.⁵ After fusing scans of CBCT of patients, CAD-CAM intermediate splint generation for Lefort I osteotomy is done along with osteotomy guide.⁶ After virtual prediction of final position of mandible with the spatial relationship with maxillofacial skeleton final splint is fabricated.

Osteotomy guides are used to ascertain the desired position of the osteotomy cuts by virtual planning. Suojanen. et.al highlighted the use of surgical guides for condylar position and inferior alveolar injury prevention in BSSO setback.⁵ Spacers in virtual planning is used in cases of asymmetries. They are fit into position for correction and are removed after fixation. Mazzoni et al. advocated the use of patient specific implants which reduced the need for splints. Implants are manufactured by sintering, or layer-by-layer technique.⁷ 3D printed models orient the surgeon regarding the positions of fixation and mini-plate adaptation.⁸ This case report depicts the use of virtual planning in a bi-jaw orthognathic surgery.

CONCLUSION

Success of orthognathic surgery is dependent on the surgical technique and accuracy of the procedure enhanced by virtual surgical planning. The adoption of computer-aided surgical simulation (CASS) is creating a paradigm shift in surgical planning for patients with CMF deformities including maxillofacial surgery, craniofacial surgery, trauma and distraction osteogenesis. Virtual planning has laid a milestone in improving the accuracy of orthognathic surgery and providing new possibilities in the visualization of craniomaxillofacial skeleton and functional movements.

REFERENCES

1. Oueis R, Waite P, Wang J, Kau C. Orthodontic-Orthognathic Management of a patient with skeletal class II with bimaxillary protrusion, complicated by vertical maxillary excess: A multi-faceted case report of difficult treatment management issues. International Orthodontics. 2020;18(1):178-190.
2. Farrell B, Franco P, Tucker M. Virtual Surgical Planning in

- Orthognathic Surgery. Oral and Maxillofacial Surgery Clinics of North America. 2014;26(4):459-473.
3. Otranto de Britto Teixeira A, Almeida M, Almeida R, Maués C, Pimentel T, Ribeiro D et al. Three-dimensional accuracy of virtual planning in orthognathic surgery. American Journal of Orthodontics and Dentofacial Orthopedics. 2020;158(5):674-683.
 4. Hammoudeh J, Howell L, Boutros S, Scott M, Urata M. Current Status of Surgical Planning for Orthognathic Surgery. Plastic and Reconstructive Surgery Global Open. 2015;3(2):307.
 5. Lin H, Lonic D, Lo L. 3D printing in orthognathic surgery – A literature review. Journal of the Formosan Medical Association. 2018;117(7):547-558.
 6. Naran S, Steinbacher D, Taylor J. Current Concepts in Orthognathic Surgery. Plastic and Reconstructive Surgery. 2018;141(6):925e-936e.
 7. Efanov J, Roy A, Huang K, Borsuk D. Virtual Surgical Planning. Plastic and Reconstructive Surgery - Global Open. 2018;6(1):e1443.
 8. Lin H, Chang HW, Wang C, Kim S, Lo LJ. Three-Dimensional Computer-Assisted Orthognathic Surgery. Annals of Plastic Surgery. 2015;74(Supplement2):S118-S126.

Literature Review

RECENT ADVANCES IN CERAMICS

*Dr.Noopura S, **Dr.Ramesh Kumar, **Dr.Elsy P Simon, ***Dr Ravi SV

Abstract

Over the last decade, it has been observed that there is an increasing interest in the ceramic materials in dentistry. Aesthetically these materials are preferred alternatives to the traditional materials in order to meet the patients' demands for improved esthetics. Dental ceramics are usually composed of non-metallic, inorganic structures primarily containing compounds of oxygen with one or more metallic or semi-metallic elements.¹ Ceramics are used for making crowns, bridges, artificial denture teeth, and implants. The use of conservative ceramic inlay preparations, veneering porcelains is increasing, along with all-ceramic complete crown preparations. The earlier ceramics are very fragile and cannot withstand the high tensile forces. Several modifications have been made in ceramics in order to address this quandary. This article discusses the various recent advances of dental ceramics.

Keywords: Ceramic, glass ceramic, feldspathic, leucite

Corresponding Author: Dr.Noopura S

** Post Graduate Student, **Professor and Head of the Department , ***Reader, Department of Conservative Dentistry, KMCT Dental College, Manassery, Kozhikode 673602, Kerala*

Introduction

A ceramic is an earthly material usually of silicate nature and may be defined as a combination of one or more metals with a non-metallic element usually oxygen. The American Ceramic Society had defined ceramics as inorganic, non-metallic materials, which are typically crystalline in nature, and are compounds formed

between metallic and non-metallic elements such as aluminium & oxygen (alumina - Al_2O_3), calcium & oxygen (calcia - CaO), silicon & nitrogen (nitride- Si_3N_4).² In dentistry, ceramics are widely used for making artificial denture teeth, crowns, bridges, ceramic posts, abutments, and implants and veneers over metal substructures.³ Ceramics are characterized



by their refractory nature, hardness, chemical inertness, biocompatibility and susceptibility to brittle fracture.⁴

Shortly after the introduction of porcelain into Europe in the early 18th century, Alexis Duchateau, a Parisian apothecary, introduced ceramics to dentistry when he successfully replaced his ivory dentures with porcelain. With the help of a Parisian dentist, Nicholas Dubois de Chemant, Duchateau, working in concert with a new, high-technology porcelain manufacturer in 1774, created a complete set of porcelain dentures.

Porcelain inlays, onlays, and crowns were introduced by Charles Land in 1886, which ultimately led to the creation of esthetic and functional ceramic restorations. However, the original dental porcelain contained a high feldspathic glass content and was extremely brittle and weak ($\sigma \sim 60$ MPa, σ stands for strength).⁵ Therefore, despite the esthetic advantage, the early version porcelain restorations were not widely applied in dentistry. All-ceramic systems use different types of crystalline phases which influence the physical, mechanical and aesthetic properties of all-ceramics. The nature, amount, particle size and coefficient of thermal expansion of crystalline phases influence the mechanical and optical

properties of the materials. In 1965 Mclean and Hughes reported that the strength and fracture toughness of feldspathic glass can be significantly improved by the addition of aluminium oxide particles (70 % vol). The castable glass-ceramic crown system⁶ and “shrink free” (Cerastore, coores Biomedical, Lake wood, Colo) ceramic systems were introduced in the 1980s with superior esthetics using new innovative processing techniques.

Later, 100% polycrystalline substructure ceramics were introduced with superior mechanical properties. However, these 100% polycrystalline materials are highly opaque and their esthetic qualities are not up to the standard. So, it can be concluded that the increase in the crystalline phase would increase the mechanical properties substantially, with compromised aesthetic properties. Therefore, it is necessary to optimize both the crystalline and glassy phases in order to attain adequate mechanical and aesthetic properties. Numerous researchers have attempted reinforcing the ceramics with various crystalline materials using innovative fabrication techniques to improve the shortcomings of all-ceramic restorations. Kelly⁷ classified all-ceramic restorations as predominantly glassy materials, particle filled glasses and polycrystalline ceramics.



All the three materials consist of feldspathic glass as the main glassy phase with varying amounts of filler particles such as opacifiers, colorants and high-melting glass particles. In addition to these filler particles, filled glasses and polycrystalline ceramics contain leucite crystals with 17-25 mass% and 40-55 mass% respectively.⁸ Based on their processing techniques all-ceramic restorations are widely classified into sintered porcelains, castable glass ceramics, machinable ceramics, slip-casted ceramics, heat pressed and injection molded ceramics.

Dental ceramics have become increasingly popular as restorative materials due to improvements in strength and the increased goodness of fit with development of pressing and CAD/CAM processes.

Recent advances in ceramics

Sintered Porcelains

Sintering is the consolidation process of ceramic powder particles through heating at high temperatures which results in atomic motion. The sintering of porcelain promotes physical-chemical reactions responsible for the final properties of the ceramic products.

Leucite-reinforced Feldspathic Porcelain

Conventional feldspathic porcelains were reinforced with approximately 45 vol% of tetragonal leucite crystals, which are responsible for high compressive strength and modulus of rupture. Optec HSP is the commercially available leucite-reinforced feldspathic porcelain. Vaidyanathan et al⁹ reported that greater leucite content of porcelain compared with conventional feldspathic porcelain for metal-ceramics leads to a higher modulus of rupture and compressive strength. Leucite reinforced ceramics are indicated to fabricate veneers due to their good optical properties. The low refractive index of these crystals makes ceramic materials translucent even with high crystalline content leading to improved flexure strength (160 - 300 MPa) which also depends on the shape and volume of the crystals.

Alumina-based Porcelain

Alumina (Al_2O_3) is the strongest and hardest oxide known¹⁰ and can be reinforced into ceramics by a mechanism called “dispersion strengthening”. Reinforcement of alumina imparts high mechanical properties as it has high modulus of elasticity (MOE); 350 GPa, and high fracture toughness, 3.5 to 4 MPa .



COTE is the same for both alumina and glass matrix.

Magnesia-based Porcelain

flexural strength and COTE ($14.5 \times 10^6/\text{°C}$) of magnesia (MgO) is very high and closely matches with that of the body and incisal porcelains designed for bonding to metal ($13.5 \times 10^{-6} / \text{°C}$). The core material is made by reacting magnesia with a silica glass within the $1100\text{--}1150\text{°C}$ temperature range that results in the precipitation of forsterite (Mg_2SiO_4) crystals which is responsible for strengthening of ceramics.

Zirconia-based Porcelain

Zirconia is a polycrystalline material reinforced into conventional feldspathic porcelain in order to strengthen them by a mechanism called “transformation toughening”.¹¹ Zirconia has cubic structure at its melting point (2680°C) and on cooling from this temperature results in crystallographic transformations such as tetragonal and monoclinic phase at 2370°C and 1170°C respectively. This crystal transformation induces internal stresses as it is accompanied by a 3% - 5% volume expansion. Stabilizing agents such as calcia, magnesia, yttria and ceria are added to partially stabilize the tetragonal phase at room temperature and to control

the volume expansion as well. This partially stabilized zirconia has high initial flexural strength and fracture toughness. Yttria stabilized zirconia (YSZ) increase fracture toughness, strength and thermal shock resistance and decrease translucency and fusion temperature.¹² Most dental zirconia ceramics are opaque and copings need to be veneered for high aesthetics.

Glass Ceramics

A glass ceramic is also called as castable glass ceramic as it is processed by using lost-wax pattern casting procedure. The first commercially available castable ceramic material for dental use is ‘Dicor’, which was developed by Dentsply international.

A glass ceramic prosthesis is fabricated in a vitreous or noncrystalline state and then converted to crystalline state by controlled devitrification process using heat treatment called as ceramming. The process of ceramming takes place in two phases such as crystal nucleation and crystal growth, which results in increasing the strength and fracture toughness of glass ceramics by interrupting the crack propagation through them under masticatory forces. The significant aspect of this ceramics is the Chameleon effect in which a part of color is picked up from adjacent tooth.¹²



Slip-Cast Ceramics

Slip-casting involves the pouring of an aqueous porcelain slip on a refractory die. The porosity of the refractory die helps condensation by absorbing the water from the slip by capillary action. Then it is fired at high temperature on the refractory die. During this heat treatment, the refractory die shrinks more than the condensed slip, and helps in easy separation. The resulting ceramic is very porous and must be either infiltrated with molten glass or fully sintered before veneering porcelain can be applied. Ceramics processed by slip-casting technique exhibit reduced porosity, and higher toughness than conventional feldspathic porcelains. However, this method may be technique sensitive in dental operatory, and also it is difficult to have accurate fit. Based on the type of core material, slipcasted ceramics are classified into Inceram-Alumina, Inceram-Zirconia and Inceram-Spinel.

Pressable ceramics

Pressable ceramics are categorized in to two generations including the first generation of heat pressed dental ceramics contains leucite as reinforcing crystalline phase (IPS Empress 1) and the second generation is lithium disilicate-based (IPS Empress2). First generation heat-pressed ceramic such as IPS Empress1 is dispersed

with 35 to 45 vol % leucite crystalline phase. Second generation heat-pressed ceramic such as IPS Empress2 contains about 65 vol % lithium disilicate as the main crystalline phase

More recently, IPS e.max Press (lithium disilicate glass-ceramic ingot for the press technique) and IPS e.max ZirPress (fluorapatite glass-ceramic ingot for the press-on technique) ceramic systems were developed by Ivoclar vivadent. IPS e.max Press is processed in the dental laboratory with the known Empress pressing equipment. This equipment is distinguished for providing a high accuracy of fit. The microstructure of IPS e.max Press is characterized as needle-like lithium disilicate crystals, which are embedded in a glassy matrix. The flexural strength of IPS e.max press is more than IPS Empress, comparatively

Machinable Ceramics

The evolution of CAD-CAM (Computer aided design and Computer aided machining) technology for the production of machined inlays, onlays, and crowns led to the development of a new generation of machinable ceramics. The advantages of this system include; impressions are not needed, which saves the dentist chair time and also avoids cross-contamination between the patient-dentist operational



field and the dental technician. Most popular systems available for machining all-ceramic restorations include CEREC (Siemens, Bensheim, Germany) system, Celay (Mikrona Technologie, Spreitenbach, Switzerland) system and Procera Alceram (Noble Biocare, USA) system.

The CEREC system was developed by Dr. Moermann. CEREC stands for “Chair side Economic Restoration of Esthetic Ceramics” and it was the first fully operational CAD-CAM ceramic. There are two commercial materials available in this system. They are Vita Mark II (Vident, Baldwin Park, CA) and Dicor MGC (Dentsply International, Inc., York, PA).

Dicor MGC is a machinable glass ceramic similar to Dicor, with the exception in the fabrication technique. This material contains 70 vol% of tetrasilicic fluoromica crystals. This higher vol% of crystalline phase addresses its superior mechanical properties. The Celay system uses a copy milling technology to manufacture ceramic inlays or onlays from resin analogs. This system is a machinable device based on pantographic tracing of resin inlay or onlay fabricated directly on to the prepared tooth or die. Commercially available Celay system material is Vita-Celay (Vident, Baldwin Park, CA). Sanidine is the major

crystalline phase in this material. Recently, In-Ceram pre-sintered slip cast alumina blocks (Vident, Baldwin Park, CA) have been developed and they can be machined with the Celay copy-milling system. This material is mainly used to make crowns and fixed partial denture

Procera All Ceram System (Nobel Biocare, USA) was introduced by Dr. Andersson,¹⁴ it was the first system which provided outsourced fabrication using a network connection.

The master die is scanned and the scanned images are sent to processing centre /laboratory through an internet. In the processing centre /laboratory, an oversized die is milled to compensate the firing shrinkage. The die is milled by a computer controlled milling machines using scanned images. Aluminium oxide powder is compacted on the die and coping is milled by a computer controlled milling machines.¹⁴

Other systems developed using milling technique were DCS Precident system with a laser scanner, Cercon System with no CAD component, and CICERO (Computer integrated crown reconstruction) system. More recently, Lava CAD/CAM System (3M ESPE, St. Paul, Minnesota) was introduced. It is



used for fabrication of zirconia framework for all ceramic restorations using yttria stabilized tetragonal zirconia poly crystals which have greater fracture resistance than conventional ceramics. Lava system uses a laser optical system to digitize information. The Lava CAD software automatically finds the margin and suggests a pontic and CAM produces an enlarged framework to compensate shrinkage



FIG. 11.6 Chair-side computer-aided design/computer-aided manufacturing system for all-ceramic restorations fabrication. (Courtesy Sirona Dental Systems, LLC, Charlotte, NC.)

New classes of materials on the horizon¹⁵

Recently, a new class of material-ceramic-polymer interpenetrating network (CPIN) material (Vita Enamic)- has been developed. The Enamic material consists of 86 wt% (75 vol%) of a feldspathic ceramic matrix into which is infiltrated by an organic phase of dimethacrylate resin

containing UDMA and TEGDMA. The fabrication process of this material involves two steps: first, a porous pre-sintered ceramic network is produced and conditioned by a coupling agent; then, the network structure is infiltrated with the monomers by capillary action. The resulting microstructure exhibits a hybrid structure with interpenetrating networks of ceramic and polymer, mimicking the interlocking of prism bands in natural teeth. The flexural strength, elastic modulus, hardness and fracture toughness of the Enamic material have been evaluated by several investigators, and revealed similar properties to those of natural tooth structure

Compared to ceramic restorative materials, Enamic has reliable millability and edge stability in terms of its ability to be fast milled into thin (< 0.5 mm) restorations with excellent precision. A full contour posterior crown takes just a little over 5 minutes to mill, while eliminating the need for post milling firing. The material is also easy to adjust and polish. Thus, it is an ideal material for chairside one-visit restorations.

CONCLUSION

The evolution in fabrication technology of dental ceramics has been outstanding over the past few decades; tremendous progress



has been made in terms of mechanical performance, with a ten-fold increase in flexural strength and fracture toughness. These new generations of all-ceramic materials present interesting options, both in terms of material selection and fabrication techniques. Success of the ceramic restoration depends on clinician's ability to select the appropriate material to match intraoral conditions and esthetic demands.

REFERENCES

- 1 Datla SR, Alla RK, Alluri VR, Babu JP, Konakanchi A. Dental ceramics: Part II-Recent advances in dental ceramics. Am J Mater Eng Technol. 2015;3(2):19-26.
- 2 Sukumaran VG, Bharadwaj N, Ceramics in Dental Applications, Trends Biomater. Artif. Organs, 20(1), 7-11, Jan 2006.
- 3 Denry I, Holloway JA, Ceramics for dental applications: A Review, Materials, 3, 351-368, Jan 2010.
- 4 Garber DA, Goldstein RE, Porcelain and Composite Inlays and Onlays: Esthetic Posterior Restorations, Quintessence, Chicago, 1994
- 5 McLean, JW. The Science and Art of Dental Ceramics. Chicago: Quintessence Publishing Co Inc.; 1979.
- 6 Lawn BR, Pajares A, Yuzang et al. Materials design in the performance of all-ceramic crowns. Biomaterials 25(14);2885-92, Jun 2004.
- 7 Kelly JR. Dental Ceramics: current thinking and trends. Dent clin N Am, 48(2): 513-530, Apr 2004.
- 8 Pilathadka S, Vahalová D, Contemporary all-ceramic materials, Part- 1, ACTA MEDICA (Hradec Králové) 2007;50(2):101-104.
- 9 Vaidyanathan TK, Vaidyanathan J, Prasad A, Properties of a new dental porcelain, Scanning Microsc 3:1023-1033, 1989.
- 10 Kelly JR, Benett P, Ceramic Materials in Dentistry: Historical Evolution and Current Practice. Aust Dent J, 56, 84-96, Jun 2011.
- 11 Jithendra Babu P, Rama Krishna Alla, Venkata Ramaraju Alluri, Srinivasa Raju Datla, Anusha Konakanchi, "Dental Ceramics: Part I - An Overview of Composition, Structure and Properties." American Journal of Materials Engineering and Technology, 3(1): 13-18, Mar 2015.



- 12 Sukumaran VG, Bharadwaj N, Ceramics in Dental Applications, Trends Biomater. Artif. Organs, 20(1), 7-11, Jan 2006
- 13 Anusavice KJ, Phillip's Science of Dental Materials, Elsevier, A division of Reed Elsevier India Pvt Ltd, New Delhi, India, 2010, 11th Edition, 655-720.
- 14 Andersson M, Oden A. A new all-ceramic crown: a dense-sintered, high purity alumina coping with porcelain. Acta Odontol Scand 51(1): 59-64, Feb 1993
- 15 Zhang Y, Kelly JR. Dental ceramics for restoration and metal veneering. Dental Clinics. 2017 Oct 1;61(4):797-819.

Literature Review

DESMOPLASTIC AMELOBLASTOMA

*Dr. Ahna Ali Akbar, *Dr. Anu, **Dr. Rajeeesh Muhammed, ***Dr. Mayeesh Radhakrishna

Summary

Ameloblastomas are neoplasms that have inspired great controversy and clinical interest, their incidence, radiographic features, treatment and behaviour are still discussed in the literature. Among the ameloblastomas, the desmoplastic variation is rare. Till date, most of the cases have been reported in Japanese, Chinese, Malaysian, Western, and African populations, with very few cases described in Indians. The male to female ratio was 3:2. The mean age at diagnosis was 33.2 years. The desmoplastic ameloblastoma (DA) is characterized by specific clinical, imaging, and histological features. Histologically, DA is characterized by small nests and strands of “compressed” odontogenic epithelium supported by pronounced collagenized stroma, scattered epithelial nests and extensively desmoplasia were prominent features of DA. In conclusion, DA present clinico-radiographic and histologic distinct features, when compared with “conventional ameloblastomas”.

Keywords

Desmoplastic ameloblastoma (DA); odontogenic tumour; Desmoplasia

Corresponding author: Dr. Ahna Ali Akbar E

Post graduate student, **Professor & Head of the Department, *Reader, Department of Oral Pathology & Microbiology KMCT Dental College, Manassery 673602, Kozhikode, Kerala*

Introduction

Odontogenic tumors (OTs) are assorted lesions derived from epithelial or ectomesenchymal tissues or both. They

range from hamartomatous or non-neoplastic tissue proliferation to malignant neoplasms with metastatic potential. In humans, tumors of the odontogenic tissues

are comparatively rare, comprising about 1% of all oral and maxillofacial biopsy specimens diagnosed.¹ Ameloblastoma is the most common clinically significant odontogenic tumor. Its relative frequency equals the combined frequency of all other odontogenic tumors excluding odontomas. Ameloblastomas are tumors of odontogenic epithelial origin. Theoretically, they may arise from rests of dental lamina, from a developing enamel organ, from the epithelial lining of an odontogenic cyst, or from the basal cells of the oral mucosa. Ameloblastomas are slow-growing, locally invasive tumors that run a benign course in most cases. They occur in three different clinico-radiographic situations, which deserve separate consideration because of differing therapeutic considerations and prognosis.² The most common histological patterns of ameloblastoma have been classified as follicular, plexiform, acanthomatous, granular cell, basal cell, desmoplastic, and keratomatous.³ DA is rare, accounting for approximately 4% to 13% of ameloblastomas.⁴

The first detailed report on the desmoplastic variant of ameloblastoma (DA) in the English literature was given by Eversole in 1984 who called it an

‘ameloblastoma with pronounced desmoplasia. However, Takigawa et al. and Uji et al. were the early ones to draw attention to this unusual variant, characterized by extensive stromal desmoplasia with small compressed nests and strands of odontogenic epithelium. Radiographically, this variant exhibited no features of conventional ameloblastoma. In 2001, Philipsen, Reichart, and Takata reviewed the 100 cases of DA reported in the literature from 1984 to 2001.³ The growing knowledge regarding the clinico-radiographical presentation and pathology of DAs has led to its categorization as a distinct variant of ameloblastoma in the World Health Organization (WHO) classification of odontogenic tumours in 2003. Other variants are solid/multicystic ameloblastoma (SMA), unicystic ameloblastoma and peripheral extraosseous ameloblastoma.³

Desmoplastic pattern

This type of ameloblastoma contains small islands and cords of odontogenic epithelium in a densely collagenized stroma. Immunohistochemical studies have shown increased production of the cytokine known as transforming growth factor β in

association with this lesion. Suggesting that this may be responsible for the desmoplasia. Peripheral columnar ameloblast-like cells are inconspicuous in the epithelial islands.²

Clinical features

Age and gender distribution

The mean age of DA patients at the initial presentation ranges from 40 to 49, and DA exhibits a similar gender distribution to other ameloblastomas.¹ The age prevalence was in the 3th to 5th decades. Whereas there were two peaks among females, in the 3rd and in the 4th decades, the males presented only a single peak in the 5th decade.⁴ more studies are needed to evaluate the true age and gender distribution of DA.³

Race

The incidence of DA among ameloblastomas ranges from 0.9% to 12.1% in different races.¹ The review by Philipsen, Reichart, and Takata has described cases of DA reported from Japanese, Western, Chinese, Malaysian, and Black populations.³ Data from different geographical regions seem to suggest a biogeographical pattern in that

the relative frequency of DA is slightly higher in Asian population.⁴

Size

In a review of 3677 ameloblastomas, Reichart et al reported that the average tumor size at the initial presentation was 4.3 cm (median, 3.0 cm). Therefore, it may be assumed that DA may be smaller than the “normal” type of ameloblastomas. There were neither statistical significance between the tumor size and localization, nor the recurrence.⁴

Location

Approximately half of the desmoplastic lesions are located in the maxilla, and the vast majority of them occur in the anterior mandible or premolar portion of the jaws.^{1,3} The maxillary sinus and mandibular ramus were involved in few cases. Whereas most lesions were one sided, few crossed the midline. Most of the patients presented with a painless swelling or a bone expansion, which was the most conspicuous clinical manifestation of the affected area.⁴ In case of maxillary sinus involvement, nasal and pharyngeal obstruction

occurred, however with a very small probability patients showed a buccal, palatal/ lingual and both a buccal and a palatal/lingual expansion.⁴

Radiographic features

The radiological information available for each reviewed case was not uniform. Tumors had mixed radiologic appearances, with poorly defined borders mimicking fibro-osseous lesions. Tumors presented as unilocular radiolucencies with specks of radiopacities and had well-circumscribed borders. Even though the tumors were located in the alveolar region, resorption of teeth was not seen.³ Computed tomography was performed in few cases usually detecting ill-defined, mixed radiolucency–radiopacity with buccal expansion.⁴ The cross-sectional occlusal radiograph of the mandibular lesions revealed a mixed radiolucent-radiopaque lesion with expansion of the buccal and lingual cortical plates. The panoramic radiograph showed the displacement. The axial section of computed tomography (CT) demonstrated permeative destruction of the buccal

bony cortex with a mesh of radio-opaque structures with ill-defined borders, suggestive of osteolysis and sclerotic changes, and the lingual bony cortex demonstrated thinning and partial destruction. The coronal CT demonstrated the sclerotic expansile destructive lesion with displacement of the teeth.⁵

Histopathology

The specimens showed few irregular epithelial islands in a densely fibrous connective stroma. The islands consisted of peripheral cuboidal cells and central spindle cells. Some of the islands showed cystic degeneration. Histologically, scattered epithelial nests and extensively desmoplasia were prominent features of DA.⁶ epithelial proliferation almost seem to be compressed and fragmented by the dense hyalinized stroma.⁷ Most desmoplastic ameloblastomas display occasional classic islands of follicular ameloblastoma among the predominant strands and cords.⁷ Typical ameloblastic columnar cells may be scant, and peripheral palisading may be absent. In the focal area, the islands have a swirled

hypercellular appearance. Osteoplasia may also be present. The surrounding stroma accompanied the cells islands are characterized for significant collagen proliferation. However, in some juxta epithelial area, loose myxoid changes can be found.⁴

Management

The types of treatment that have been used include both radical and conservative surgical excision, curettage, chemical and electrocautery, radiation therapy or a combination of surgery and radiation. The surgical plan should be influenced strongly by whether the lesion involves the mandible or maxilla. Maxillary lesions behave distinctly from mandibular lesions. The higher cancellous bone percentage in the maxilla facilitates the spread of ameloblastoma.⁷

Discussion

In 1984, Eversole established the report on DA to the English literature thereby describing three cases and called it an ‘ameloblastoma with pronounced desmoplasia’. In the WHO’s Histopathological Typing of

Odontogenic tumors 2005, DA is included as separate clinicopathological entity and classified ameloblastoma into four types as solid/multicystic, extra osseous, desmoplastic, and unicystic. The term “hybrid lesions” was introduced by Waldron and El Mofty reporting a condition in which DA was present close to follicular or plexiform ameloblastoma and Wakoh et al. presented a case of a patient demonstrating follicular type ameloblastoma with desmoplasia, in whom radiological findings suggested the coexistence of a fibro osseous lesion with a solitary cystic lesion and proposed it to be hybrid follicular/DA.^{1,8}

The majority of the cases has been reported particularly in Chinese residing in Malaysia and Hong Kong, Malaysians, Japanese and Afro-Caribbeans. Reports from various geographical regions hint at relatively higher frequency of desmoplastic ameloblastoma in Asians. However, more systematic studies on desmoplastic ameloblastoma are necessary to justify such suggestions.⁸ The etiologic factors described relate to the onset of the lesion after a local trauma, inflammation,

nutritional deficiencies, mutations and/or molecular alterations, where different signalling pathways participate. More recent theories indicate the existence of genetic anomalies related to the appearance of ameloblastomas, enabling less aggressive treatments.⁹

DA may develop in all ages; however, people of the 4th and 5th decade are more prone to be affected. No gender predilection of DA has been reported. Usually, the DA variation is smaller in size than other types of ameloblastoma. DA occurs in the anterior or premolar regions of the jaws and there is not any difference in prevalence between the maxilla and mandible. This represents a contrast with classic ameloblastomas, which are usually found in the posterior mandibular regions presenting a mandible to maxilla ratio of 5:1. The main symptom at first clinical examination of DA is a painless swelling, with frequently buccal expansion. Tooth displacement were frequently been seen.⁴ Tooth displacement is a common feature of DA. It has been reported to occur in almost 90% of cases, while root

resorption has been reported in approximately a quarter of cases.¹⁰

Frequently, the tumor is asymptomatic, the tumefaction is painless. and the expansion of the involved bone is the commonly observed clinical manifestations. Radiographically, other types of ameloblastomas are classically described as a unilocular or multilocular radiolucencies with well-defined borders, whereas DAs are usually described as poorly defined in most cases. In the series by Reichart et al. 51.1% of the tumors were described as unilocular, whereas 48.9% were described as multilocular or multicystic.⁴

The DA usually appears in the anterior and premolar regions as a mixed radiolucent and radiopaque lesion sometimes mimicking a benign fibro-osseous lesion. Approximately half of the reported lesions showed diffuse radiological borders and mimicking fibro-osseous lesions or malignant tumors. The lamina dura also was involved. The radiographic appearance may indicate that this tumor is more aggressive than other variants of ameloblastoma.⁴

Histologically, the odontogenic epithelium of DA form irregular, stellate, or follicular islands and cords, and the centers of such lesions often appear hypercellular and contain spindle-shaped or squamous cells. The most striking feature which separates DA from conventional ameloblastoma is the presence of extensive stromal desmoplasia with an abundance of thick collagen fibers which compress the odontogenic epithelial islands. Marked tumor growth factor- (TGF-) β expression has been reported in DA, but not in conventional ameloblastomas implying that TGF- β plays a part in the formation of the desmoplastic matrix. Scientists have also indicated an association between desmoplasia and the incidence of mucous cell metaplasia in ameloblastoma. Unlike with the conventional ameloblastomas, a strong positive reaction for collagen type VI has been observed in DA indicating active production of connective tissue within the stroma of DA. Previous studies report that DA tumor cells display variable S100 protein and desmin expression decreased cytokeratin 19 expression; and strong p63, caspase-3,

and Fas expression compared with conventional ameloblastoma cells. These expressions might contribute to the distinct characteristics of DA.¹⁰ Kishino et al. demonstrated oxytalan fibres in the stromal tissue of one case, suggesting that the tumor had derived from the epithelial rest of Malassez in the periodontal membrane of a neighbouring tooth.³

Conclusion

The DA is a rare variant of ameloblasoma. DA resemble fibro osseous lesions in clinical and radiographic features, histopathologic findings give the conclusive diagnosis. Treatment also varies with fibro osseous lesion and DA. Because of its aggressive nature a complete resection and long term follow up is required to check any recurrence and even prognosis.

Reference

1. Ahire MS, Tupkari JV, Chettiankandy TJ, Thakur A, Agrawal RR. Odontogenic tumors: A 35-year retrospective study of 250 cases in an Indian (Maharashtra) teaching institute. Indian J Cancer 2018; 55:265 72.

2. Neville, Brad W. Oral and Maxillofacial Pathology. St. Louis, Mo: Saunders/Elsevier, 2009
3. Sivapathasundharam B, Einstein A, Syed RI. Desmoplastic ameloblastoma in Indians: report of five cases and review of literature. Indian J Dent Res. 2007 Oct-Dec;18(4):218-21. doi: 10.4103/0970-9290.35836. PMID: 17938502.
4. Sun ZJ, Wu YR, Cheng N, Zwahlen RA, Zhao YF. Desmoplastic ameloblastoma - A review. Oral Oncol. 2009 Sep;45(9):752-9. doi: 10.1016/j.oraloncology.2009.01.016. Epub 2009 Jul 23. PMID: 19631576; PMCID: PMC6022750.
5. Athota A, Nagalaxmi V, Gandhi Babu D B, Nagabhushana D, Asif SM. Desmoplastic ameloblastoma in the anterior mandible crossing the midline: A rare variant. J Indian Acad Oral Med Radiol 2009; 21:134-8
6. Savithri V, Janardhanan M, Suresh R, Kumar RV. Desmoplastic ameloblastoma with osteoplasia: Review of literature with a case report. J Oral Maxillofac Pathol. 2013 May;17(2):298-301. doi: 10.4103/0973-029X.119784. PMID: 24250098; PMCID: PMC3830246
7. RRajendran;B Sivapathasundharam; William G Shafer NewDelhi: Elsevier/Reed Elsevier, 2009.
8. Sharma Lamichhane N, Liu Q, Sun H, Zhang W. A case report on desmoplastic ameloblastoma of anterior mandible. BMC Res Notes. 2016 Mar 16; 9:171. doi: 10.1186/s13104-016-1961-2. PMID: 26984790; PMCID: PMC4793556.
9. Cadavid, A.M.H., Araujo, J.P., Coutinho-Camillo, C.M. et al. Ameloblastomas: current aspects of the new WHO classification in an analysis of 136 cases. Surg Exp Pathol 2, 17 (2019). <https://doi.org/10.1186/s42047-019-0041-z>
10. Masayasu Iwase, Airi Fukuoka, Yoko Tanaka, Naoyuki Saida, Eriko Onaka, Sanae Bando, Gen Kondo, "Hybrid Desmoplastic/Follicular Ameloblastoma of the Mandible: A Case Report and Review of the Literature", Case Reports in Pathology, vol. 2017,

Article ID 7031414, 6 pages, 2017.

<https://doi.org/10.1155/2017/7031414>

Literature Review

CALCIFYING ODONTOGENIC CYST (COC)

*Dr Anu.PV, *Dr Ahna Ali Akbar, **Dr Rajeesh Mohammed, ***Dr Usha Balan

Abstract

The calcifying odontogenic cyst (COC), also known as “Gorlin Cyst” is a benign odontogenic cyst that occurs in the gnathic bone. This cyst is part of a spectrum of lesions characterized by odontogenic epithelium containing “ghost cells,” with a propensity to calcify.¹ It’s a relatively uncommon odontogenic lesion characterized by varied clinical, radiographical features and biological behaviour and can exhibit either as a cystic or a solid lesion. It has been known by different names and classified and sub-classified into various types.² This article discusses the literature regarding the various terminologies, classifications, clinical & histopathological features of COC.

Key Words: Calcifying odontogenic cyst, Ghost cell

Corresponding Author: Dr Anu.PV

* Post Graduate Student, **Professor and Head of the Department, ***Reader, Department of Oral Pathology, KMCT Dental College, Manassery, Kozhikode 673602, Kerala

Introduction

The calcifying odontogenic cyst (COC) was first described by Gorlin *et al.* in 1962. According to Altini and Farman, a similar condition had previously been mentioned in German literature in 1932 by Rywkind. Earlier it was thought to be an oral presentation of dermal calcifying

epithelioma of Malherbe.³ Although it may occur in soft tissue, COC is most commonly found within bone due to the presence of embryonic epithelial rests in these bones and a majority of them are remnants of odontogenic apparatus.¹

The calcifying odontogenic cyst (COC) is a developmental odontogenic cyst and

constitute about 0.3–0.8% of all odontogenic cysts.⁴ It is a heterogeneous lesion and shows extreme diversity in its clinical and histopathological features, as well as in its biological behaviour and there has always been a confusion and disagreement on the terminology and classification of this lesion.⁵

Concepts and Classifications:

Several classifications of COC have been suggested in literature, each trying to separate the cystic from solid variants, but none has been universally accepted. The solid variant of COC represent the ultimate phase of the evolution of COC, not necessarily a separate entity.

There are two different concepts or schools of thought depending on the nature of COC.⁶ The first concept is “monistic,” in which all COCs are neoplastic in nature, even though the majority are cystic and appear to be non-neoplastic and the second “dualistic” concept posits that COC contains two entities: a cyst and a neoplasm. Praetorius *et al* in 1981, framed a classification based on dualistic concept and proposed the term dentinogenic ghost cell tumour (DGCT) for the neoplastic variant.

In 1991, Buchner classified COC into peripheral COC and central COC based on clinical grounds and further subclassified each of them into cystic or neoplastic variants and included rare malignant variant of COC in this classification. Hong *et al.* in 1991, followed the dualistic concept and divided COC into cystic and neoplastic types. The cystic type is further subdivided into proliferative, non-proliferative, ameloblastomatous and odontoma associated and used a term epithelial odontogenic ghost cell tumour (EOGCT) for the solid variant.⁷

In 1998, the new dualistic classification of the so-called COC was given by Toida.⁶ He stated that in above classifications the term “cystic” used synonymous for “non-neoplastic” was incorrect and mentioned that there may be lesion with cystic architecture and extensive proliferating capacity. Toida proposed a classification in which he called CGCOC for the cystic variant and used the term calcifying ghost cell odontogenic tumour

(CGCOT) for the neoplastic variant. He further subdivided the neoplastic group into cystic CGCOT and solid CGCOT, to include

neoplasm showing cystic architecture and neoplasm with solid pattern.⁷

Li and Yu (2003) proposed a more concise terminology based on likely differences in biologic behaviour of the COC and its related lesions and classified the lesions into the following three groups:

1. Cysts
2. Benign tumours
3. Malignant tumours.

They suggested that the term COC should be used specifically for the unicystic lesions with or without an associated odontoma. Other suggested classifications of COCs were by Reichart *et al.*, 2004, and Praetorius in 2006. From the above-described classifications, it is plausible that the dualistic concept finds more favour among the researchers.⁷

WHO Classification

The approach of WHO toward CGCOC was different and mostly followed monistic concept. In 1971, WHO described the lesion as non-neoplastic cystic lesion and preferred to use the term COC. In 1992, WHO

classified this lesion under odontogenic tumour but continued to use the term calcifying odontogenic cyst. This terminology was misleading and could not explain the complete behaviour of the lesion.⁵ So, in 2005, WHO again renamed the lesion as calcifying cystic odontogenic tumour arising from odontogenic epithelium with ectomesenchyme, which can be associated or not with the formation of hard tissue. In 2017, the WHO reclassified this lesion as COC and included it in the group of odontogenic and non-odontogenic developmental cysts.⁷

Table 1: Classification of calcifying odontogenic cyst (Praetorius *et al*-1981)

Type	Description
1	Cystic
1a	Simple unicystic with little or no dentinoid
1b	Odontoma producing type
1c	Ameloblastomatous
2	Neoplastic variant Dentinogenic ghost cell tumour

Table 2: Classification of calcifying odontogenic cyst (Buchner, 1991)

Type	Description
<u>A</u>	Peripheral COC
	Cystic
	Neoplastic
<u>B</u>	Central COC
	Cystic
	1. Associated with Odontoma
	2. Associated with odontogenic tumours (Other than odontoma)
	3. Clear cell or pigmented variant
	Neoplastic variant
	Malignant COC

Table 3: Classification by Toida (1998)

Category	Type
Cyst	CGCOC
Neoplasm	CGCOT
	1. Benign CGCOT Cystic CGCOT Solid CGCOT
	2. Malignant CGCOT
Combined lesion	Odontoma Ameloblastoma Other odontogenic lesions

CGCOC = Calcifying ghost cell odontogenic cyst, CGCOT = Calcifying ghost cell odontogenic tumour

Different terminologies for COC

Gorlin et al. (1962)	Calcifying odontogenic cyst
Gold (1963)	Calcifying ghost cell odontogenic tumour (CGCOT)
Bhaskar (1965)	Keratinizing calcifying odontogenic cyst (KCOC)
Fejerskov and Krogh (1972)	Calcifying ghost cell odontogenic tumour (CGCOT)
Freedman et al. (1975)	Cystic calcifying odontogenic tumour (COCT)
Praetorius et al. (1981)	Dentinogenic ghost cell tumour (DGCT)
Ellis and Shmookler (1986)	Epithelial odontogenic ghost cell tumour (EOGCT)
Colmenero et al. (1990)	Odontogenic ghost cell tumour (OGCT)
Shear (1994)	Odontogenic ghost cell ameloblastoma (OGCA)
Wirshberg et al. (1994)	Odontocalcifying odontogenic tumour (OOT)
WHO classification (2005)	Calcifying cystic odontogenic tumour (CCOT)

Clinical presentation

The COC normally appears as a painless, slow-growing tumour, which affects the maxilla and mandible equally, showing a strong predilection for the anterior segment (incisor/canine area). It does not show any gender predilection, generally affects the young adults in the third to fourth decade of

life.⁸ Intraosseous lesions may produce a hard bony expansion. Extraosseous lesions usually appears as pink to red, circumscribed and elevated masses measuring up to 4 cm in diameter.⁶

Radiographic features

Radiographically, these lesions appear as unilocular, well-defined radiolucency, although multilocular radiolucency may also occur occasionally. Radiopaque structures, either irregular calcifications or tooth-like densities, may also be present within the lesion occasionally and opacities tend to be denser if the cyst is associated with a complex odontoma.¹ The cyst may cause lingual expansion and displacement of teeth along with the resorption of adjacent teeth in a few cases. Occasionally COC may cause perforation of the cortical plate.^{1,6}

Histopathology

The definitive diagnosis of COC is made histologically, due to the lack of characteristic clinical and radiological features, as well as the variable biological behaviour of the lesion. The histological features of a classic calcifying odontogenic cyst are characteristic. The microscopic features of lesion show fibrous capsule with a lining of odontogenic epithelium. The basal layer is made up of ameloblast-like columnar or cuboidal cells of 4–10 cell thickness, overlined by loosely arranged epithelial cells similar to stellate reticulum

of the enamel organ. Anucleated, eosinophilic, epithelial cells retaining their basic cellular outline, present either in the epithelial lining or connective tissue called “ghost cells” is a characteristic finding. These ghost cells may undergo calcification and lose their cellular outline to form sheet-like area.

Irregular masses of calcified structure indicating dysplastic dentin may present in association with basal layer denoting the inductive nature of the odontogenic epithelium.^{1,6,3} Melanin deposits are also seen in the epithelial lining in some cases.⁶ Confocal laser scanning microscopy observations have disclosed that COC ghost cells auto fluoresce. But possibly due to presence of hard keratin autofluorescence intensities are variable.⁹

Immunohistochemically, amelogenin protein is expressed chiefly in ghost cells. CK 19 protein and Bcl-2 protein is expressed mainly in the epithelial lining cells, whereas ghost cells are devoid of staining. In COC lining epithelial cells are sporadically positive for Ki-67 antigen. COCs with varying histological features have neoplastic potential and may not be separate entities.^{10,6}

Conclusion

Calcifying odontogenic cyst (COC) is a rare lesion and a thorough clinical, radiological and histological work-up thus becomes mandatory for arriving at a correct diagnosis and an effective plan for the treatment of the lesion accordingly. A regular follow-up protocol is important, especially when a particular histological work-up dictates that to rule out any future recurrence of the lesion as well as to rule out any possibility for malignant transformation of the persisting or recurring pathology.

Management of intraosseous COC is mainly by enucleation, with a low rate of recurrence, occurring in <5% of cases. However, if it is associated with another odontogenic tumour, the treatment and prognosis are likely to be same as for the associated tumour and a long-term follow-up of such patients should be performed.

Financial support and sponsorship

Nil

References

1. Santos, Hellen Bandeira de Pontes et al. "Calcifying Odontogenic Cyst

with Extensive Areas of Dentinoid: Uncommon Case Report and Update of Main Findings." *Case reports in pathology* vol. 2018 8323215. 10 May.2018.

doi:10.1155/2018/8323215

2. Jeddy N, Balaguhan S. Calcifying ghost cell odontogenic cyst: A review on terminologies and classifications. *J Oral Maxillofac Pathol* 2012; 16:450-3
3. Vatsyayan A, Adhyapok AK, Debnath SC, Malik K. Calcifying Odontogenic Cyst: Case Report and Review of Literature. *Int J Dent Med Res* 2014;1(4):69-75
4. Balaji SM, Rooban T. Calcifying odontogenic cyst with atypical features. *Ann Maxillofac Surg* 2012; 2:82-5.
5. Thinakaran M, Sivakumar P, Ramalingam S, Jeddy N, Balaguhan S. Calcifying ghost cell odontogenic cyst: A review on terminologies and classifications. *J Oral Maxillofac Pathol* 2012; 16:450-3.
6. Negi BS, Danish I, Gupta P, Sabharwal R. Calcifying

- odontogenic cyst – A review. J Sci Soc 2020; 47:3-7.
7. Arruda JA, Silva LV, Silva L, Monteiro JL, Álvares P, Silveira M, Sobral AP. Calcifying odontogenic cyst: A 26-year retrospective clinicopathological analysis and immunohistochemical study. J Clin Exp Dent. 2018 Jun 1;10(6): e542-e547. doi: 10.4317/jced.54528.
 8. Chandran A, Nachiappan S, Selvakumar R, Gunturu S, Lakshmi UV, Bharathi K, *et al.* Calcifying epithelial odontogenic cyst of maxilla: Report of a case and review and discussion on the terminology and classification. J Microsc Ultrastruct 2021; 9:98-102.
 9. Makarla S, Bhat M, Bavle RM, Kristam P. A confocal view of the calcifying odontogenic cyst: Report of two cases. Orofac Sci 2014; 6:131-6. Korean J Pathol. 2014;48(3):175-187
 10. Suk Keun Lee and Yeon Sook Kim. Current Concepts and Occurrence of Epithelial Odontogenic Tumours: II. Calcifying Epithelial Odontogenic Tumour Versus Ghost Cell Odontogenic Tumours Derived from Calcifying Odontogenic Cyst. The Korean Journal of Pathology 2014; 48: 175-187.