

The Implications of Endocrinology in Orthodontics – Literature Review

SUMMARY

Endocrinopathies have a variety of orofacial presentations which span from dental malocclusion to facial disfigurement. These characteristics depend on the nature and severity of the condition. An orthodontist should understand the body's physiological processes to be able to timely determine the optimum intervention and plan treatment stages accordingly in compromised individuals. Communication between the two specialties should be well coordinated and should help facilitate quality health care to the patient. This review was aimed to impart the basic knowledge and the pivotal guidelines for orthodontic management in these conditions. Systemic conditions require multidisciplinary management and the dental team should aim to provide quality oral health care to enhance the overall quality of life and the orthodontist plays a vital role in helping patients achieve physical and psychological health.

Key words: Endocrine System Diseases, Orthodontics, Hormones

Adeel Tahir Kamal¹, Hafiz Taha Mahmood², Mubassar Fida¹

¹ Section of Dentistry, Department of Surgery, The Aga Khan University Hospital, Karachi, Pakistan

² King Abdul Aziz Hospital, Ministry of Health, Saudi Arabia

REVIEW PAPER (RP)

Balk J Dent Med, 2020;8-13

Introduction

The success of orthodontic treatment lies in identifying the patient's needs and concerns and addressing them with the best hardware at an orthodontist's disposal. For achieving timely orthodontic correction, it is imperative that the patient is either disease free or the disease is in a controlled state¹. It is essential to understand the basics of human physiology and the interaction between medicine and orthodontic science to provide the best treatment outcome with the least undesirable side effects².

In the current era, more adults are seeking orthodontic treatment than before and this age group is affected by complicated medical conditions and their corresponding drug regimens. A prompt medical and drug history of the patient allows the orthodontist to know their patient and focus not only on the dentition and facial esthetics but also the patient's overall systemic health³.

The human body is regulated by hormones and any alteration can significantly affect orthodontic treatment and its outcome⁴. The endocrinologist is a specialist who deals with hormonal imbalances and helps manage these disorders. Orthodontic tooth movement involves

successive bone remodeling and complex interaction of local and systemic hormones, cytokines and chemokines. With the help of an endocrinologist, orthodontic treatment can be successful in patients who suffer from growth and bone metabolism related pathologies⁵.

A close communication with the endocrinologist is essential to provide quality care to orthodontic patients. A complete understanding of the patient's medical condition can help an orthodontist plan and execute treatment effectively⁶. Knowledge of the physiological processes and potential risks during orthodontic therapy can aid in planning mechanics and employing suitable appliances. This multidisciplinary approach to treatment can prove to be a significant benefit in terms of regular appointments and follow ups with monitoring of disease control or progression.

Endocrinological disorders have oral manifestations which are characteristic. Since an orthodontist usually sees their patients routinely on a 3-4 week basis, they are best suited to monitor a patient's progress if medically compromised⁵. In this review, the objective is to highlight the common disorders (Table 1), the diagnosis and the endocrinological and orthodontic management.

Table 1. Endocrinopathies in Orthodontics

Endocrinopathies in Orthodontics		
Condition	Significance	Comments
Diabetes Mellitus	Periodontal disease	Monitor control of diabetes.
Hyperthyroidism	↑ BMR, possible osteoporosis	Inquire control of disease
Adrenal Insufficiency	↓ tolerance to stress, delayed healing	Inquire steroid dosages
Osteoporosis	ONJ, delayed tooth movement	Inquire medications
Osteopetrosis	↑ bone mass, delayed dentition	Avoid orthognathic surgery
Vitamin D Deficiency	Delayed eruption, dental abscesses	Inquire nutritional disturbances
Fibrous Dysplasia	Facial disfigurement, malocclusion	Consider delaying treatment

Growth Hormone Abnormalities

Growth Hormone Excess

The pituitary gland is one of the most important endocrine glands in the human body. It is composed of anterior and posterior lobes, each contributing to the regulation of a number of physiological processes such as stress and growth³. It produces several hormones such as growth hormone (GH), luteinizing hormone (LH), prolactin (PRL), adrenocorticotrophic hormone (ACTH) and thyroid stimulating hormone (TSH).

An excessive production of growth hormone after adolescence causes acromegaly^{6,7}. The characteristic extra-oral features include a prominent forehead, growth of the nose and ears, deepening of the nasolabial folds and mandibular prognathism^{8,9}. When examined intra-orally, a common presentation of these patients is macroglossia. This can be attributed to the presence of obstructive sleep apnea syndrome. Patients present with a deep voice which is associated with laryngeal hypertrophy and enlargement of the sinuses¹⁰.

With the evaluation of significant symptoms in the craniofacial area and dental occlusion, Herrmann *et al.*¹¹ concluded that patients with acromegaly require exquisite oral and maxillofacial examination and excellent coordination among endocrinologists, dentists and oral surgeons when conducting treatment. A case report indicates that intervention in forms of transphenoidal surgery, medication and radiation therapy may be required before any orthodontic treatment begins¹².

Growth Hormone Deficiency

Children with growth hormone deficiency can suffer from inadequate growth due to an isolated deficiency or a combined disorder. Although they have normal growth for the first 6 months of life, growth reduces significantly thereafter¹³. Craniofacial development is hampered and leads to immature facial appearance, small facial dimensions and profile convexity.

Investigations have revealed that growth hormone deficiency related pathologies have significant gender dimorphism. Cephalometric analysis in males reveals an increased posterior facial height, short cranial base, mandibular length, total facial height and a retrognathic

facial type¹⁴⁻¹⁹. In addition, the mandibular ramus heights and corpus lengths have also been found to be reduced¹⁸. Females were found to have short anterior and posterior cranial base lengths and mandibular ramus heights^{15,16}.

Early intervention in children with a short stature and a known deficiency of growth hormone can result in effective correction of skeletal discrepancy²⁰. Several studies reported that patients treated with growth hormone replacement therapy have significant improvements in overall facial dimensions with improved mandibular ramal and basal lengths²⁰⁻²². However, orthodontic intervention did not contribute to significant improvements in the craniofacial skeleton and plays a greater role in alleviating dental malocclusion due to micrognathia²².

Diabetes Mellitus

Diabetes Mellitus (DM) is an endocrine disorder characterized by a triad of hyperglycemia, increased micturition and thirst. The etiology is either due to insufficient insulin production by the pancreas or the unresponsive behavior of body cells to insulin. If left uncontrolled or untreated, acute complications such as diabetic ketoacidosis and non-ketotic coma can occur. Long term chronic complications include cardiac stroke, renal failure, foot ulcers and eye damage. Recent studies have been reported that there are three types, type I (insulin-dependent DM), type II (non-insulin dependent DM) and type III which has been proposed for Alzheimer's disease where there is insulin resistance in the brain²³⁻²⁵.

An orthodontist must have comprehensive knowledge about how to manage their diabetic orthodontic patients. It is important to understand the pathophysiology of diabetes and its deleterious effects on periodontal health. It is imperative to note that periodontal consequences may exist in both types of diabetes. Periodontitis is the most common complication due to significantly reduced number and impaired function of polymorphonuclear leukocytes and poor collagen metabolism. This results in slow or impaired neutrophil chemotaxis and macrophage functions leading to delayed and compromised wound healing. In type I diabetes, it has been reported that there may be delayed skeletal

maturation and reduced angular and linear measurements on cephalometric examinations²⁴.

Orthodontic Considerations

In uncontrolled insulin dependent DM or non-insulin dependent DM ($Hb_{A1c} \geq 9\%$) patients are prone to periodontal breakdown. As a general rule, orthodontic treatment should always be initiated when the periodontium is sound and disease free. The orthodontist should educate patients about the potential side effects associated with orthodontic treatment. This may include microangiopathies that may cause the patient to experience iatrogenic odontalgia, sensitivity, pulpitis or in rare cases loss of tooth vitality. Patients should be advised to take the medicines prescribed by their diabetologist. Patients should be appointed in the morning hours and advised to take their usual meal and medications before arriving at the dental clinic.

Thyroid and Parathyroid Disorders

Hormones secreted by the thyroid gland maintain physiological functioning of the brain, heart and various muscles, whereas altered thyroid function may affect functioning of these organs²⁶. Alterations may be either due to an increased activity (hyperthyroidism) or decreased activity (hypothyroidism) of the thyroid gland.

Children with hypothyroidism have dental characteristics such as delayed tooth eruption, enamel hypoplasia and anterior open bite, whereas children with hyperthyroidism may suffer from accelerated tooth eruption, macroglossia and maxillary and mandibular osteoporosis. The impact of variations in thyroid function within the normal or subclinical range and their effects on dental tissue in healthy children need to be further investigated.

Orthodontic Considerations

Orthodontic therapy should be instituted in patients with adequately managed thyroid disease. In hyperthyroidism, an enlarged tongue may pose problems during treatment. The bone turnover can also influence orthodontic tooth movement. High bone turnover in hyperthyroidism can increase the amount of tooth movement compared to normal or low bone turnover states in adult patients. Abuabara²⁷ reported an increased risk of external apical root resorption related to hypothyroidism due to low bone turnover.

Vitamin D Deficiency

Vitamin D deficiency has been recognized as a global issue²⁸. In the recent past, effective measures to control this condition have reduced the risk of suffering from this deficiency.²⁸ Vitamin D deficiency in children is called rickets and osteomalacia in adults. Genetic causes and variants of this condition include vitamin D resistant (type I-II) and x-linked hypophosphatemic rickets (Table 2)²⁹.

Table 2. Genetic Etiologies of Vitamin D Conditions

Genetic Etiologies of Vitamin D Conditions	
Vitamin D Resistant Rickets (Hypophosphatemic)	X-linked dominant
Vitamin D Deficiency Rickets	Nutritional
Type I Vitamin D Dependent	Autosomal Recessive
Type II Vitamin D Dependent	Autosomal Recessive

Bone formation is a series of events involving the deposition of osteoid which is later mineralized. During new bone formation, the failure of the mineralization leads to Rickets. Bone remodeling brings about change in existing bone and a failure of remineralization in this process is known as osteomalacia. The early management of this condition is critical with the need to identify skeletal abnormalities such as delayed development and bowing of legs, craniofacial abnormalities such as frontal bossing and delayed dental eruption and enamel hypoplasia.

Hypophosphatemic vitamin D resistant rickets with 1- α hydroxylase deficiency may present with muscle weakness, seizures and tetany. Dental manifestations include hypoplastic enamel that has yellow to brown discoloration, defective dentin mineralization, gingivitis and periodontitis. Radiographic features include large tooth pulp chambers and shortened roots. Histologically, there is abnormal enamel matrix and dysplastic dentin. A common clinical presentation entails the formation of channels between the pulp chamber and dentinoenamel junction which allow microorganisms to enter the pulp causing dental abscesses²⁹.

Orthodontic Considerations

Nutritional supplementation has been recommended for infants, children and pregnant females. Early diagnosis of this condition is required to prevent the development of adverse effects. Patients with the x-linked disorder are advised good oral hygiene and may require dental restorations such as crowns.

Fibrous Dysplasia

Fibrous dysplasia is a benign developmental disorder of the skeletal tissue. It occurs due to defective osteoblastic differentiation and maturation which results in destruction and replacement of normal bone with fibrous tissue³⁰. A patient may present between the ages of 3-13 years with extra-oral findings such as facial asymmetry and gingival swelling which may be evident intra-orally³⁰.

McCune Albright syndrome is classically defined as a triad of fibrous dysplasia, café-au-lait spots and precocious puberty³¹. Other complications that may occur include estrogen secreting ovarian cysts and a few cases may report hyperthyroidism, cortisol, growth

hormone excess and hyperprolactinemia. Café-au-lait spots are associated with this syndrome and have a typical presentation and unilateral distribution on the body. The features related to this condition include well defined radiological lesions with thin cortices and a ground glass appearance resulting from calcification of fibrous tissue.

Orthodontic Consideration

Patients with this condition may present with significant dental complications such as numerous carious teeth, facial pain originating from the maxilla or mandible, facial disfigurement and dental malocclusion. An interdisciplinary approach involving the periodontist, endodontist and orthodontist can help manage the oral health conditions. Previous reports^{31,32} indicate prolonged orthodontic treatment times and a greater risk of relapse in these patients. Delaying treatment till after attaining skeletal maturity is preferred. Bone pain in these patients is commonly managed with bisphosphonate therapy, however the risk of osteonecrosis of the jaws is not commonly encountered due to the doses administered.

Adrenal Disorders

Adrenal insufficiency occurs when the adrenal cortex is unable to produce adequate levels of cortisol and aldosterone³³. The etiology includes autoimmune disorders, infectious agents, genetic, metastatic, hemorrhagic conditions, infiltrative disorders, surgery and drugs. Recent prevalence rates include 4-6 cases/million/year³³.

The symptoms reported by a majority of patients include postural dizziness, joint and muscle pain, abdominal pain, fatigue, salt craving, loss of appetite and vomiting. Indicative signs of the disease include skin hyperpigmentation, hypotension and weight loss. These symptoms rapidly decline after hormone replacement therapy is started although many patients may still report salt craving and postural dizziness³⁴.

Orthodontic Considerations

Patients may be under corticosteroid therapy and their regime should be evaluated for the past year³⁵. Short term steroid administration leads to reduced bone turnover and a decrease in orthodontic tooth movement. In contrast, long term steroid administration hastens bone turnover leading to increased orthodontic tooth movement. Short term administration is favorable in cases of areas with increased anchorage requirement. Patients undergoing long term steroid administration should be recalled at a two week interval due to chances of rapid orthodontic tooth movement.

Steroid cover should be considered when planning minor oral surgical procedures. Orthodontic appointments should be scheduled with strict management and coordination to maintain minimum psychological and physical stress to these patients. This reduces the risk of

inducing an acute adrenal crisis, however in emergency situations steroids should be available for I/M or I/V administration³⁶.

Osteoporosis

Osteoporosis is a condition characterized by a loss of mineral substance from bone, leading to bone fragility. It most commonly affects postmenopausal women and results in 1.5 million fractures per year in the United States³⁷. The prevalence of osteoporosis varies depending on whether it is defined by fracture incidence or by low bone mineral density (BMD) (a T-score of 2.5 or less)³⁸. The risk of an osteoporotic fracture is 50% in white women^{39,40}. Fractures of the hip and spine result in a dramatic reduction in the quality of life and life expectancy.

Orthodontic Considerations

Orthodontic treatment must include the consideration of problems such as bone loss, retention instability and temporomandibular dysfunction³⁶. Problems associated with medications must also be considered. Estrogen replacement therapy decreases the rate of tooth movement⁴¹. However, if these drugs are not used during orthodontic treatment in patients with osteoporosis, resorption of alveolar bone and possibly tooth roots could occur. Use of bisphosphonates (BP) can affect orthodontic treatment by delaying tooth eruption, inhibiting tooth movement⁴², impairing bone healing and causing BP-induced osteonecrosis of the jaws (ONJ). BP inhibits osteoclasts, decreases microcirculation and thus impedes tooth movement⁴³. Extraction protocols and the use of temporary anchorage devices should be avoided⁴⁴.

Osteopetrosis

Osteopetrosis is a group of rare bone disorders within the family of sclerosing bone dysplasias characterized by reduced osteoclastic bone resorption resulting in a high bone mass (Figure 1) ⁴⁵. Rather than conferring strength, the overlying dense bone architecture belies a structural brittleness that predisposes to fracture. The disruption of normal bone modeling and remodeling can give rise to skeletal deformity and dental abnormalities and can interfere with mineral homeostasis. In addition, expansion of bone into marrow cavities and cranial nerve foramina can compromise hematologic and neurologic function, respectively. The former may manifest as profound anemia, bleeding, frequent infections, and hepatosplenomegaly from extramedullary hematopoiesis. The latter can lead to blindness, deafness, and nerve palsies^{46,47}.

Orthodontic Considerations

The extra-oral manifestations of osteopetrosis include facial growth anomalies. Intra-orally, there may be malformed teeth, unerupted teeth and delayed

development of the dentition. Recurrent osteomyelitis of the mandible is also common. It is necessary to first manage the condition through controlling hypercalcemia and anemia. Bone marrow transplant should follow⁴⁸. Orthodontic management to settle dental occlusion can be performed to improve function, however orthognathic surgery or distraction can result in serious consequences⁴⁹.



Figure 1. Increased Bone Density in Osteopetrosis

Conclusions

The objective of this review was to discuss the orthodontic considerations in patients suffering from endocrinological disorders and highlight essential considerations for the management of these patients. Systemic conditions require multidisciplinary management and the dental team should aim to provide quality oral health care to enhance the overall quality of life. The orthodontist can provide the patient with better oral function and help improve self confidence in a difficult time.

References

1. Graber LW, Vanarsdall RL, Vig KW, Huang GJ. Orthodontics: Current Principles and Techniques. 5 th ed. Elsevier Health Sciences; 2016.
2. Patel A, Burden DJ, Sandler J. Medical disorders and orthodontics. J Orthod, 2009;36:1-21.
3. Kovacs K, Horvath E, Vidal S. Classification of pituitary adenomas. J Neurooncol, 2001;54:121-127.
4. Vilar L, Vilar CF, Lyra R, Naves LA. Acromegaly: clinical features at diagnosis. Pituitary, 2017;20:22-32.
5. Melmed S, Kleinberg D. Anterior pituitary. In: Reed Larsen P, Kronenberg HM, Melmed S, Polonsky KS, editors. Williams textbook of Endocrinology. 10th ed. Philadelphia: Saunders; 2003.
6. Choi SH, Fan D, Hwand MS, Lee HK, Hwang CJ. Effect of growth hormone treatment on craniofacial growth in children: idiopathic short stature versus growth hormone deficiency. J Formos Med Assoc, 2017;116:313-321.
7. Miranda-Rius J, Brunet-Lobet L, Lahor-Soler E, de Dios-Miranda D, Gimenez-Rubio A. GH-secreting pituitary macroadenoma (acromegaly) associated with progressive dental malocclusion and refractory CPAP treatment. Head Face Med, 2017;13:7.
8. Naves LA, Mercado M, Duarte FG, Vilar BF, Vilar L. Acromegaly – an overview. In: Vilar L, editor. Endocrinologia Clínica (Clinical Endocrinology). 6th ed. Rio de Janeiro: Guanabara Koogan; 2016. p. 56-70.
9. Davidopoulou S, Chatzigianni A. Craniofacial morphology and dental maturity in children with reduced somatic growth of different aetiology and the effect of growth hormone treatment. Prog Orthod, 2017;18:10.
10. MacGillivray MH. Disorders of growth and development. In: Felig P, Baxter JD, Broodu E, Frohman LA, editors. Endocrinology and Metabolism. 2nd Edition. New York: McGraw-Hill Book Co; 1987.
11. Herrmann BL, Mortsch F, Berg C, Weischer T, Mohr C, Mann K. Acromegaly: a cross-sectional analysis of the oral and maxillofacial pathologies. Exp Clin Endocrinol Diabetes, 2011;119:9-14.
12. Vitral RWF, Tanaka OM, Fraga MR, Rosa EAR. Acromegaly in an orthodontic patient. Am J Orthod Dentofacial Orthop, 2006;130:388-390.
13. Bevis RR, Hayles AB, Isaacson RJ, Sather AH. Facial growth response to human growth hormone in hypopituitary dwarfs. Angle Orthod, 1977;47:193-205.
14. Salas-Flores R, González-Pérez B, Barajas-Campos RL, Gonzalez-Cruz B. Changes on craniofacial structures in children with growth-hormone deficiency. Rev Med Inst Mex Seguro Soc, 2010;48:591-595.
15. Keller EE, Sather AH, Hayles AB. Dental and skeletal development in various endocrine and metabolic diseases. J Am Dent Assoc, 1970;81:415-419.
16. Konfino R, Pertzalan A, Laron Z. Cephalometric measurements of familial dwarfism and high plasma immunoreactive growth hormone. Am J Orthod, 1975;68:196-201.
17. Pirinen S, Majurin A, Lenko HL, Koski K. Craniofacial features in patients with deficient and excessive growth hormone. J Craniofac Genet Dev Biol, 1994;14:144-152.
18. Poole AE, Greene IM, Buschang PH. The effect of growth hormone therapy on longitudinal growth of the oral facial structures in children. Prog Clin Biol Res, 1982;101:499-516.
19. Cantu G, Buschang PH, Gonzalez JL. Differential growth and maturation in idiopathic growth-hormone-deficient children. Eur J Orthod, 1997;19:131-139.
20. Oliveira-Neto LA, Melo Mde F, Franco AA, Oliveira AH, Souza AH, Valença EH, et al. Cephalometric features in isolated growth hormone deficiency. Angle Orthod, 2011;81:578-583.

21. Van Erum R, Mulier M, Carels C, Verbeke G, de Zegher F. Craniofacial growth in short children born small for gestational age: effect of growth hormone treatment. *J Dent Res*, 1997;76:1579-1586.
 22. Kjellberg H, Wikland KA. A longitudinal study of craniofacial growth in idiopathic short stature and growth hormone-deficient boys treated with growth hormone. *Eur J Orthod*, 2007;29:243-250.
 23. Sonwane S, Shweta RK, Kumar SB, Shett RGK. Chronic congenital systemic disorder- a hurdle in orthodontic treatment plans: meta-analysis. *Int J Med Res Health Sci*, 2016;5:239-247.
 24. Giannini C, Mohn A, Chiarelli F. Growth abnormalities in children with type 1 diabetes, juvenile chronic arthritis and asthma. *Int J Endocrinol*, 2014;14:1-10.
 25. De la Monte SM, Wands JR. Alzheimer's disease is type 3 diabetes – evidence reviewed. *J Diabetes Sci Technol*, 2008;2:1101-1113.
 26. Vucic S, Korevaar TIM, Dharmo B, Jaddoe VWV, Peters RP, Wolvius EB et al. Thyroid function during early life and dental development. *J Dent Res*, 2017;96:1020-1026.
 27. Abuabara A. Biomechanical aspects of external root resorption in orthodontic therapy. *Med Ora Patol Oral Cir Bucal*, 2007;12:610-613.
 28. Fiscoletti M, Stewart P, Munns CF. The importance of vitamin D in maternal and child health: a global perspective. *Public Health Rev*, 2017;38:19.
 29. Hanna AE, Sanjad S, Andrary R, Nemer G, Ghafari JG. Tooth development associated with mutations in hereditary vitamin D-resistant rickets. *JDR Clin Trans Res*, 2018;3:28-34.
 30. Burke AB, Collins MT, Boyce AM. Fibrous dysplasia of bone: craniofacial and dental implications. *Oral Dis*, 2017;23:697-708.
 31. Dumitrescu CE, Collins MT. McCune-Albright syndrome. *Orphanet J Rare Dis*, 2008;3:12.
 32. Akintoye SO, Boyce AM, Collins MT. Dental perspectives in fibrous dysplasia and McCune Albright syndrome. *Oral Surg Oral Med Oral Pathol Oral Radiol*, 2013;116:1-12.
 33. Reddy K, Anitha E. Orthodontic management of medically compromised patients. *Ann Essences Dent*, 2009;1:1-11.
 34. Erichsen MM, Lovas K, Skinningsrud B, Wolff AB, Undlien DE, Svartberg J, et al. Clinical, immunological, and genetic features of autoimmune primary adrenal insufficiency: observations from a Norwegian registry. *J Clin Endocrinol Metab*, 2009;94:4882-4890.
 35. Bensing S, Hulting AL, Husebye ES, Kampe O, Lovas K. Epidemiology, quality of life and complications of primary adrenal insufficiency: a review. *Eur J Endocrinol*, 2016;175:107-116.
 36. Maheshwari S, Verma SK, Ansar J, Prabhat KC. Orthodontic care of medically compromised patients. *Indian J Oral Sci*, 2012;3:129-137.
 37. Hernandez CJ, Guss JD, Luna M, Goldring SR. Links between the microbiome and bone. *J Bone Miner Res*, 2016;31:1638-1646.
 38. Weaver CM. Diet, gut microbiome, and bone health. *Curr Osteoporos Rep*, 2015;13:125-130.
 39. Weaver C, Gordon C, Janz K, Kalkwarf H, Lappe J, Lewis R, et al. The National Osteoporosis Foundation's position statement on peak bone mass development and lifestyle factors: a systematic review and implementation recommendations. *Osteoporosis Int*, 2016;27:1281-1386.
 40. Takaishi Y, Arita S, Honda M, Sugishita T, Kamada A, Ikeo T, et al. Assessment of alveolar bone mineral density as a predictor of lumbar fracture probability. *Adv Ther*, 2013;30:487-502.
 41. Miyajima K, Nagahara K, Iizuka T. Orthodontic treatment for a patient after menopause. *Angle Orthod*, 1996;66:173-178.
 42. Bartzela T, Türp JC, Motschall E, Maltha JC. Medication effects on the rate of orthodontic tooth movement: a systematic literature review. *Am J Orthod Dentofacial Orthop*, 2009;135:16-26.
 43. Igarashi K, Mitani H, Adachi H, Shinoda H. Anchorage and retentive effects of a bisphosphonate (AHBuBP) on tooth movements in rats. *Am J Orthod Dentofacial Orthop*, 1994;106:279-289.
 44. Graham JW. Bisphosphonates and orthodontics: Clinical implications. *J Clin Orthod*, 2006;40:425-428.
 45. Tolar J, Teitelbaum SL, Orchard PJ. Osteopetrosis. *N Engl J Med*, 2004;351:2839-2849.
 46. Faden MA, Krakow D, Ezgu F, Rimoin DL, Lachman RS. The Erlenmeyer flask bone deformity in the skeletal dysplasias. *Am J Med Genet A*, 2009;149:1334-1345.
 47. Wu CC, Econs MJ, Dimeglio LA, Insogna KL, Levine MA, Orchard PJ, et al. Diagnosis and management of osteopetrosis: consensus guidelines from the osteopetrosis working group. *J Clin Endocrinol Metab*, 2017;102:3111-3123.
 48. Krishnan V, Davidovitch Z. *Integrated Clinical Orthodontics*. Wiley-Blackwell; 2012.
 49. Khoja A, Fida M, Shaikh A. Pycnodysostosis with special emphasis on dentofacial characteristics. *Case Rep Dent*, 2015;2015: 817989.
- Conflict of Interests:** Nothing to declare.
Financial Disclosure Statement: Nothing to declare.
Human Rights Statement: None required.
Animal Rights Statement : None required.
- Received on July 21, 2019.**
Revised on September 1, 2019.
Accepted on December 11, 2019.
-
- Correspondence:
Adeel Tahir Kamal
Aga Khan University Hospital
Karachi, Pakistan
e-mail: adeelkamal_01@hotmail.com