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Case Report | **Pediatric Dentistry and Orthodontics**

Dental Treatment of Cystic Fibrosis for Pediatric Patient – Case Report

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Abstract

Cystic fibrosis (CF) is the most common, life-threatening, autosomal-recessive disorder among Caucasians. Some of the mutations are very rare, and some represent individual sequence changes in the gene. In this case report, we present the dental treatment of CF in a 5 years old Saudi female. She has poor oral hygiene, poor dietary intake, generalized mild plaque induced gingivitis, multiple carious teeth, and a negative behavior. In addition, clinical and radiographic examinations indicated the presence of taurodontism and congenital absence of lingual frenum. We discuss the effect of the disease process on dental and oral health and management in the dental setting.

Keywords: Cystic fibrosis, dental rehabilitation, general anesthesia, medically compromised, lingual frenum, taurodontism.

INTRODUCTION

Cystic Fibrosis (CF) is a terminal, multisystem disorder with an autosomal recessive inheritance pattern (Abdulrahman Rasheed, 2019). This disease causes a disturbance in the ion channels which consequently alters the normal epithelial secretions into a viscous and thickened layer in the lungs, pancreas, biliary tract and reproductive organs (Harrington, Barry, & Barry, 2016). CF has been described as the most common genetic lethal disorder among Caucasians (Abu-Zahra *et al*., 2019; Afify & Zawawi, 2012). CF is common in many countries worldwide, including developed and developing countries with an annual incidence of (1000) cases and a prevalence of (70) thousand individuals (Chi, 2013; Grosse *et al*., 2004). The largest CF population in the range of the Arabian Gulf and the Middle East is reported in Saudi Arabia due to consanguineous marriages. The prevalence of CF varies considerably in the country, with highest reported in eastern, central, and western regions at rates of (37%), (28%) and (22%) respectively. Considerably lower rates are recognized in the southern region (8%) and northern region (5%) (Banjar, 1999).

This genetic disease has been linked to chromosome 7 with multiple mutations of a single gene (Cystic Fibrosis Transmembrane Regulator [CFTR]) (Chi, 2013). Consequently, affecting the regulation of cellular chloride channels which indirectly regulates sodium, potassium and carbonate ions flow through different epithelioid ion channels and transporters. Thus, producing secretions that are more mucus in nature (Abdulrahman Rasheed, 2019). Clinical findings in conjugation with biochemical or genetic testing are utilized as diagnostic methods of CF (Naehrig, Chao, & Naehrlich, 2017). Approximately, 1600 mutations of CFTR are detected with 10% of cases are identified at birth or during the first three years of life due to being symptomatic (Filbrun, Lahiri, & Ren, 2016). Hence, newborn screening of CF has been developed as Immunoreactive Trypsinogen (IRT) and sweat chloride test which is considered the gold standard in CF diagnosis (Filbrun *et al*., 2016; Naehrig *et al*., 2017). Collaborative efforts developed to improve life expectancy of CF patients through earlier diagnosis and palliative treatment that has extended their lifespan from only a few months to 40 years of age (Naehrig *et al*., 2017).

Effect of CF on Respiratory System

The most reported cause of morbidity and mortality of CF has been attributed to respiratory disease (Davies, Alton, & Bush, 2007). The previously mentioned thick mucus secretions represent a persistent and ideal habitat for the harboring pathogens; chronic infection and continuous tissue destruction lead to

bronchiectasis which is manifested as reproductive cough, shortness of breath and limitation of physical activity over time (Harrington *et al*., 2016). Preventing acute episodes of respiratory disease is by utilizing targeted nebulized and oral antibiotics to suppress the level of infection (Döring, Flume, Heijerman, & Elborn, 2012). Such acute exacerbation ultimately progresses into failure of the respiratory system which necessitates the need for supportive oxygen therapy or lung transplantation (Harrington *et al.*, 2016). In conjugation to the lower respiratory tract, unfortunately, CF affects the upper respiratory tract as well. Sinuses may become chronically harbored by pathogens. Nasal polyps and sinusitis are commonly presented (Gysin, Alothman, & Papsin, 2000). Furthermore, CF patients are at risk of vestibular problems and sensory-neural hearing loss as a result of a long-term exposure to antibiotics to treat respiratory infections (Farzal, Kou, St John, Shah, & Mitchell, 2016).

Effect of CF on the Digestive System

CF patients experience maldigestion, malabsorption, liver and pancreatic disease, rectal prolapse, intestinal obstruction and neonatal meconium ileus due to abnormal secretions of the bile and pancreas. Most individuals have pancreas dysfunction with exocrine pancreatic insufficiency (Harrington *et al*., 2016). The co-occurrence of malabsorption and hypermetabolism lead to chronic constipation, bowel obstruction, intussusception and gastrointestinal reflux. Thus, CF patients require a high calorie diet to compensate for malnutrition. Furthermore, nutritional intake is critical to CF patients' health and survival (Harrington *et al*., 2016; Moursi, Fernandez, Daronch, Zee, & Jones, 2010). The earliest clinical feature is detected in 20% of infants diagnosed with CF as meconium ileus. The condition is described as the obstruction of the terminal ileum by feces (Naehrig *et al*., 2017).

Effect of CF on Bone, Skin and the Reproductive System

One of the most challenging manifestations in patients with CF is bone disease, including systemic glucocorticoids, malnutrition and vitamin D osteoporosis and osteopenia which occur due to deficiency (Plant, Goss, Plant, & Bell, 2013). Low-impact fractures may occur as a result of Osteoporosis which is treated by bisphosphonate therapy. Hence, CF patients may be at risk of medication related osteonecrosis (Conwell & Chang, 2014). In addition, arthropathy musculoskeletal abnormalities are commonly presented as chronic joint pain and have been referred to as Cystic Fibrosis Related Arthritis (CFRA). Another severe but rare complication of CF is vasculitis which mostly involves the skin and is often linked with arthralgias (Harrington *et al*., 2016). Patients with CF have salty tasting skin due to excessive excretion of chloride in their sweat and it is considered as one of the key diagnostic tests for CF termed as sweat chloride test (Kessler & Andersen, 1951). Although infertility occurs in most male patients due to the congenital absence of the vas deferens which prevent semen production. Parenting is deemed possible for CF male patients through advanced medical procedure by surgical extraction of spermatozoa (McCallum *et al*., 2000).

Oral Health in Children with CF

Sugar-containing food is consumed more frequently by children with CF as a result of their need to maintain a high caloric and salt intake. Despite these dietary recommendations, caries incidence has been reported to be lower than in a healthy population of the same age (McCallum *et al*., 2000). The impact of long-term antibiotic and pancreatic enzyme replacement therapy on the oral microbiota may be linked to the lower caries rate (Littleton & White, 1964; Mahaney & McCoy, 1986). Increased levels of salivary calcium and phosphate in CF patients are incorporated into the enamel surface may be a post-eruptive maturational process that gives the tooth more resistant to demineralization (Primosch, 1980). Moreover, xerostomia is commonly reported in CF patients as a consequence of salivary glands disruption and medications (Harrington *et al*., 2016).

Maintaining the welfare of patients diagnosed with CF is of importance to their health, nevertheless, dental and oral health in these patients is indispensable to their quality of life (Nährlich & Zimmer, 2013). Extensive treatment is necessary as CF patients age; lung transplant might be indicated in advanced disease status. Therefore, regular dental care will aid towards the prevention of extreme episodes of dental disease which might hinder necessary medical treatment (Abu-Zahra, Antos, Kump, & Angelopoulou, 2019; Narang, Maguire, Nunn, & Bush, 2003). Caries prevention and risk reduction of dental diseases are obtainable by adhering to oral health measures, which improve the oral health of CF patients by 60% to 90% (Abu-Zahra *et al*., 2019). This case report will discuss the effect of the disease process on oral health and the dental care of pediatric patients diagnosed with Cystic Fibrosis which also includes dental treatment of Taurodontism.

CASE PRESENTATION

A 5 years old Saudi female attended pediatric dentistry clinic at King Saud University Dental Hospital – King Khalid University Hospital for dental treatment with a chief complaint by her father “My daughter has several cavities and previous abscesses”.

Medical history showed that the patient is a known case of cystic fibrosis diagnosed at age of 4 years by two sweat chloride tests, she completed full term birth by cesarean section and her immunization is up to date. She is an only child; her mother is a 30-year-old housewife and her father is a 34-year-old governmental employee. Both parents are medically fit.

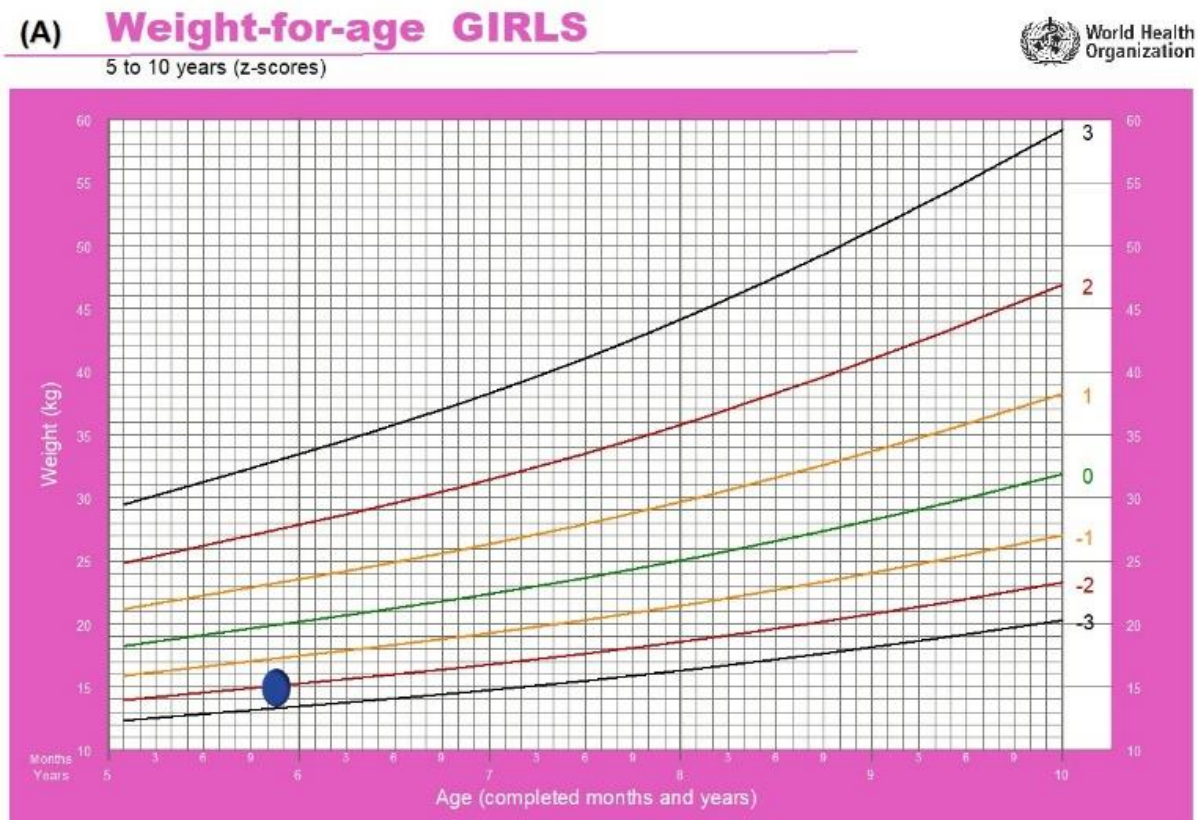
However, they are first-degree relatives, middle class, with a history of familial CF.

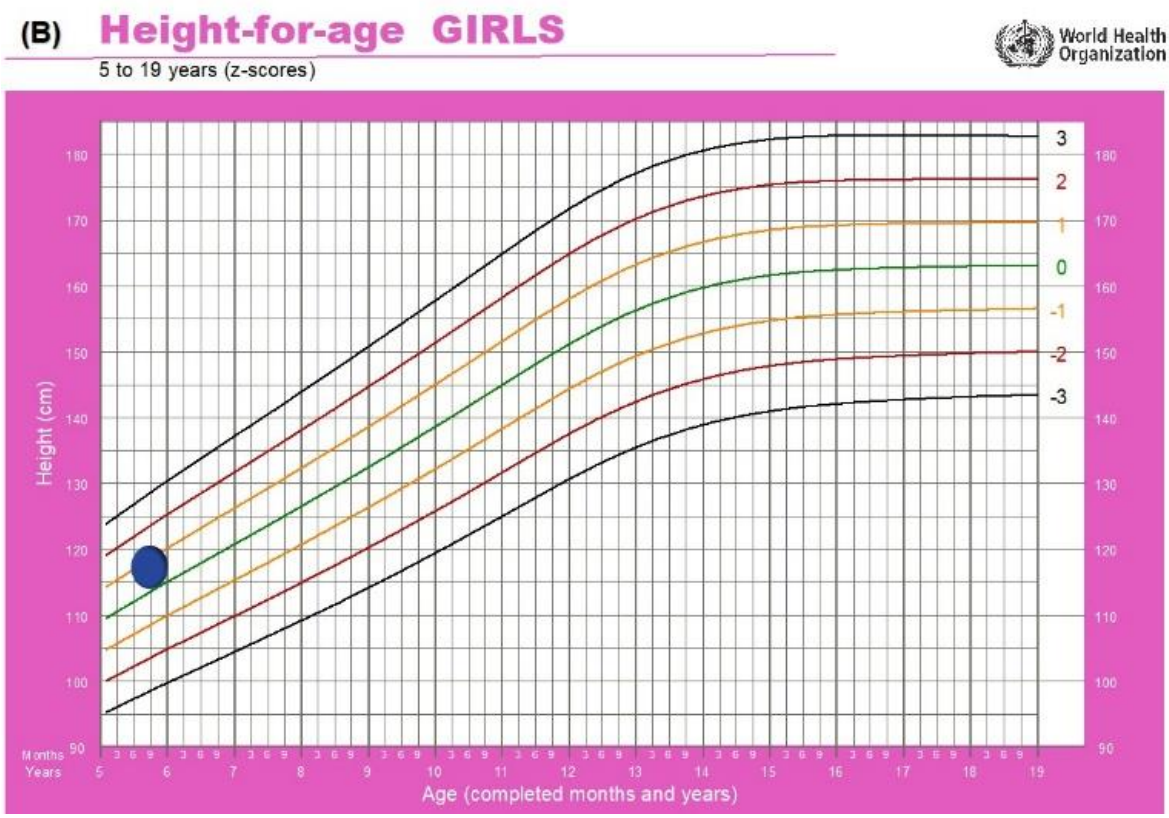
The patient is on the following medications; daily A, D, E and K vitamin replacements, Ventolin 2.5mg twice daily, NACL (3%) 3mL twice daily, daily chest physical therapy, and Tobramycin 300mg once/month.

The patient was prescribed nutritional supplements to compensate for the lack of appetite and poor absorption attributed to pancreatic insufficiency. Furthermore, the patient is prescribed a high calorie-diet of 1600kcal/day and 20mg protein/day. The patient was advised to drink 2 bottles of nutritional shakes each day for six months (500ml/day). Infancy feeding of breastfeeding for 2 months, bottle feeding for 24 consecutive months with no report of night feeding and no history of pacifier use or other oral habits as well as irregular brushing without assistance. No previous dental visits and no history of trauma. The child has a negative behavior (Frankl II) along with positive parents' behavior.

INVESTIGATIONS

Fig-1: Extra Oral Examination (A) Frontal view (B) Lateral view, convex profile (C) Nail clubbing





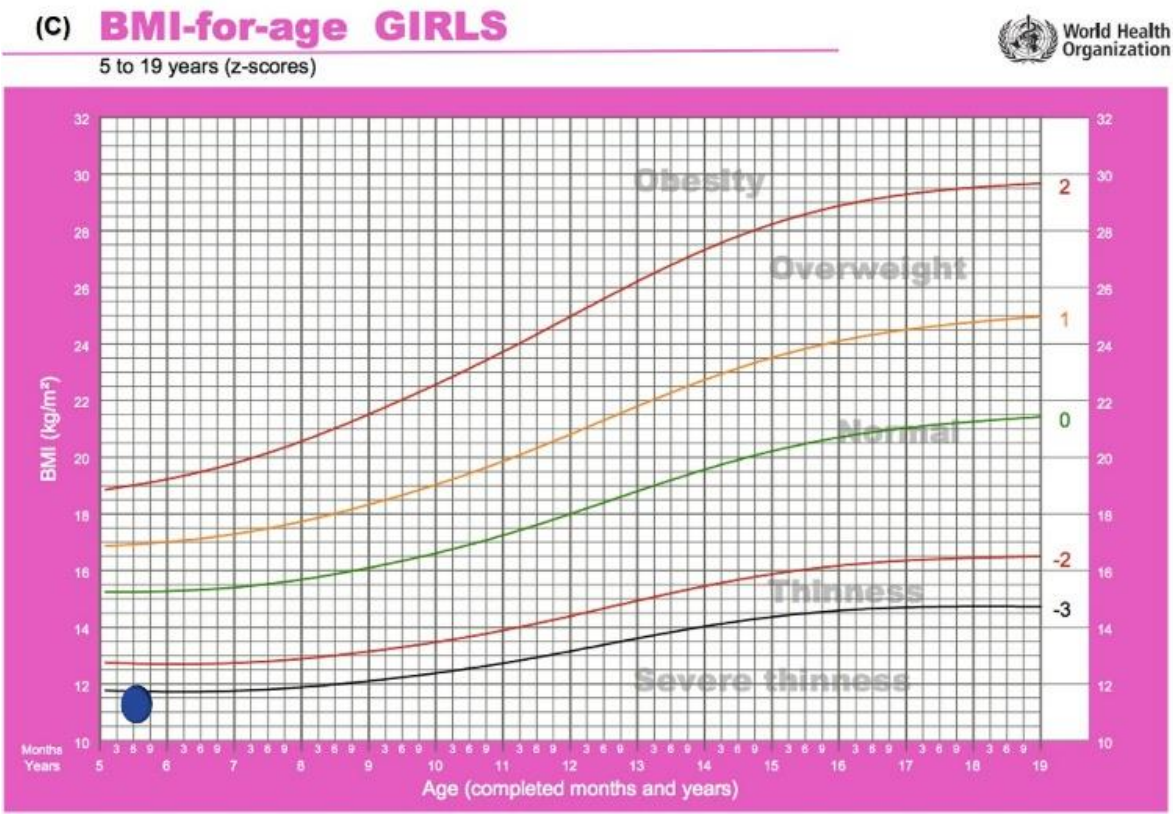


Fig-2: The circle represents the patient in comparison of her age group, (A) underweight with 14.35 Kg, (B) Average height of 114 cm and (C) Body mass index of 11 which is considered sever thinness.

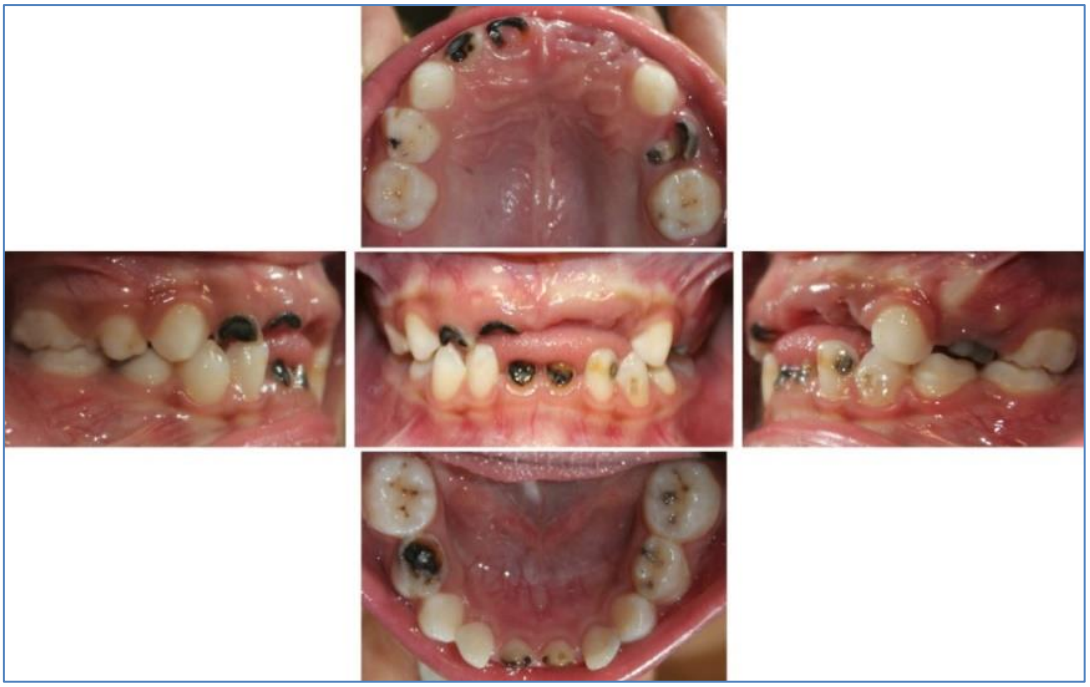


Fig-3: Pre-Operative Intra-Oral photographs. Notice absence of lingual frenum

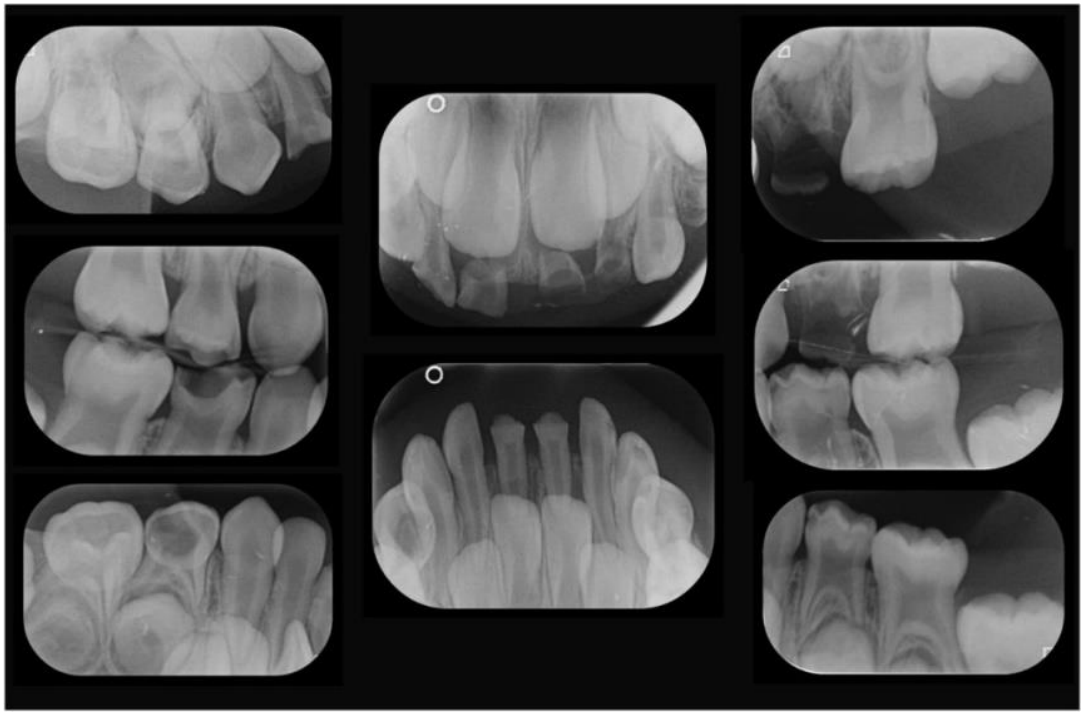


Fig-4: Pre-Operative radiographs, notice taurodontism in primary molars.

DIAGNOSIS

The patient is 5 years, 5 months old Saudi female, with a known case of Cystic Fibrosis, failure to thrive, and recurrent respiratory exacerbations. She has poor oral hygiene, poor dietary intake, generalized mild plaque induced gingivitis, multiple carious teeth, and a negative behavior (Frankle II). Patient is medically compromised, requires multiple dental needs, and have acute situational anxiety.

Patient is regarded to be underweight with average height in relation to her age group, along with a BMI of 11 which is considered as severe thinness (Figure 2). The patient has symmetrical face with a convex profile, dry lips and nail clubbing of the hands (Figure 1). Functional assessment revealed normal TMJ and mandibular movement with breathing difficulties (wheezing). Absence of lingual frenum in the floor of the mouth and a gingival abscess related to the maxillary left first primary molar. The child is in

primary dentition phase with poor OH, U-shape maxillary arch, overjet and overbite are not applicable and no crossbite was detected. She has mesial step molar classification and class I canine classification on both sides (Figures 3& 4).

To conclude the problem list of the case is as follows: Cystic fibrosis, inadequate nutrition intake, insufficient weight gain. Dental problem list consisted of: visible plaque deposits and cavitated teeth, taurodontism, erosion, missing lingual frenum, poor oral hygiene with negative behavior.

TREATMENT

To be treated under general anesthesia, she was cleared from her physician as her overall health was well and chest was clear. Her pediatrician recommended to continue with her current treatment regimen of: Tobramycin nebulizers (300) mg twice daily - alternate every (28) days, stress on good chest physical therapy daily with Ventolin and (3%) NACL.

Following physician's recommendations admitted as in-patient. On the day of surgery, dental treatment performed under general anesthesia started with prophylaxis. Following Federation Dentaire Internationale (FDI) numbering system; Resin composite restorations were placed in all second primary molars, lower left canine and lower left lateral incisor (FDI: #55, 65, 75, 73, 72, 85), Mineral-trioxide-aggregate (MTA) Pulpotomy of lower left first primary molar (FDI: #74), Stainless steel crown performed on the upper right first primary molar and lower left first primary molar (FDI: #54, 74) and extraction of hopeless teeth under local anesthesia to reduce postoperative pain in recovery period upper incisors, upper right first primary molar, lower central incisors and lower right first primary molar (FDI: #52,51,61,62,64,71,81,84). Pre-fabricated space maintainer (DeNovo space maintainer) was place in the maxillary arch from upper left second primary molar to the primary canine (FDI: #65 to #63) and mandibular arch from lower right second primary molar to the primary canine (FDI: #85 to #83). Patient's recovery was uneventful and post-operative visit was scheduled after 2 weeks followed by 6 months recall visit.

Outcome and follow-up

Post-operative visit of the patient after 6 months

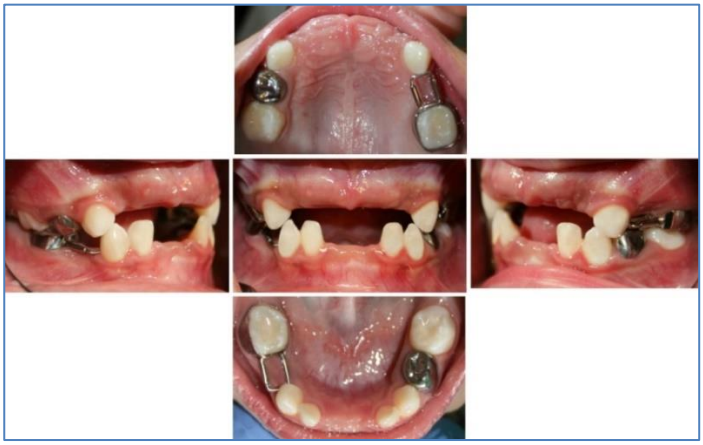


Fig-5: Post-Operative Intra-Oral photographs, 6 months recall

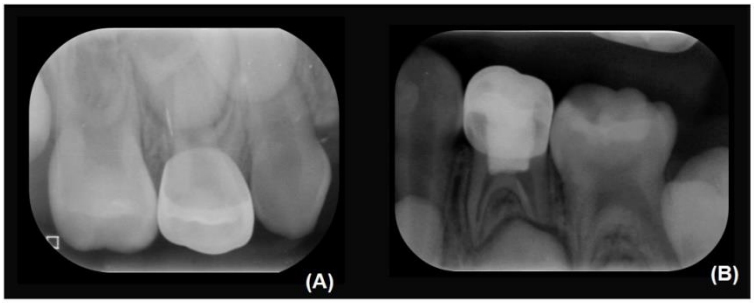


Fig-6: Post-Operative radiographs, 6 months recall of (A) Upper right primary molars and (B) Lower left primary molars.

DISCUSSION

According to the American Academy of Pediatric Dentistry guidelines, one of the most important purposes of this dental area is to provide "both primary and comprehensive preventive and therapeutic oral health care to individuals with Special Health Care Needs (SHCNs)", as an integral part of the pediatric dentistry practice. In this same context, the term SHCNs refers to those children with "any

physical, developmental, cognitive, or emotional impairment or limiting condition that requires medical management, healthcare intervention, and/or the use of specialized services or programs" (Gómez-González, Rosales-Berber, De Ávila-Rojas, Pozos-Guillén, & Garrocho-Rangel, 2020). CF patients are considered to have a high risk for dental diseases as a consequence of their nutritional intake of high calorie diet and medications with high percentage of sugar along with the association of gastroesophageal reflux (Barry, Fleming, & O'Connor, 2009; Scott, O'Loughlin, & Gall, 1985). The current evidence contradicts the previous assumption as the literature reports low caries levels along with markedly decrease in caries rates of CF patients in comparison of their healthy siblings (Jagels & Sweeney, 1976).

Xerostomia is a frequent condition in CF patients because of medications and salivary gland dysfunction (Harrington *et al*., 2016). Mucous secreting glands demonstrate CFTR protein therefore changing their structure and function (Mandel, Kutscher, Denning, Thompson, & Zegarelli, 1967). On the other hand, serous parotid glands are not affected which is explained due to elevated buffering capacity of secreted saliva and an alkaline environment (Di Sant'Agnese & Davis, 1976; Kinirons, 1983). Xerostomia might be exacerbated by mouth breathing due to chronic rhino-sinusitis (Brihaye, Jorissen, & Clement, 1997). Absence of proper lubrication will lead to food and plaque accumulation on teeth and gingiva thereby contributing to periodontal disease and caries development. Saliva can be stimulated pharmacologically and by sugar-free chewing gum, saliva substitute, and fluoride application will improve patients' quality of life (Plemons, Al-Hashimi, & Marek, 2014; Villa, Connell, & Abati, 2015).

Teeth discoloration of CF patients has been attributed to antibiotics use during dental development as tetracyclines, doxycycline, linezolid, and carbapenems (Harrington *et al*., 2016). Moreover, presence of dental anomaly along with the detection of enamel related abnormalities have markedly increased in CF pediatric patients (Azevedo, Feijó, & Bezerra, 2006; Narang *et al*., 2003). Furthermore, an experimental study concluded that low expression of CFTR contributes to hypomineralization of enamel as it is significant for pH regulation during enamel development (Sui, Boyd, & Wright, 2003).

Taurodontism is a morpho-anatomical variation in the tooth which the tooth's body is enlarged on the expense of the roots. Enlargement of the pulp chamber leading apically displaced furcation area (Mena, 1971). There have been numerous hypotheses about what causes taurodontism. Its occurrence has been linked to various syndromes and genetic abnormalities it has associated with rare syndromes likes Williams syndrome, McCune-Albright syndrome, and Van der Woude syndrome (Manjunatha & Kovvuru, 2010). In addition to several anomalies and developmental syndromes such as amelogenesis imperfecta and ectodermal dysplasia, Tricho-Dento-Osseous syndrome, Mohr syndrome, Down's syndrome, and Wolf-Hirschhorn syndrome (Manjunatha & Kovvuru, 2010).

A significant finding of this case report is related to the detection of taurodontism in the primary dentition along with the fact that according to the literature taurodontism has not been reported in CF patients. Nevertheless, the incidence of taurodontism in primary dentition is (0.3%) compared to a higher percentage in permanent dentition of 5.67 to 14% (Bäckman & Wahlin, 2001). In Saudi Arabia specifically, taurodontism was the least frequently reported dental anomaly of 0.1% (Afify & Zawawi, 2012). Despite its rarity, taurodontism increases the risk of pulp exposure and must be emphasized due to its impact on different dental treatments. Furthermore, root canal system complexities represent a challenge during endodontic treatment due to buccal orifices proximity and extraction of those tooth is frequently challenging due to apically placed furcation area (Manjunatha & Kovvuru, 2010).

In conjugation of hard tissue discoloration caused by antibiotics, soft tissue staining has been reported as well, mainly the tongue which manifested as black hairy tongue. Another frequent condition is oral candidiasis which is a consequence of inhaled corticosteroids (Balfour-Lynn & Welch, 2014; Khasawneh, Moti, & Zorek, 2013).

No literature has reported the congenital absence of lingual frenulum in CF patients; however, such finding has been linked to Ehler-Danlos syndrome infantile hypertrophic pyloric stenosis. The lingual frenum absence is rare in healthy patients but, it was reported in an adult patient (Filfilan & Almazrooa, 2020; Savasta *et al*., 2021). Lingual frenum supports tongue movement and provides support of ventral tongue to the floor of the mouth; its' absence result in loss of control on tongue movements thus affecting speech and deglutition (Felemban & Mawardi, 2019).

Erosion of two central incisors was caused by the use of inhalers. Regular use of inhalers or nebulizers would increase risk of tooth decay and erosion (Manuel, Kundabala, Shetty, & Parolia, 2008). Repetitive exposure and acidic environment provided by medications such as bronchodilators, corticosteroids, and anticholinergic drugs weakens the tooth structure. Such clinical manifestation is frequently present in patients with bronchitis. This finding is noted in this report by lower centrals being badly affected (Manuel *et al*., 2008).

CONCLUSION

Dental prevention is crucial due to treatment limitations in CF patients, through periodic professional care and high adherence to oral hygiene instructions. Moreover, nutritional intake plays an important factor to CF patients' wellbeing and survival, thus the dental team should not advise their patients to reduce the amount of intake of meals and beverages guided by their high-calorie diet. Parental education and encouragement of periodic dental care is importance as oral health should be advised as part of CF healthcare team as frequent application of oral hygiene in CF children has been related to their parents increased health awareness and motivation (Narang *et al*., 2003). Establishing appropriate dental home regimen by guiding CF patients brush twice daily with fluoridated toothpaste and floss regularly followed by regular recall visits every 3 months and radiographic imaging as necessary every 6 months to assess the status of the dentition, proper oral hygiene habits, apply fluoride and provide restorative treatment.

Disclosure

The author reports no conflicts of interest in this work.

REFERENCES

- Abdulrahman Rasheed, R. (2019). Cystic Fibrosis Diagnosis and Management in Children: A Simple Literature Review. *Archives of Pharmacy Practice, 10*(3), 4.
- Abu-Zahra, R., Antos, N. J., Kump, T., & Angelopoulou, M. V. (2019). Oral health of cystic fibrosis patients at a north american center: A pilot study. *Med Oral Patol Oral Cir Bucal, 24*(3), e379-e384. doi:10.4317/medoral.22756
- Afify, A. R., & Zawawi, K. H. (2012). The prevalence of dental anomalies in the Western region of saudi arabia. *ISRN Dent, 2012*, 837270. doi:10.5402/2012/837270
- Azevedo, T. D., Feijó, G. C., & Bezerra, A. C. (2006). Presence of developmental defects of enamel in cystic fibrosis patients. *J Dent Child (Chic), 73*(3), 159-163.
- Bäckman, B., & Wahlin, Y. B. (2001). Variations in number and morphology of permanent teeth in 7-year-old Swedish children. *Int J Paediatr Dent, 11*(1), 11-17. doi:10.1046/j.1365-263x.2001.00205.x
- Balfour-Lynn, I. M., & Welch, K. (2014). Inhaled corticosteroids for cystic fibrosis. *Cochrane Database Syst Rev*(10), Cd001915. doi:10.1002/14651858.CD001915.pub4
- Banjar, H. (1999). Geographic distribution of cystic fibrosis transmembrane regulator gene mutations in Saudi Arabia. *East Mediterr Health J, 5*(6), 1230-1235.
- Barry, S., Fleming, P., & O'Connor, M. (2009). Prescribing sugar-containing medicines for children--are we forgetting "primum non nocere"? *Ir Med J, 102*(9), 298-300.
- Brihaye, P., Jorissen, M., & Clement, P. A. (1997). Chronic rhinosinusitis in cystic fibrosis (mucoviscidosis). *Acta Otorhinolaryngol Belg, 51*(4), 323-337.
- Chi, D. L. (2013). Dental caries prevalence in children and adolescents with cystic fibrosis: a qualitative systematic review and recommendations for future research. *Int J Paediatr Dent, 23*(5), 376-386. doi:10.1111/ipd.12042
- Conwell, L. S., & Chang, A. B. (2014). Bisphosphonates for osteoporosis in people with cystic fibrosis. *Cochrane Database Syst Rev, 2014*(3), Cd002010. doi:10.1002/14651858.CD002010.pub4
- Davies, J. C., Alton, E. W., & Bush, A. (2007). Cystic fibrosis. *Bmj, 335*(7632), 1255-1259. doi:10.1136/bmj.39391.713229.AD
- Di Sant'Agnese, P. A., & Davis, P. B. (1976). Research in cystic fibrosis (first of three parts). *N Engl J Med, 295*(9), 481-485. doi:10.1056/nejm197608262950905
- Döring, G., Flume, P., Heijerman, H., & Elborn, J. S. (2012). Treatment of lung infection in patients with cystic fibrosis: current and future strategies. *J Cyst Fibros, 11*(6), 461-479. doi:10.1016/j.jcf.2012.10.004
- Farzal, Z., Kou, Y. F., St John, R., Shah, G. B., & Mitchell, R. B. (2016). The role of routine hearing screening in children with cystic fibrosis on aminoglycosides: A systematic review. *Laryngoscope, 126*(1), 228-235. doi:10.1002/lary.25409
- Felemban, R., & Mawardi, H. (2019). Congenital absence of lingual frenum in a non-syndromic patient: A case report. *Journal of Medical Case Reports, 13*, 56. doi:10.1186/s13256-018-1966-7
- Filbrun, A., Lahiri, T., & Ren, C. (2016). *Handbook of Cystic Fibrosis*.
- Filfilan, R. O., & Almazrooa, S. A. (2020). Double lingual frenulum: a case report. *J Med Case Rep, 14*(1), 116. doi:10.1186/s13256-020-02440-7
- Gómez-González, A., Rosales-Berber, M., De Ávila-Rojas, P., Pozos-Guillén, A., & Garrocho-Rangel, A. (2020). Pediatric Dental Management of an Uncommon Case of Mucopolysaccharidosis Type IV A (Morquio A Syndrome): A Case Report of a Three-Year Follow-Up. *Case Rep Dent, 2020*, 2565486. doi:10.1155/2020/2565486
- Grosse, S. D., Boyle, C. A., Botkin, J. R., Comeau, A. M., Kharrazi, M., Rosenfeld, M., & Wilfond, B. S. (2004). Newborn screening for cystic fibrosis: evaluation of benefits and risks and recommendations for state newborn screening programs. *MMWR Recomm Rep, 53*(Rr-13), 1-36.
- Gysin, C., Alothman, G. A., & Papsin, B. C. (2000). Sinonasal disease in cystic fibrosis: clinical characteristics, diagnosis, and management.

Pediatr Pulmonol, 30(6), 481-489. doi:10.1002/1099-0496(200012)30:6<481::aid-ppul8>3.0.co;2-n

- Harrington, N., Barry, P. J., & Barry, S. M. (2016). Dental treatment for people with cystic fibrosis. *Eur Arch Paediatr Dent, 17*(3), 195-203. doi:10.1007/s40368-016-0229-9
- Jagels, A. E., & Sweeney, E. A. (1976). Oral health of patients with cystic fibrosis and their siblings. *J Dent Res, 55*(6), 991-996. doi:10.1177/00220345760550065101
- Kessler, W. R., & Andersen, D. H. (1951). Heat prostration in fibrocystic disease of the pancreas and other conditions. *Pediatrics, 8*(5), 648-656.
- Khasawneh, F. A., Moti, D. F., & Zorek, J. A. (2013). Linezolid-induced black hairy tongue: a case report. *J Med Case Rep, 7*, 46. doi:10.1186/1752-1947-7-46
- Kinirons, M. J. (1983). Increased salivary buffering in association with a low caries experience in children suffering from cystic fibrosis. *J Dent Res, 62*(7), 815-817. doi:10.1177/00220345830620070801
- Littleton, N. W., & White, C. L. (1964). Dental findings from a preliminary study of children receiving extended antibiotic therapy. *J Am Dent Assoc, 68*, 520-525. doi:10.14219/jada.archive.1964.0111
- Mahaney, M. C., & McCoy, K. S. (1986). Developmental delays and pulmonary disease severity in cystic fibrosis. *Hum Biol, 58*(3), 445-460.
- Mandel, I. D., Kutscher, A., Denning, C. R., Thompson, R. H., Jr., & Zegarelli, E. V. (1967). Salivary studies in cystic fibrosis. *Am J Dis Child, 113*(4), 431-438. doi:10.1001/archpedi.1967.02090190077005
- Manjunatha, B. S., & Kovvuru, S. (2010). Taurodontism –A Review on its etiology, prevalence and clinical considerations. *J Clin Exp Dent, 2*, 1-5. doi:10.4317/jced.2.e187
- Manuel, S. T., Kundabala, M., Shetty, N., & Parolia, A. (2008). Asthma and dental erosion. *Kathmandu Univ Med J (KUMJ), 6*(23), 370-374. doi:10.3126/kumj.v6i3.1714
- McCallum, T. J., Milunsky, J. M., Cunningham, D. L., Harris, D. H., Maher, T. A., & Oates, R. D. (2000). Fertility in men with cystic fibrosis: an update on current surgical practices and outcomes. *Chest, 118*(4), 1059-1062. doi:10.1378/chest.118.4.1059
- Mena, C. A. (1971). Taurodontism. *Oral Surg Oral Med Oral Pathol, 32*(5), 812-823. doi:10.1016/0030-4220(71)90308-2
- Moursi, A. M., Fernandez, J. B., Daronch, M., Zee, L., & Jones, C. L. (2010). Nutrition and oral health considerations in children with special health care needs: implications for oral health care providers. *Pediatr Dent, 32*(4), 333-342.
- Naehrig, S., Chao, C. M., & Naehrlich, L. (2017). Cystic Fibrosis. *Dtsch Arztebl Int, 114*(33-34), 564-574. doi:10.3238/arztebl.2017.0564
- Nährlich, L., & Zimmer, K. P. (2013). Neonatal cystic fibrosis screening--time to begin! *Dtsch Arztebl Int, 110*(20), 354-355. doi:10.3238/arztebl.2013.0354
- Narang, A., Maguire, A., Nunn, J. H., & Bush, A. (2003). Oral health and related factors in cystic fibrosis and other chronic respiratory disorders. *Arch Dis Child, 88*(8), 702-707. doi:10.1136/adc.88.8.702
- Plant, B. J., Goss, C. H., Plant, W. D., & Bell, S. C. (2013). Management of comorbidities in older patients with cystic fibrosis. *Lancet Respir Med, 1*(2), 164-174. doi:10.1016/s2213-2600(13)70025-0
- Plemons, J. M., Al-Hashimi, I., & Marek, C. L. (2014). Managing xerostomia and salivary gland hypofunction: executive summary of a report from the American Dental Association Council on Scientific Affairs. *J Am Dent Assoc, 145*(8), 867-873. doi:10.14219/jada.2014.44
- Primosch, R. E. (1980). Tetracycline discoloration, enamel defects, and dental caries in patients with cystic fibrosis. *Oral Surg Oral Med Oral Pathol, 50*(4), 301-308. doi:10.1016/0030-4220(80)90411-9
- Savasta, S., Bassanese, F., Hruby, C., Foiadelli, T., Siri, B., Gori, V., . . . Marseglia, G. L. (2021). Absence of lingual frenulum in children with Ehlers-Danlos Syndrome: a retrospective study of forty cases and literature review of a twenty years long debate. *Minerva Pediatr (Torino), 73*(3), 230-235. doi:10.23736/s0026-4946.19.05530-0
- Scott, R. B., O'Loughlin, E. V., & Gall, D. G. (1985). Gastroesophageal reflux in patients with cystic fibrosis. *J Pediatr, 106*(2), 223-227. doi:10.1016/s0022-3476(85)80291-2
- Sui, W., Boyd, C., & Wright, J. T. (2003). Altered pH regulation during enamel development in the cystic fibrosis mouse incisor. *J Dent Res, 82*(5), 388-392. doi:10.1177/154405910308200512
- Villa, A., Connell, C. L., & Abati, S. (2015). Diagnosis and management of xerostomia and hyposalivation. *Ther Clin Risk Manag, 11*, 45-51. doi:10.2147/tcrm.S76282