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Hereditary Dental Diseases – Clinical Diagnosis and Strategies for Treatment and Rehabilitation

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Abstract

AIM: The research has been aimed at optimization of approaches to diagnosis, prevention, and treatment strategies to the hereditary dental diseases based on the analysis of modern relevant information.

METHODS: Using the methods of content analysis and cluster analysis, the information included in periodicals, as well as educational and non-regulatory publications for the period of 2011–2019, was systematized and structured; the analysis of sources devoted to modern approaches to the diagnosis, prevention, and treatment of hereditary dental diseases, their genetic etiology, with the description of clinical cases and illustrations for each example, was conducted; hereditary dental diseases were classified; based on a comparative analysis, approaches to the diagnosis, treatment, and prevention of these diseases were optimized.

RESULTS: The most significant hereditary dental diseases have been identified, the classification of approaches to their diagnosis and treatment has been presented, the scheme of drug therapy has been optimized depending on the pathology.

CONCLUSION: The systematic analysis of information on hereditary dental diseases with the description of clinical cases for each nosology has been carried out for the 1st time, and the approaches to their diagnosis and treatment have been optimized with due consideration of domestic and foreign experience.

Introduction

Hereditary diseases occupy an important place in modern medicine [1], [2]. It should be noted that this section is the least studied one in dentistry, therefore, analysis of literature data on the problems of hereditary diseases affecting hard tissues of teeth is of particular interest to dental science and practice and is becoming the subject of research today.

There are a number of domestic and foreign studies devoted to hereditary dental diseases with descriptions of clinical cases and illustrations for each example.

The significance of systematization of such studies on hereditary dental diseases is due to the development of treatment standards, inclusion in modern teaching aids, incorporation in the clinical practice of a dentist, and the conduct of further scientific research.

The research has been aimed at optimization of approaches to the diagnosis, prevention, and treatment strategies of the hereditary dental diseases based on the systematization and analysis of relevant modern information.

Methods

Using the method of content analysis and cluster analysis, information and analytical studies were carried out; information included in periodicals, as well as in educational and non-regulatory publications for the period of 2011–2019, was systematized and structured; sources devoted to modern approaches to the diagnosis, prevention, and treatment of hereditary dental diseases, their genetic etiology, with the description of clinical cases and illustrations for each example, was analyzed; hereditary dental diseases were classified; based on comparative analysis, approaches to the diagnosis, treatment, and prevention of hereditary dental diseases were optimized.

Results

According to the information and analytical studies, the following diseases are considered to be

among the serious hereditary diseases in dentistry: Amelogenesis imperfect (AI), dentinogenesis imperfecta (DI), dentin dysplasia (DD), and marble bone disease (MBD). The etiological factor of these pathologies is mutations in the genes that lead to various dentofacial abnormalities.

AI is a hereditary disease induced by genetic mutations and characterized by violation of the tooth enamel formation. Both temporary and permanent teeth are affected. Inheritance can be of autosomal dominant, autosomal recessive, X-linked, or autosomal dominant type, with the latest being the most common one [1], [2], [3].

AI should be differentiated from other dental disorders caused by teeth development violation under the influence of environmental factors (fluorides, tetracyclines, etc.).

In 1991, the cause of AI was announced to be the mutations in the AMELX gene which encodes an extracellular matrix protein produced by ameloblasts during enamel formation. Since then, scientists have found that this disease was also induced by disorders in at least another 18 genes [1]. Some genes encode enamel proteins, both structural (amelogenin, enamelin, ameloblastin, and c4orf26) and enzyme (kallikrein 4 and MMP20) ones, other genes encode transcription factors (MSX2 and DLX3), cellular proteins (WDR72, FAM83H, and COL17A1), cellular receptor (ITGB6), and calcium transporter (SLC24A4) [2].

The color of the teeth varies from light yellow to dark brown. Vestibular surfaces of teeth are more affected than the oral ones. The surfaces are rough. Preserved enamel is chalky, without gloss, easily detachable. As a result of exposure of dentin, increased sensitivity to thermal and mechanical stimuli is noted [3].

According to the Witkop and Sauk classification (1976), there are four clinical forms of AI [4], [5].

1. The hypoplastic AI implies quantitative deficiency of enamel characterized by its partial or full decrease. The enamel is thin, but mineralized, in rare cases, it can be completely absent. The enamel surface is rough, with point defects or larger lesions, with vertical and horizontal grooves. There are no contact points between adjacent teeth. The teeth color varies from yellow to light brown. As a rule, patients with this type of pathology do not complain of hyperesthesia, however, under the influence of chemical and thermal stimuli, they may experience short-term painful sensations [2].

Clinical case

A 4–5-year-old patient came to the Center for Rare Diseases in Paris. According to her mother, the girl complained of pain during eating, hyperesthesia when brushing her teeth, and, in addition, the poor appearance of her teeth. When examining the oral cavity, hypoplastic AI was revealed.

Figure 1 shows intraoral photographs of a patient with hypoplastic AI. The teeth are yellow in color with rough surface and characteristic brown spots. The enamel is sufficiently thinned and hypoplastic, which may look like false microdontia with multiple diastema. The molars are the most affected, the height of the crowns is greatly reduced (a, c). In addition, the child has an open bite (b).

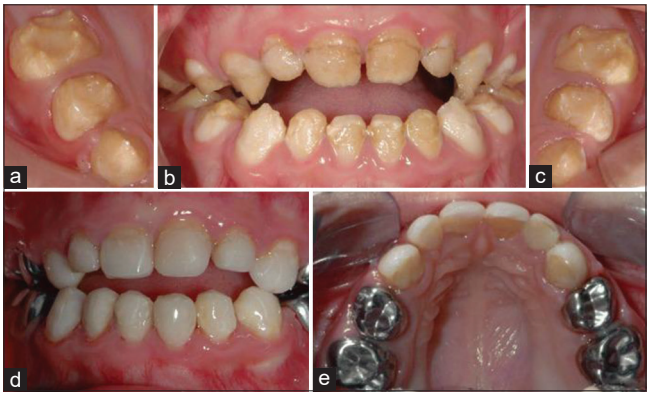

Figure 1: (a-e) Intraoral photographs as an example of hypoplastic AI before and after its treatment

Treatment

Due to the fact that in this case, it was necessary to prevent pain and maximally preserve intact hard tissues to provide correct occlusion and restore aesthetics, the treatment consisted of placing metal crowns on molars and restoring the anterior teeth with composite. Figure 1 illustrates the treatment result: Molars were covered with stainless steel crowns, incisors and canines were restored using composite materials (d, e) [6]. After treatment, the patient was under the supervision of doctors for a year for assessing the quality of dental restoration and the oral hygiene level.

2. Hypomineralized (hypocalcified) AI is the most severe form of AI. The mineral component of the enamel is strongly reduced, thus, some areas or sometimes even the entire surface of the crown lack hardness. The teeth are dark yellow or brown in color due to enamel underdevelopment and partial or complete dentin exposure. As a result, patients often complain of pain during chewing (due to dentin exposure to various kinds of irritants: Chemical, thermal, and mechanical) and brushing. On radiographs, enamel and dentin are visualized like tissues of the same density. Such patients are usually very restless and anxious due to persistent toothache [2].

Clinical case

An 8-year-old patient turned to the Paris Center for Rare Diseases with complaints of pain when

the teeth were affected by the temperature changes, which deteriorated her oral hygiene. There were also complaints of snoring during sleeping, probably due to unerupted maxillary lateral incisors. Moreover, the patient experienced pain while chewing, brushing her teeth and, even when breathing, complained of esthetics due to mockery and insults of schoolmates. At the oral cavity examination, temporary and permanent teeth (the first molars and the incisors) were identified, the diagnosis of a hypomineralized AI was made.

Figure 2 presents intraoral photographs and orthopantamogram (OPG) of an 8-year-old patient. Enamel of permanent teeth (incisors) is yellowish, of temporary teeth (molars) – with brown spots (a). A significant enamel loss of molars is observed. In addition, the patient has open bite. The radiograph clearly shows the significant reduction of enamel thickness. The upper jaw is underdeveloped (c).

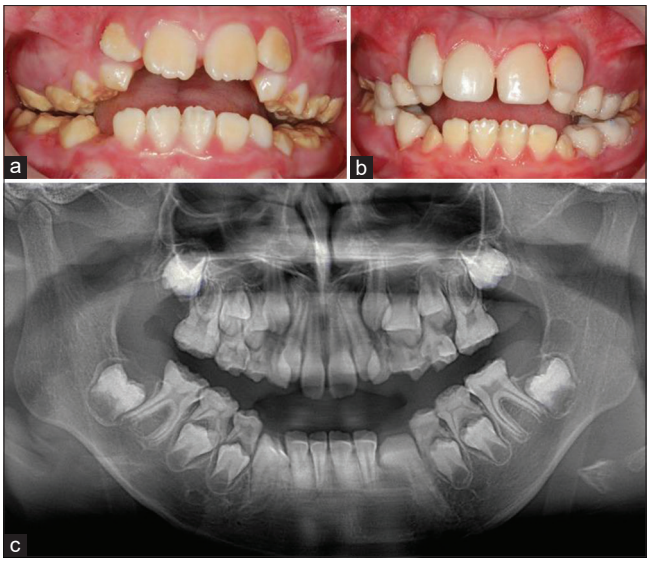

Figure 2: (a-c) Intraoral photographs and orthopantamogram of a patient affected by hypomineralized AI

Treatment

Treatment in this case implied maximum preservation of the intact tissues and vitality of permanent teeth, as well as reestablishing esthetics and the most vital functions: Chewing, breathing, and swallowing. Esthetic appearance of the permanent anterior teeth was created with veneers and temporary posterior teeth were restored with composites (b) [2].

3. Hypomaturized AI: In healthy enamel, proteins are usually destroyed to ensure the final formation of crystals, however, with this pathology, there is a defect associated with the violation of the destruction of the matrix protein. The enamel is opaque, white or brown, of normal thickness, but very brittle due to an excess of protein and lack of mineral component, which leads to its often chipping. The radiograph shows gradual decrease in enamel opacity nearby the enamel-dentin junction. This is the simplest form of AI. Patients do not complain of hypersensitivity, thus, dissatisfaction with their general dental looks serves as the main reason for going to the doctor [7].

Clinical case

A 7-year-old girl turned to the children's dental clinic at the university in Istanbul. During oral examination, both temporary and permanent teeth were revealed. The diagnostics results confirmed that the pathology was caused by defects in the SLC24A4 gene [7].

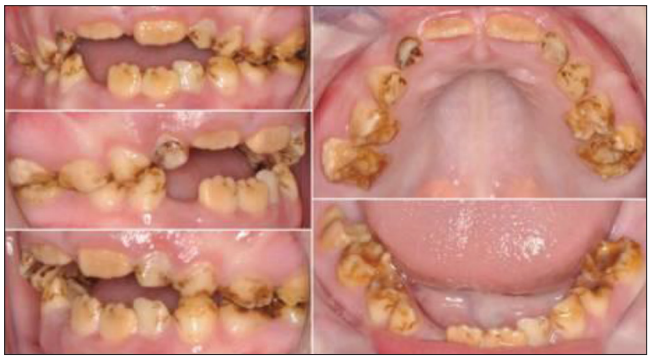

Figure 3: Intraoral photographs of a patient with hypomaturized AI

Figures 3 and 4 demonstrate intraoral photographs and OPG of the clinical case with hypomaturized AI: The enamel is rough, sufficiently worn out, almost completely brown, in the cervical areas the tooth surface looks a little better. The teeth are mainly of normal size and shape. The bite is open, with disocclusion of the anterior teeth [7].

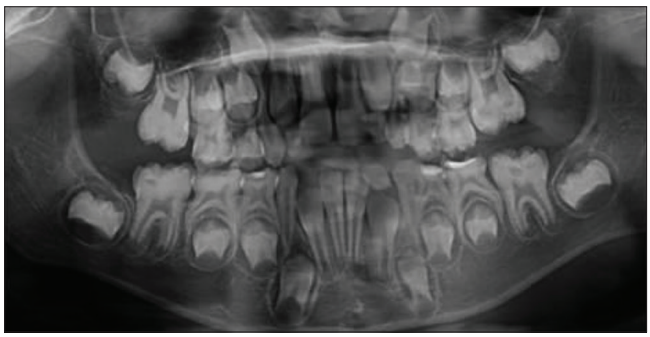

Figure 4: Orthopantamogram of a patient with hypomaturized AI

The enamel-dentin border is practically invisible on the radiograph; it is difficult to distinguish enamel from dentin [7].

Treatment

The treatment consisted of creating a healthy appearance of dentition, namely, performing restoration of the anterior teeth with composites and placing crowns on molars.

4. Hypoplastic-hypomaturized AI: This type of AI combines enamel hypoplasia and taurodontism ("bovine tooth").

Radiograph (Figure 5) shows abnormally large tooth cavities, bifurcations and trifurcations shifted to the apex [8], [9].

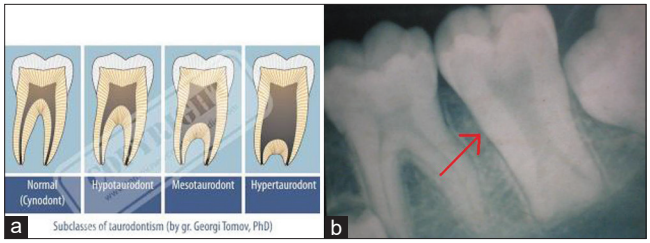

Figure 5: (a and b) Scheme of hypoplastic-hypomaturized AI development and bitewing radiograph of a clinical case

Treatment

Hypoplastic-hypomaturized AI requires carrying out endodontic treatment combined with composite restorations or metal-ceramic crowns (also called porcelain-fused-to-metal crowns).

Like many pathologies induced by genetic mutations, hereditary diseases are rarely encountered in dentistry. However, according to Witkop, dentin abnormalities are much more common than those of tooth enamel. In this regard, DI and DD belong to the group of hereditary dentin diseases [10]. These pathologies are inherited autosomally dominantly and are characterized by an abnormal dentin structure of both temporary and permanent teeth. On radiographs, the teeth crowns are in the shape of a bulb, and the pulp chambers are significantly reduced. Underlying dentin demineralization causes a shift in the enamel and its detachment from the dentin, which leads to its weakening and wear.

DI is an autosomal dominant disease characterized by severe hypomineralization and dentin structure alteration. Dentin extracellular matrix is comprised type I collagen (90%) and non-collagenous proteins (10%), including dentin sialoprotein (DSP), dentin glycoprotein (DGP), and dentin phosphoprotein (DPP). These proteins are essential for the process of dentinogenesis. They are encoded by a single gene – dentin sialophosphoprotein (DSPP) – and undergo some post-translational modifications (glycolysis and phosphorylation) to maintain and control mineralization [10]. This pathology is caused by mutations in the DSPP gene, resulting in types II and III of DI. DI-I manifests itself as one of the symptoms of osteogenesis imperfecta (OI), which, in its turn, is caused by mutations in other genes (more often they are COL1A1 or COL1A2) [11].

In case of DI, teeth are yellow-brown, dentin is transparent, with noted fast attrition. The teeth roots are short. The inorganic substances amount is significantly reduced in dentin, there is more water than should normally be.

In the original Shields classification, three types of DI are distinguished.

DI-I is considered as one of the symptoms of OI of types 1b, c, 2, 3, 4b, 9, and 10.

DI-II (Stainton-Capdepont syndrome) is not associated with the violation of the bone formation process. Clinically, it is characterized by abnormal amber (yellow) or opalescent (milky white with yellowish or bluish hues) dentin, the teeth have "worn out" appearance, the crowns are barrel shaped, with the narrowed neck and short roots, the tooth cavity is absent, which can be seen on radiographs.

DI-III is characterized by opalescent temporary and permanent teeth with obvious areas of abrasion and with large pulp chambers [12], [13].

1. DI-I appears to be one of the symptoms of OI. Temporary and permanent teeth are of typical amber, grayish or bluish color, translucent, with significant abrasion. As can be seen on the radiograph, the teeth roots are short and narrow. Dentin hypertrophy leads to obliteration of the tooth pulp chamber both before and after eruption. The severity of the pathological process depends on the characteristics of the patient's body: In some patients, the tooth cavity can be completely obliterated, while in others, it looks normal.

Clinical case

Figure 6 shows the image of the oral cavity of a 15-year-old girl with DI-I caused by mutation in the COLIA2 gene. The teeth are of a characteristic gray-blue color, the bite is open with disoccluded anterior teeth (a). On the OPG, the pulp chambers of almost all teeth are calcified, crowns are in the form of bulbs, necks are narrowed (b). The second maxillary molars are impacted (indicated by arrows) [11].

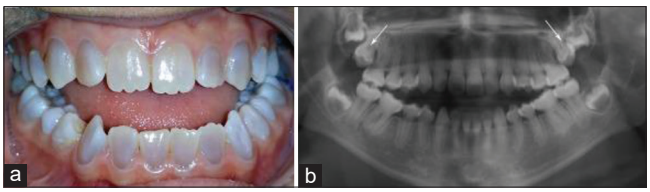

Figure 6: (a and b) Intraoral photograph and orthopantamogram of a patient with DI-I (osteogenesis imperfecta)

Treatment

Treatment of patients with OI should be carried out with extreme caution due to high risks of injuries and fractures of the teeth and jaws. It is recommended to place porcelain (anterior teeth) or metal (posterior teeth) crowns.

2. DI-II (Stainton-Capdepont syndrome according to Groshnikov): The signs of DI-II are very similar as for DI-I, the only difference is the absence of OI. Normal teeth are not found in this type of disease, unlike type I of DI. In rare cases, patients experience hearing loss. Stainton-Capdepont syndrome appears to be a hereditary disease that affects both enamel and dentin of temporary and permanent teeth. The syndrome is inherited by half of the off-springs from one of the parents and is not gender linked. According to etiology, the disease is characterized by the violation of the mesoderm and ectoderm germ layers functions. Teeth are early erupted. Enamel changes the color to grayish or brownish one. The teeth crowns are of a bulb shape with specific narrowing of the neck. The teeth roots are shortened. Patients complain of gum, cheek, and tongue injuries resulting from early abrasion of crowns and sharp incisal edges. Dentin after exposure gets brown color, calcification of the pulp cavity occurs. While conducting electroodontodiagnosis, one can note a sharp decrease or even complete absence of electric excitability of the pulp. In dentin, the content of minerals decreases, the amount of water and the organic component increase [13].

Treatment

For such clinical cases, prosthetic treatment is required (cementing of crowns).

Clinical case

Figure 7 shows temporary teeth of a 6-year-old boy (a-c) and his permanent teeth at the age of 8 (d-f). Temporary teeth are brownish, sufficiently worn out, with complete pulp space obliteration in the erupted teeth. Teeth crowns are of a bulb shape, the roots are short. Temporary teeth are affected much more strongly than permanent ones [10].

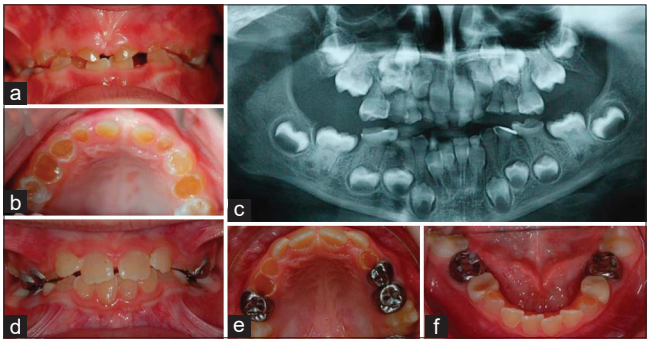

Figure 7: (a-f) Intraoral photographs and orthopantamogram of a patient with DI-II

Treatment

Posterior teeth were prosthetically treated with metal crowns, and anterior teeth were restored with composite materials.

3. DI-III: It was first found among residents of Brandywine in the states of Maryland and Washington, thus, these teeth are now called Brandywine. Clinical signs are similar to those of DI-I and DI-II, the difference consists in possible spontaneous exposure of temporary teeth pulp. Permanent teeth are more often affected with DI-III. Teeth look like shells in radiographs, being hollow inside due to a thin layer of hypotrophic dentin, the roots are short.

Figure 8 shows the radiograph of shell teeth of a patient with DI-III, which are characterized by large size, and an abnormally large pulp chamber due to the absence of secondary dentin. As the roots are short, temporary teeth may fall out earlier [10].

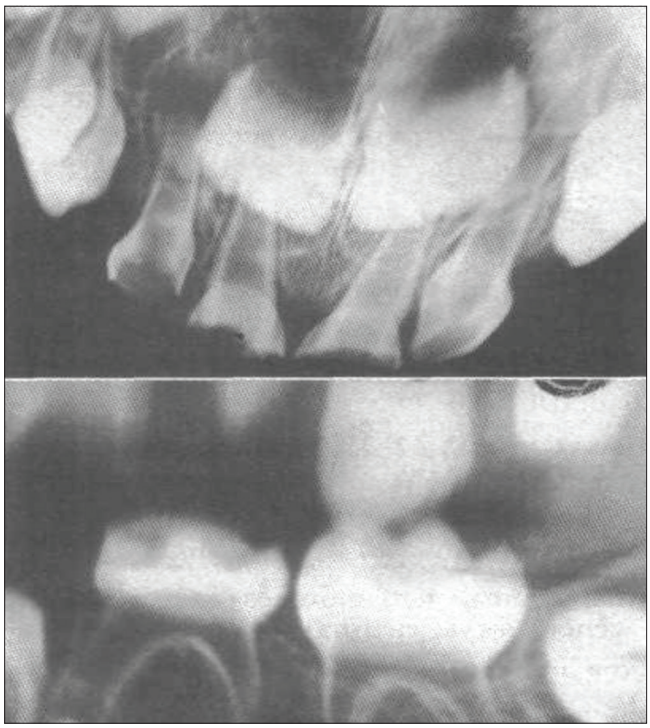

Figure 8: Radiographs of shell teeth of a patient with DI-III

Treatment

Endodontic and prosthetic treatment of such teeth is necessary.

DD, as has been mentioned earlier, is also attributed to hereditary diseases of dentin. Two types of DD are distinguished.

In case of DD-I (root DD), teeth usually do not differ from normal ones: They have a characteristic shape, color, and size. As a rule, there are complaints of pain as the teeth are temperature sensitive, as well as complaints of periodontal diseases and exacerbations of

chronic pulpitis and periodontitis. Radiograph displays roots being short, underdeveloped, sharp, conical, with apical narrowing, with the bifurcation weakly expressed, or even completely absent. Bone tissue resorption is observed around the root apex. With this pathology, pulp chamber obliteration occurs even before tooth eruption. Electrical excitability is reduced.

Treatment

Treatment involves teeth extraction and prosthetic therapy [14].

Clinical case

Figure 9 shows intraoral photograph where the teeth are of normal color (a), the crowns shape is also characteristic of their healthy state, however, the roots are significantly reduced, the root tip is conical (b). In addition, bull teeth (taurodontism) can be observed [10].

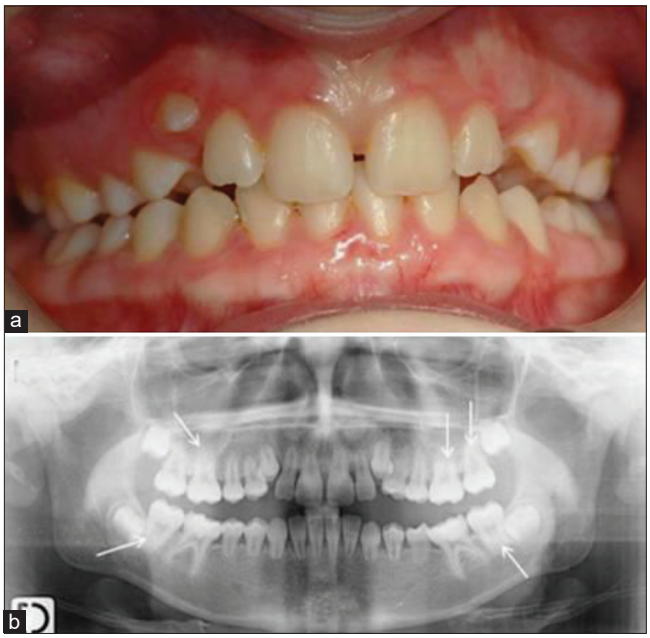

Figure 9: (a and b)Intraoral photograph and orthopantamogram of a patient with DD-I

DD-II (coronal DD) is characterized by the appearance of permanent teeth crowns being close to normal, however, enlarged thistle-like pulp chambers are seen radiographically. The root canals are narrow and deformed, denticles (dental pulp stones) are also revealed.

Treatment

No treatment is required.

Clinical case

Figure 10 shows intraoral images and OPG of temporary teeth of a 4-year-old girl (a-c) and her

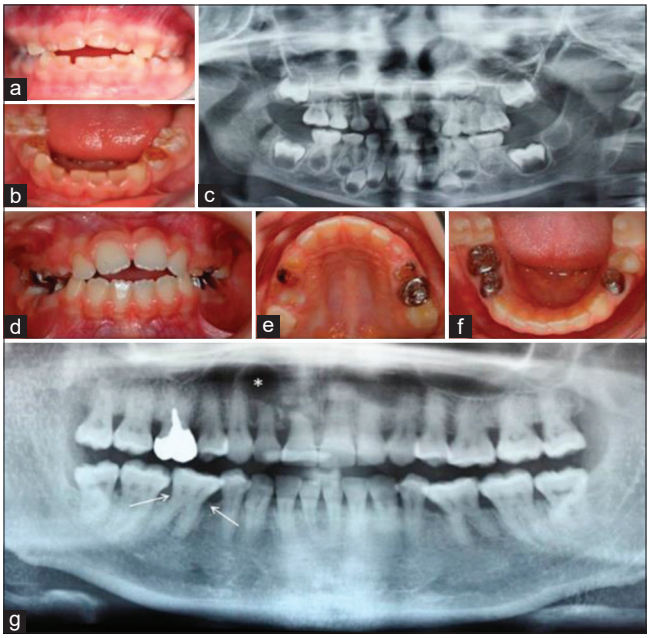

Figure 10: (a-g) Intraoral photographs and orthopantamogram displaying teeth with DD-II

permanent teeth at the age of 10 (d-f). Temporary teeth are of a specific “amber” color, the crowns are strongly worn out, erupted teeth pulp chambers are partially obliterated, crowns are of an onion shape, the roots are short. Permanent teeth are of normal color and almost not worn out. Specific thistle-shaped pulp chamber is shown on OPG. The roots are short [10].

MBD (congenital family osteopetrosis, osteosclerosis, and Albers-Schoenberg disease) is also considered to be a rare genetic disease characterized by an increase in bone mass and volume due to impaired osteoclast function. Osteoclasts are highly specialized cells responsible for dissolution of the mineral component of bones and the destruction of the organic matrix. These processes are vital for the constant renewal of bone tissue and the maintenance of mineral homeostasis. Bones become more prone to osteomyelitis due to lower vascularization. The disease is characterized by impaired formation of skeletogenic tissue and insufficient formation of myelogenic one. Pathology is inherited autosomally recessively or autosomally dominantly.

MBD is usually manifested in two clinical forms: Benign (autosomal dominant) and malignant (autosomal recessive). With benign (adult) form of MBD, no special symptoms are revealed, and a malignant (infantile) form of the disease usually has a fatal outcome. Due to high-quality medical care, the life duration of such children can be extended for several years.

In the oral cavity, MBD has several characteristic manifestations, which include late teeth eruption, teeth malformations, partial adentia, enamel hypoplasia, impaired dentinogenesis, enamel and dentin hypomineralization, tooth injuries, underbite (mandibular prognathism), odontomas, and thickening

of the bone plate. Teeth extraction should be limited due to the proneness to various injuries and osteomyelitis. Such patients should always maintain high oral hygiene level. In addition, the application of fluorides is recommended to reduce the tendency to develop caries.

Figures 11 and 12 show the changes characteristic of MBD (infantile disease): Lack of significant number of teeth and a strong narrowing and, even, obliteration of the tooth canals [15].

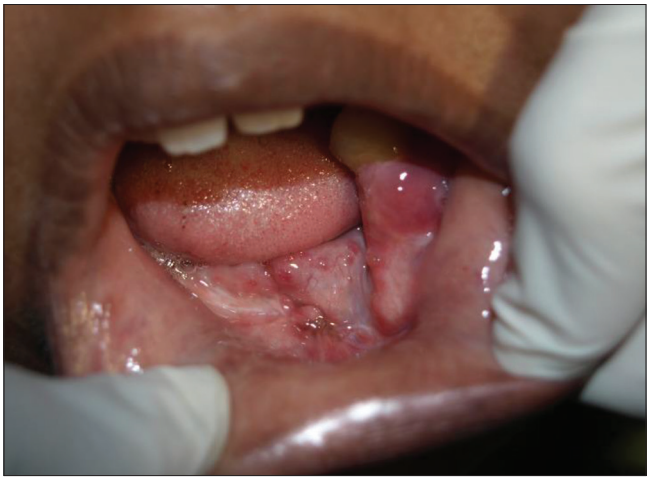

Figure 11: Intraoral photograph displaying manifestations of autosomal recessive marble bone disease

Teeth of patients with this pathology are more prone to caries. The factors leading to osteonecrosis and tooth decay are as follows: Narrowing of the channels with the neurovascular bundles nourishing and innervating the teeth and jaws, obliteration of the bone cavities, and teeth pulp chambers.

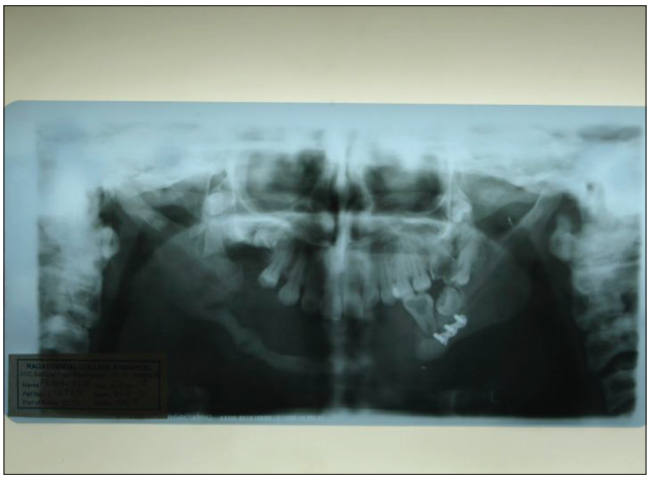

Figure 12: Orthopantamogram of a patient with autosomal recessive marble bone disease

Bone marrow spaces vascularization and partial obliteration of the mandibular canal lead to a decrease in bone resistance to various infections. Patients become more prone to infections due to granulocytopenia. Severe infections tend to proceed during a long period of time and are, as a rule, accompanied by anemia and neutropenia.

The disease occurs in both children and adults. When the disease begins in the prenatal period, children often die at a fairly early age being affected by anemia, osteomyelitis, pneumonia, etc. Abnormal bone formation and bone marrow replacement with connective tissue lead to a decrease in hematopoiesis. Extramedullary hematopoiesis occurs causing leukoerythroblastic anemia and thrombocytopenia. The liver and spleen of such a patient are enlarged. Hemolysis resulting from an enlarged spleen exacerbates anemia and thrombocytopenia.

Differential diagnosis includes other diseases that cause osteosclerosis: Hypervitaminosis D, hypoparathyroidism, intoxication with fluoride, lead, beryllium, Paget's disease, diffuse bone metastasis from breast cancer (which is osteoblastic, while most metastases are osteolytic), and blood diseases (myelofibrosis, leukemia, and sickle cell anemia).

Patients with such a disease should constantly be under the supervision of a doctor since they are highly prone to infections and various kinds of fractures (injuries). In some patients, osteomyelitis of both jaws develops. External manifestations are wide nostrils, depressed root of the nose, wide-spaced eyes, and puffy lips.

This pathology can be diagnosed using X-rays. Bone condensing becomes visible outwardly resembling marble. In the skull, this process is especially pronounced: Sclerosis of the frontal and maxillary sinuses, as well as of ethmoidal labyrinths, is observed. Jaw bone is also condensed: In the lower jaw, for example, it is impossible to distinguish bone marrow spaces from the spongy substance. The upper jaw is less frequently sclerosed. The chest is deformed, the skeletal bones are injured even under minor impacts.

Blood test reveals a high content of calcium and phosphorus. The amount of phosphatase is normal.

MBD, respectively, also affects the teeth, disrupting their development and creating multiple carious lesions.

No pathogenetic treatment is offered, therefore, symptomatic one is used. With a malignant form of MBD, blood transfusion is recommended, which temporarily improves the well-being of the patient. Benign form of MBD cannot be treated, it proceeds without symptoms and is accidentally detected on a radiograph.

For the prevention of osteomyelitis with MBD, health of the teeth should be carefully monitored and, in extreme cases, the poor teeth should be removed.

The main treatment is bone marrow transplantation. Erythropoietin can be used to treat anemia. Injuries and osteomyelitis are treated as usual. In both infantile and adult forms of osteopetrosis, Actimmune injections (interferon gamma-1b) can be given. This drug slows the progression of malignant infantile osteopetrosis causing increased bone

resorption and production of red blood cells. In the oral cavity, if necessary (in case of complete or partial adentia), prosthetic treatment should be performed. Any treatment should be as conservative as possible. Fish oil, Vitamin D, as well as calcium, fluoride, and phosphorus preparations are strictly contraindicated.

It is impossible to prevent osteopetrosis, as this is a genetically determined disease. Careful monitoring is necessary for a pregnant woman for the timely diagnosis of fetus genetic disorders and the subsequent provision of necessary therapy so that the life of the unborn child could be as close to normal as possible [15]

Treatment

Restoration of teeth affected by hereditary diseases can lead to their rapid further destruction stipulated by demineralization of enamel and dentin. Therefore, treatment should begin with a comprehensive and long-standing remineralization therapy for strengthening dental tissues before prosthetics and reducing teeth hypersensitivity.

At the moment, there are many drugs that can be used to alleviate or prevent the deterioration of the patient's condition [16]. Remineralization therapy consists in applying special gels, varnishes, and solutions to previously cleaned teeth and rinsing the oral cavity for the active substances to penetrate into hard tissues and restore the normal tooth structure [17], [18]. The use of electrophoresis is advisable for increasing the bioavailability of remineralizing drugs. This method is much more effective than rinsing and topical applications, since under the influence of current, ions actively penetrate into the hard dental tissues. Electrophoresis is used for older children, adolescents, and adults, however, it is not indicated for young children, since adequate and controlled behavior is necessary during the procedure. The disadvantages of this method are the need for special equipment, the use of several drugs, the direct participation of a dentist, the complexity of the procedure, etc.

Calcium gluconate (Calcii gluconas) or calcium salt of gluconic acid is the white powder, odorless, and tasteless, readily soluble in water, practically insoluble in alcohol and ether [19]. It is used as the means of remineralization therapy, applied for the prevention and treatment of caries and non-carious dental lesions, especially in patients suffering from rickets and osteomalacia, for therapy of intestinal toxicosis (mainly in infants), as well as while treatment with corticosteroids. It is also applied as an antiexudative agent reducing vascular permeability indicated for patients with allergic diseases and immediate hypersensitivity reactions, including drug allergies, used to prevent and stop postoperative bleeding. No contraindications are known. No side effects are caused by topical application. In the superficial layers of enamel, calcium ions combine with fluorine ions to form calcium fluoride.

For remineralization therapy, 10% solution of calcium gluconate is used for applications. First, tooth enamel needs to be cleaned from the deposits (tartar, plaque, and calculus) and isolated from saliva. Next, enamel is processed with the solution of hydrogen peroxide (1%) and dried. Then, a swab moistened with 10% calcium gluconate solution is applied to the surface of the teeth for 15–20 min. Every 5 min, swabs must be changed. In conclusion, an application of 0.5–2% sodium fluoride solution for 5 min is needed. After the procedure, the patient should refrain from eating and drinking coloring beverages during 2 h.

If the course of remineralization is prescribed for preventive purposes, the patient should have 3–5 sessions. The course, consisting of 10–30 procedures, is prescribed for medicinal purposes. Sessions should be held daily or every other day. Electrophoresis is sometimes done using 10% solution of calcium gluconate, the course consists of 10–12 procedures. The drug does not irritate the mucous membrane of the gastrointestinal tract and other tissues.

The effectiveness of remineralization is determined by applying 2% methylene blue solution available as powder, tablets of 0.25 (for children), 0.5, and 0.75 g; 10% solution in ampoules of 1, 2, 3, 5, and 10 ml.

Calcium lactate (Calcii lactas) can also be used for teeth remineralization. It is more effective than calcium gluconate, as it contains higher amount of calcium (13%). Calcium lactate is contained in numerous therapeutic toothpastes and chewing gums.

Calcium hydroxide: It is used as an anti-inflammatory, osteotropic, and antiseptic agent, promoting the activation of metabolic processes of pulp cells, and stimulating the secondary dentin formation [19].

Calcium glycerophosphate (Calcii glycerophosphas) is an odorless white powder, with bitter taste, which stimulates the hard tissues remineralization due to the content of calcium and phosphorus ions, enhances anabolic processes, and has a general strengthening and tonic effect. Calcium glycerophosphate is indicated for the treatment of initial caries, various pathologies associated with demineralization, non-carious lesions, prevention of dental caries, and rickets. No contraindications and side effects have been observed.

During application, calcium ions contact with fluorine ions, and calcium fluoride is formed in the demineralized areas of teeth. This powder can be used in conjunction with iron-containing drugs and multivitamins. In dentistry, this drug is prescribed topically and per os. For topical applications and electrophoresis, 2.5% drug solution is used. The drug is applied for 15 min, and every 5 min, it is necessary to change the swab moistened with the solution. The alternative variant is to

use a calcium glycerophosphate tablet, moisten it with 2–3 drops of distilled water and apply the resulting mass to the areas of demineralization also for 15–20 min. After completion of the calcium glycerophosphate application, the remaining product should be carefully removed with a dry swab, then the treated enamel areas must be coated with fluoride varnish. The course consists of 10–12 procedures, every other day, and is held combined with Vitamins B1 and B6 intake. To prevent caries, the course is carried out during 1 month in spring and autumn. Calcium glycerophosphate is also contained in many toothpaste and is available as powder and tablets of 0.2 and 0.5 g [19].

Sodium fluoride (Natrium fluoratum) synonyms: Fluossen and Koreberon. The main indication is enamel remineralization. The solution penetrates well into the superficial enamel layers due to its increased permeability. Sodium fluoride reacts chemically with calcium ions resulting in calcium fluoride. Fluorine enters into reaction with one of the main components of hard dental tissues – hydroxyapatite, replaces the hydroxyl group in it, and, thereby, promotes the formation of hydroxyfluoroapatite and fluoroapatite. Fluorides get accumulated within the enamel, reduce its permeability, and increase the acid resistance. Remineralization therapy is indicated for the treatment of initial caries, non-carious lesions of hard dental tissues (hypoplasia, hyperesthesia, etc.). Sodium fluoride is contraindicated in case of detected fluorosis and high fluoride content in drinking water and food.

Sodium fluoride is prescribed both per os and topically. It is not recommended to prescribe calcium preparations in combination with sodium fluoride. When taking tablets, the dosage must be strictly observed, otherwise, there is a risk of fluoride intoxication (fluorosis) when the dosage exceeding 2 mg/l of fluorine enters the body during the day. Topically, the drug can be used in the form of applications, electrophoresis, and rinses. Sodium fluoride solution (2%) is applied as independent prophylactic courses or immediately after the application of calcium gluconate solution. In the first case, fluoride is applied to demineralized areas for 2–3 min. It is necessary to carry out 2–4 applications every 3–5 days. It is advisable to undergo 3–4 courses of remineralization therapy per year. Sodium fluoride in the form of a gel should be applied with maximum caution, especially with children, since the patient can swallow part of the drug, which is undesirable. By electrophoresis, 0.2% sodium fluoride solution is introduced from the cathode at a current strength of 30 μA. Rinsing is carried out with 2% solution after cleaning the teeth from plaque and tartar deposits. The procedure must be performed every year for 9 months. It is prescribed for both children and adults.

The drug comes in powder, tablets of 0.015 g and 0.02 g; 0.05% and 0.2% rinse solutions [3].

Remodent (Remodentum) is a complex preparation for remineralization consisting of 4.35% Ca, 0.15% Mg, 16% Na, 30% Cl, 0.2% K, 1.36% P, 44% of organic substances, and other elements (Mn, Fe, Zn, and Cu). The organic part of the powder is freeze-dried bone meal from the young cattle jaws.

The drug is indicated for caries prophylaxis, treatment of non-carious dental lesions, and hyperesthesia. It is used for topical applications and rinses (for patients with hyperesthesia). Remodent is applied as 3% solution for 20 min, every 5 min, it is necessary to update the swab. One course includes 15–20 applications of a drug with the frequency of 2 times a week. For rinsing, 1–2% solution of drug is used within 3 min after teeth pre-brushing. Rinsing of the oral cavity is carried out 3–4 times a week, one course includes 40 rinses.

The drug comes in 1, 2, and 3% solutions, powder, tablets, toothpastes, and gels [3].

Profokar is transparent liquid with small amount of white deposits and salty taste. It is a complex product including calcium, phosphorus, magnesium, chlorine, iron, zinc, potassium, copper, sodium, and lead. Unlike Remodent, Profokar contains fluorine as well. Demineralizated long bones of cattle serve as the organic basis of the drug. It is used for topical applications and rinses [20].

Belagel Ca/P (developed by VladMiVa) was created on the basis of the Remodent preparation and has a prolonged action ensured by the formation of a film from which ions of phosphorus, calcium, magnesium, and potassium gradually enter the enamel. This drug contains no fluoride. If fluorination is necessary, Belagel F or Belak F preparations can be used [21].

Profilac is fluorine-based varnish. The drug is based on cedar balsam, which does not allow the active component of fluoride to settle on the bottom of the bottle. The main action is remineralization and stabilization of tooth enamel. The high activity of fluoride ions contributes to their rapid penetration into enamel. As a result of action of calcium ions, calcium fluoride is formed. The drug is indicated for caries prophylaxis, treatment of initial caries, dental hyperesthesia, enamel erosion, hypoplasia, and dry mouth. Profilac is contraindicated for patients with allergy to the components of the drug. Side effects include allergic reactions (rarely).

Use along with calcium preparations contributes to the formation of calcium fluoride strengthening the enamel and increasing its acid resistance. In addition, hydroxyapatites, after interaction with fluorine, turn into more durable structures – fluorapatites.

Dosage and administration: The drug is applied with a brush or a swab to the affected teeth areas, previously cleaned from deposits, for 2–3 min. Within 2 h after the procedure, eating and drinking are excluded. Fluoride varnish can be used both independently, and after application of calcium-containing drugs (to consolidate the result). For remineralization treatment,

the procedure can be conducted 4–8 times a year. For teeth sensitivity treatment, the course should consist of 2–3 applications during 10 days.

All previously listed fluorine-containing drugs have one disadvantage. Calcium fluoride formed during the interaction of drugs with calcium and fluoride ions often remains on the enamel surface. Therefore, the doctor often has to repeat remineralization courses. An alternative can be the use of the German drug – enamel-sealing liquid – providing deep fluoridation of hard dental tissues.

Belak-F: The drug is based on the natural polysaccharide – chitosan. The main action of chitosan consists in replenishing the mineral composition of the hard dental tissues and eliminating hypersensitivity. Fluorine actively penetrates into the tooth enamel and, interacts with the calcium ions, promotes the formation of calcium fluoride.

Indications, contraindications, side effects, and drug interactions are similar to that of Profilak. Belak-F is indicated for treating caries at the spot stage and non-carious lesions (hypoplasia, erosion, wedge-shaped defect, and hyperesthesia). The course of using the drug consists of four applications with an interval of 3 days. It can be applied after the application of calcium preparations [21].

Enamel-sealing liquid (deep fluoride) (in German “Tiefenfluorid Schmelzversiegelungsliquid”) is used for deep fluorination. It consists of two liquids: No. 1 – anhydrous magnesium silicate fluoride with calcium and copper ions, No. 2 – finely dispersed calcium hydroxide suspension; sodium fluoride (as a stabilizer) and distilled water. As a result of these liquids interaction, enamel forms crystals of calcium fluoride, magnesium fluoride, and copper fluoride in a silica gel. This effect persists for 0.5–1 years after application. The drug provides deep fluoridation and sealing of pores of enamel, tubules of dentin, and cement. The crystals formed in the enamel are in a gel that protects them from mechanical stress. Interaction of enamel-sealing liquid with mineral components of saliva leads to constant release of fluorine providing long-term dental tissues mineralization.

Enamel-sealing liquid is indicated for prevention and treatment of caries, dentin hypersensitivity, and non-carious lesions. No contraindications and side effects have been identified.

Mode of administration: Liquid No. 1 is applied on pre-cleaned and dried demineralization areas with a swab or brush for 30–60 s. Then, liquid No. 2 is applied in the same manner. Since the second liquid is a suspension, it must be shaken before the use for even particles distribution. After 30–60 s, the mouth should be rinsed, preferably with distilled water. The procedure should be repeated 2 times a year.

Special instructions are to avoid contact with eyes. The drug comes in two 5 ml bottles [6].

Conclusion

The content analysis of the study was limited to sources for the period of 2011–2019.

The results of the studies have shown that the most significant hereditary dental diseases are considered to be AI, DI, and DD, as well as severe congenital anomaly – MBD – directly affecting hard dental tissues. The etiology of these diseases is stipulated by genetic mutations.

Hereditary dental diseases should be differentiated from other dental disorders caused by teeth development violation under the influence of environmental factors.

The treatment of such diseases is symptomatic and esthetic: The visual defects caused by these pathologies are eliminated by remineralization therapy, orthopedic/orthodontic treatment, and surgery. In addition, preventive conversation with patients about maintaining oral hygiene has to be conducted.

Therapeutic treatment is now considered to be the least invasive way to deal with these abnormalities. Drugs compensate for the lack of mineral components in the hard dental tissues, preventing their further destruction and restoring aesthetic appearance of teeth.

Effectiveness and safety of each drug should be taken into account before conducting remineralization therapy.

It is imperative for a modern dentist to know and constantly study hereditary dental diseases, their symptoms, and clinical manifestations for detecting pathologies in patients at the earliest possible time, making correct diagnoses and choosing the appropriate treatment strategies (therapeutic, orthopedic/orthodontic, or surgical).

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