Ectodermal dysplasia, an odontological point of view

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Abstract

Introduction: Ectodermal dysplasia (ED) consists of rare genetic disorders in which it is mainly characterized by abnormalities of tissues derived mainly from the ectoderm, sometimes tissues of mesodermal origin. It has a frequency of one in 17,000 births, mainly males.

Objective: To analyze the literature on ectodermal dysplasia and its application in dentistry. To investigate information on etiology, genetics, general and oral manifestations, and its treatment.

Methodology: A research search was carried out in PubMed, PMC and Google Scholar with the words “ectodermal dysplasia”, “genetics”, “oral manifestations”, “treatment” and “clinical manifestations”.

Results: The factor of ED was found to be of genetic origin. The mutations are X-linked. The most affected structures are the skin, hair and nails; this is due to its ectodermal origin. The oral manifestations can appear in the shape of the teeth, size, number of teeth present and can even affect the normal development of the alveolar ridge. The use of removable prosthesis and the placement of implants are the most applied treatments to improve the conditions of the patients.

Conclusions: The most affected structures are those of ectodermal origin; while in the oral cavity we can present a partial absence of the dentition, together with alterations of the alveolar bone structures and even patients can come to suffer from cleft palate and cleft lip. There is no specific treatment, but to treat the afflictions presented by means of implants and prosthesis.

Keywords: ectodermal dysplasia, etiology, treatment

1. Introduction

Ectodermal dysplasia (ED) is composed of a group of rare genetic disorders characterized mainly by abnormalities of tissues derived primarily from the ectoderm, such as hair, teeth, skin, sweat glands, and nails, along with occasional dysfunction of tissues of mesodermal origin [1, 2]. Performing some treatment to correct their condition during infancy may have better results than one applied at a later stage of development. Prosthetic treatment, either fixed with implants or removable, is the most frequent treatment in these patients, so there should be good planning for better results [3].

The literature has found 345 reported cases with ED, of which 206 are mainly due toEDA gene mutations. In 2017, the HGMD Professional 2017 gene mutation database recorded 314 mutations in the EDA gene [4]. So, we have that the most frequent type of mutation consists of substitutions occurring in a single base pair in coding regions. There are many different types of ectodermal dysplasias; each type of dysplasia is caused by a specific mutation in some genes. The most common phenotypes of dysplasia are of the anhidrotic or hypohidrotic type (HED known as Christ-Siemens-Touraine Syndrome/ EDA known as Clouston Syndrome); this disorder is X-linked, which has a frequency of one in 17,000 live births in the general population [5].

Studies have found that ED manifests mainly by upper maxillary retrusion caused by underdevelopment, will have a forward and upward displacement of the lower jaw and a collapsed anterior facial height; while the palatal arch usually presents in a high manner and a cleft palate may be present. The patient usually presents an absence of teeth caused by poor alveolar bone growth, as well as hypodontia and anodontia [5, 6, 7], so it is here when the dentist challenges his skills and employ some treatment.
Nowadays there is a great lack of attention to patients with disabilities, some of them are born with these disabilities and some others acquire them during life; there comes a time for the dentist that becomes a great challenge in the care of these patients, such is the case of patients with Ectodermal Dysplasia. ED is a syndrome that will have many manifestations in the face and mouth, among other conditions, so the main objectives of this research was to investigate information about the etiology, genetics, the way it manifests and the treatment plan.

2. Materials and Methods
Articles on the subject published through the PubMed, SCOPUS and Google Scholar databases were analyzed, with emphasis on the last 5 years. The quality of the articles was evaluated using PRISMA guidelines, i.e., identification, review, choice and inclusion. The quality of the reviews was assessed using the measurement tool for evaluating systematic reviews (AMSTAR-2) [8]. The search was performed using Boolean logical operators AND, OR and NOT. It was realized with the words ‘genetics’, ‘ectodermal dysplasia’, ‘oral manifestations’, ‘treatment’ and ‘clinical manifestations’. The keywords were used individually, as well as each of them related to each other.

3. Results & Discussion
3.1 Etiology
ED has a great multisystemic involvement, which will cause certain alterations in the structures of ectodermal origin; it not only affects this structure, but can also compromise the mesoderm, of genetic origin. In the literature we can find that the ectoderm and endoderm are present at the end of the first week after fertilization, while the mesoderm will form in the third week, where it is formed by the product of the invagination of the ectoderm. The ectoderm will give rise to the central and peripheral nervous system, tooth enamel, sebaceous and sweat glands and the epithelium of organs [1,9]. The incidence of the different EDs can vary, but is estimated at 7:10 000 live births [10]. There are about 150 different variants of ED described in the literature. The most frequent is X-linked recessive inheritance; this disease tends to manifest mainly in males [10,11-14]. The first recorded cases of ED were reported in the year 1792, since that time various characteristic signs related to dysplasia have been identified.

Generally, the manifestations can affect the person in all senses; there are social problems that can have an impact on the quality of life of the individual [7]. ED can also be initiated by autosomal mutations, where those of the ED1 gene have been found to be responsible for 58% of cases. The condition will be delineated into two forms mainly, known as (HED) hypohidrotic or anhidrotic (Christ-Siemens-Touraine syndrome) where endocrine glands are absent or markedly diminished and hydrotic (Clouston syndrome) with normal endocrine glands. The two types show similarities in the involvement of teeth and hair, although the nails and sweat glands show a different pattern [2,15,10]. HED is the most frequent of all dysplasias and brings with it hypodontia, hypohidrosis and hypotrichosis and presents an infant mortality rate between 2 and 20%, all this is going to depend on the precocity of diagnosis and treatment protocols [4,11-13,17,18]. Anhidrotic ectodermal dysplasia is considered another classification of these dysplasias, which consists of sparse hair, dental hypoplasia and anhidrosis [14].

Ectodermal dysplasia is of genetic origin and has generally been found to affect mainly the ectoderm and sometimes the mesoderm; it is mainly due to autosomal mutations. It encompasses a wide variety of types, where the hypohidrotic and hydrotic types are the most frequent, appearing mainly in males.

3.2 Genetics
ED is mainly due to maldevelopment of ectodermal derivatives in embryonic life. X-linked hypohidrotic ED has been mapped to the long arm of the Xq12-q13.1 band [14,19,22]. We found that 60% to 80% of women have some degree of hypodontia. Prenatal testing would be possible for pregnant women at increased risk if pathogenic variants in the family were known [14,23].

In some studies, genetic testing marked a mutation of the EDA gene c.911A → G. Also in Y304 mediated, trimerization of EDA and cysteine replacement was found to abrogate protein secretion. A pregnancy with two male sex twins was shown on ultrasonographic examination without dental germs [24]. ED is also caused by mutation in the PKP1 gene and this form is characterized by generalized skin fragility, alopecia, nail dystrophy, plantar palmar dystrophy and painful fissures [25]. In other studies, a Val472Glyfs 28 mutation was found, where there is not much information, but it leads to premature protein termination [26]. The most frequent presentation of HED is caused by pathogenic variants of the EDA gene in Xq13.1. This gene tends to encode ectodysplasin, which is usually a molecule involved in epithelial-mesenchymal communication during the skin development process. Other genes that can be associated with this dysplasia are the EDAR, EDARADD and WNT10A genes, where it will present a recessive or dominant inheritance pattern [16,27-29].

Studies have shown that the hypohidrotic subtype is X-linked. Pathogenic variants in the EDA gene have been found to exist in Xq13.1, EDAR, EDARADD and WNT10A.

3.2 General manifestations
Some specific signs will be present in certain areas of the body such as skin, hair and nails. The peri skin may even show fine wrinkling with some hyperpigmentation and hypoplasia in the midface, highlighting protruding lips. It has also been found that the nails may also have a dystrophic and brittle appearance [25,26,30].

Studies have been found, where affected individuals with the hypohidrotic form often show heat intolerance due to a reduced number of sweat glands and this in turn results in a mortality rate of approximately 30% in early childhood if the disease is not properly diagnosed and treated [14,13,31]. They also tend to present with asymmetric development of the alveolar ridge, changes in nasal secretions from concretions that are solidified secretions in the ducts, a depressed nasal bridge, decreased sebaceous secretions, some dry eye symptoms, fragile appearing skin, a lack of dermal ridges, persistent peri-orbital hyperpigmentation, pneumonia and some asthma-like symptoms related to abnormal bronchial glands, hoarse voice, mid-facial hypoplasia. While physical growth and psychomotor development are within normal limits [23].

These patients usually present with dysmorphic features, oligodontia, friable scaly skin, hypoplastic sebaceous glands where they exhibit decreased sweating, hypoplastic salivary glands exhibiting dry oral mucosa and hypoplastic glands. Generally, these patients are vulnerable to allergic diseases such as bronchial asthma, allergic rhinitis, food allergy, pneumonia, otitis media, among others [2]. Oligodontia tends
to result in decreased oral intake, causing poor nutrition and reduced tears leading to corneal erosion. Most of the subtypes of this disease present the same signs and symptomatology, the most affected structures are the skin, hair, nails; this is because it is of ectodermal origin. It is important to employ early diagnosis as well as treatment because sometimes the conditions can increase the mortality rate at an early age.

3.3 Oral manifestations

The most common oral manifestations include anodontia, hypodontia, retained teeth, loss of vertical dimensions of occlusion, deformed teeth, deficient alveolar growth, prominent lips \([1, 2, 27, 32, 33]\),

It has been found that central incisors, canines and first molars in the maxilla and in the mandible are the canines, first premolars and molars are the pieces that present the highest percentage; with less probability we find the anterior teeth \([1]\), The absence of teeth can result from poor development of the alveolar bone. Some patients may also present cleft lip and palate \([34]\). Regarding the shape and size of the teeth, they are usually small in size, conical, bulbous or taurodontic in shape and usually have a large space between each tooth. Studies have shown that enamel is prone to decay and mechanical damage. Sometimes atrophic inflammation of the mucosa of the oral cavity, hoarse voice and difficulty in swallowing may be present \([35]\). Defects in the number of teeth is a very common problem in these dysplasias. Third molars usually do not develop in 25% of the world's population. The number of teeth can range from more than a dozen, through several, or the lack of all permanent teeth and even, in some cases the lack of both dentitions is present \([4, 31, 35, 36]\). Studies have found that the most frequent missing teeth are the upper lateral incisors, upper and lower premolars \([37]\). The oral manifestations can occur in the shape of the teeth, size, the number of teeth present and can even affect the normal development of the alveolar ridge, making it a challenge when planning treatment, because the bone can compromise the results.

3.4 Treatment

There is no definitive pharmacologic treatment for ectodermal dysplasia. Patients are usually treated depending on the ectodermal structures affected \([38]\). Dental care through prosthetic rehabilitation at an early age can help children with ED develop speech, chewing and swallowing skills, along with improved facial support ratio and temporomandibular joint function \([23, 34, 39]\).

The union of teeth that present a conical shape in young individuals will improve esthetics and chewing ability. Sometimes it is necessary to use treatments such as orthodontics and dental implants; it has been shown that implants in the anterior portion of the mandibular arch have had very good results in children when they are treated at an early age, while in adults the aim is to obtain good esthetics and a functional appliance. There is also a tendency to implement therapies aimed at oral lubrication and caries control \([2, 23, 39, 40]\). Other treatments that can be applied are bone grafts in sinus lift procedures, in the placement of implants and any other treatment that can be used to align the dentition by orthodontics \([41]\). The use of light clothing, air conditioning for the environment, both at home and in the office, a cold-water atomizer, use of artificial tears and application of petroleum jelly for mucosal protection in these patients is recommended \([42]\). Prostheses ranging from fixed prostheses, removable prostheses, implant-retained prostheses, implant-supported prostheses or some other combination depending on the degree of disease of the patient can be used. The application of removable prostheses with numerous retention clasps is recommended to ensure a good development of the prosthetic base bone structure. Adaptation is usually necessary because of the bony structural changes in the base, together with the shape of the few remaining teeth in the dental arch. The use of a tin foil is recommended to protect the dry oral mucosa from the traumatic impact of plaque, along with the application of good hygiene technique to the patient \([4, 10]\). Treatment planning should be carried out and treatment should be started as soon as possible after diagnosis, all this is in order to have good control in terms of esthetic, functional and psychological aspects; so that we can have control in the different stages and improve the quality of life of patients \([2, 10]\). Before treatment with Covid-19, complete isolation is recommended, hospital visits should only be for emergencies, good hand washing with disinfection is very important, but the risks of using these products that may cause dermatologic damage should be taken into account \([43]\).

It is essential to start treatment as soon as possible to prolong the patient's life and give him/her a better quality of life. It is a challenge when deciding to start therapy because patients tend to suffer from deformities in the oral cavity. The use of removable prosthesis and the placement of implants are the most applied treatments to improve the patients' conditions.

4. Conclusions

Ectodermal dysplasia has an incidence of 7 persons per 10000 born and its origin is genetic. The most affected structures are the skin, hair, nails; while in the oral cavity we can present a partial absence of the dentition, along with alterations of the structures of the alveolar bone and even patients may suffer from cleft palate and cleft lip. As for the treatment for dysplasia, there is no established treatment, it is only to give attention to the alterations caused by dysplasia. The use of dental implants and prosthesis at an early age has favored the life span of patients.

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