

**HYPOHYDROTIC ECTODERMAL DYSPLASIA
(Christ-Siemens-Touraine syndrome)**

**N.B.Prabhavathi*¹, Lakshmi Sowjanya .N¹, J.Mastanaiah²,
B.Samyuktha Rani¹**

¹ *Dept. of pharmacology, st.ann's college of pharmacy, Nayunipalli,
chirala.*

² *Dept. of pharmacology, Sana College of pharmacy, kodad,
Nalgonda dist.*

Correspondence author:

N.B.Prabhavathi
Asst.professor
St.Ann's college of pharmacy
Nayunipalli, Chirala.
E.Mail : prabhacology@rediffmail.com

Summary

The present review mainly discusses the detailed disease information. Hypohydrotic ectodermal Dysplasia (Christ - Siemens Touraine syndrome) is a rare genetic disorder that affects several ectodermal structures. The condition is usually inherited as

X – Linked recessive trait, in which gene is carried by females and manifested in males. The manifestations may vary in individuals and usually involves skin, hair, nail, sweat and sebaceous glands. The incidence in male is estimated at 1 in 100,000 births, the carriers-incidence is probably around 17.3 in 100,000 women most patients with EDA have a normal life expectancy and normal intelligence. However, the lack of sweat glands may lead to hyperthermia, followed by brain damage or death in early infancy, if unrecognized. Thus an early diagnosis is important. Families with EDA should therefore be offered genetic counseling. Currently the genes and gene products are defined, but the function of the proteins is not fully known. Once the exact function is known, we can understand the embryogenesis and morphogenesis of the ectodermal structures. It is quite possible that these kinds of observations of gene function and interaction may form the basis of new therapeutic methods in the future.

Key words: Hypohydrotic ectodermal Dysplasia, Christ - Siemens Touraine syndrome, EDA.

Introduction

Ectodermal dysplasia (ED) is not a single disorder, it is a large and complex group of disorders defined by the abnormal development of two or more structures derived from the embryonic ectoderm layer [1,2]. These are congenital, diffuse and non progressive disorders. More than 192 distinct disorders have been described till date. Most common of them are X-linked recessive anhidrotic (Christ-Siemens-Touraine syndrome) and hidrotic ectodermal dysplasias (Clouston syndrome) [3]. It is also rare and non progressive and presents a triad of partial or total absence of sweat glands, hypotrichosis, and hypodontia [4]. In addition, there are other signs and symptoms that can be found depending on the involvement of the ectodermal tissue [5]. The ectoderm, one of three germ layers present in the developing embryo, gives rise to the central nervous system, peripheral nervous system, sweat glands, hair, nails, and tooth enamel [6]. As a result, patients of ED exhibit the following clinical sign: hypotrichosis, hypohidrosis, and cranial abnormalities. The patients often exhibit a smaller than normal face because of frontal bossing, a depressed nasal bridge, the absence of sweat glands results in very smooth, dry skin and/or hyperkeratosis of hands and feet. Oral traits may express themselves as anodontia, hypodontia, and conical teeth. Anodontia also manifests itself by a lack of alveolar ridge development [7, 8]. The earliest recorded cases of ED were described in 1792. Since then, nearly 200 different pathologic clinical conditions have been recognized and defined as ED. These disorders are considered relatively rare, 1 in 10,000 to 1 in 100,000 births [9, 10].

Classification

Current classification of ectodermal dysplasias is based on clinical features. Freire-Maia and Pinheiro proposed the first classification system of the ectodermal dysplasias in 1982 [11], with additional updates in 1994 and 2001[12,13]. Their original classification system stratified the ectodermal dysplasias into different subgroups according to the presence or absence of (1) hair anomalies or trichodysplasias, (2) dental abnormalities, (3) nail

abnormalities or onychodysplasias, and (4) eccrine gland dysfunction or dyshidrosis.

Overall, the ectodermal dysplasias were classified into either group A disorders, which were manifested by defects in at least 2 of the 4 classic ectodermal structures as defined above, with or without other defects, and group B disorders, which were manifested by a defect in one classic ectodermal structure (1-4 from above) in combination with (5) a defect in one other ectodermal structure (ie, ears, lips, dermatoglyphics). Eleven group A subgroups were defined, each with a distinct combination of 2 or more ectodermal defects (eg, 2-4, 1-2-3, 1-2-3-4 from above). The group B disorders were indicated as 1-5, 2-5, 3-5, or 4-5 (from above).

Lamartine reclassified the ectodermal dysplasias into the following 4 functional groups based on the underlying pathophysiologic defect: those are

- (1) cell-to-cell communication and signaling,
- (2) Adhesion,
- (3) Development, and
- (4) Other [14].

Priolo and Laganà reclassified the ectodermal dysplasias into 2 main functional groups:

- (1) defects in developmental regulation/epithelial-mesenchymal interaction and
- (2) defects in cytoskeleton maintenance and cell stability[15].

Other classification systems categorize the ectodermal dysplasias based on defects in cell-cell communication and signaling, adhesion, transcription regulation, or development [16].

Several ectodermal dysplasia syndromes may manifest in association with midfacial defects, mainly cleft lip, cleft palate, or both. The 3 most commonly recognized entities are (1) ectodermal dysplasia, ectrodactyly, and clefting (EEC) syndrome; (2) Hay-Wells syndrome or ankyloblepharon, ectodermal dysplasia, and cleft lip/palate (AEC) syndrome; and (3) Rapp-Hodgkin syndrome, all of which are caused by mutations in the *TP63* gene.

Etiopathology

Molecular genetic pathogenesis:

The molecular pathogenesis of hypohidrotic ectodermal dysplasia (HED) is poorly understood. The gene responsible for X-linked HED, *EDA*, produces ectodysplasin-A, a protein that is important for normal development of ectodermal appendages including hair, teeth, and sweat glands. Evidence is accumulating that ectodysplasin-A is important in several pathways that involve ectodermal-mesodermal interactions during embryogenesis. Defects in the molecular structure of ectodysplasin-A may inhibit the action of enzymes necessary for normal development of the ectoderm and/or its interaction with the underlying mesoderm and that leads to HED.

EDA

Normal allelic variants. *EDA* comprises 12 exons, eight of which encode the transmembrane protein ectodysplasin-A [17]

Normal gene product. Ectodysplasin-A has 391 amino acid residues with a short collagenous domain (Gly-X-Y) that is homologous to the protein in the *tabby* mouse [18], demonstrated that ectodysplasin-A is a trimeric type II protein that colocalizes with cytoskeletal structures at the lateral and apical surfaces of cells, suggesting that it is a novel member of the tumor necrosis factor (TNF)-related ligand family that plays a role in early epithelial-mesenchyme interactions. Several isoforms of ectodysplasin are expressed in keratinocytes, hair follicles, and sweat glands.

Pathologic allelic variants. More than 60 mutations have been identified in *EDA*, including nucleotide substitutions (missense, nonsense, and splicing), small deletions and insertions, and gross deletions [19].

Abnormal gene product. Mutations in *EDA* lead to ectodysplasin A molecules that are unable to regulate epithelial-mesenchyme interactions, leading to abnormal ectodermal appendages. Several mutations in the *EDA* gene produce ectodysplasin A molecules that resist cleavage by furin and are consequently unable to be converted to their active forms and mediate the cell-to-cell signaling that regulates morphogenesis of ectodermal appendages [20].

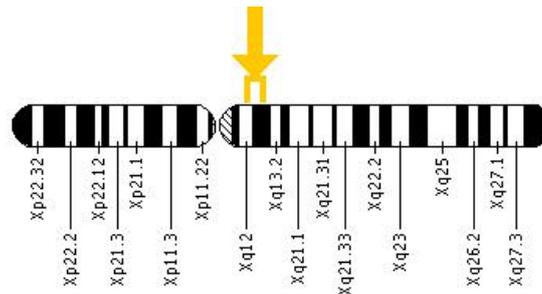


Fig 1: site of EDA gene location

EDAR

Normal allelic variants. The human *EDAR* gene has 12 exons. *EDAR* is homologous to the mouse downless gene.

Normal gene product. *EDAR* encodes a 448-amino acid protein that contains a single transmembrane domain with type 1 membrane topology. The protein probably functions as a multimeric receptor and is related to the TNFR family. It forms a ligand-receptor pair with ectodysplasin.

Pathologic allelic variants. Several mutations have been identified in the *EDAR* gene, including deletions and transitions [21-24]. Those responsible for autosomal recessive HED exhibit loss of function, while those responsible for autosomal dominant HED exhibit a dominant negative effect [25]. At least two of the dominant negative mutations are not associated with the HED phenotype.

Abnormal gene product. The defective proteins encoded by mutations in *EDAR* are unable to bind with ectodysplasin.

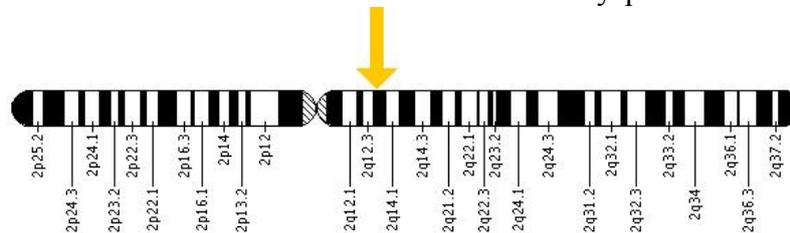


Fig :2 site of EDAR gene location

EDARADD

Normal allelic variants. The human *EDARADD* gene has two isoforms, each with six exons encoding 205 and 215 amino acid proteins. *EDARADD* is homologous to the mouse crinkled gene.

Normal gene product. The protein encoded by *EDARADD* is similar to the death domain, MyD88, a cytoplasmic transducer of

Toll/interleukin receptor signaling [Headon et al 2001]. It also contains a Traf-binding consensus sequence. It is coexpressed with tumor necrosis factor receptor superfamily member EDAR in epithelial cells during the formation of hair follicles and teeth. It interacts with the death domain of EDAR and links the receptor to signaling pathways downstream.

Pathologic allelic variants. A transition at nucleotide 424 of the *EDARADD* gene, leading to a glutamine-to-lysine (p.Glu142Lys) amino acid substitution in the encoded protein, has been identified in an inbred family with autosomal recessive HED [26]. Another family with autosomal dominant HED has been found to have a heterozygous c.335T>G mutation in the *EDARADD* gene, indicating that both recessive and dominant forms of HED can be caused by *EDARADD* mutations [27].

Abnormal gene product. The *EDARADD* mutation alters the charge of an amino acid in the resultant gene, rendering it incapable of performing its function.

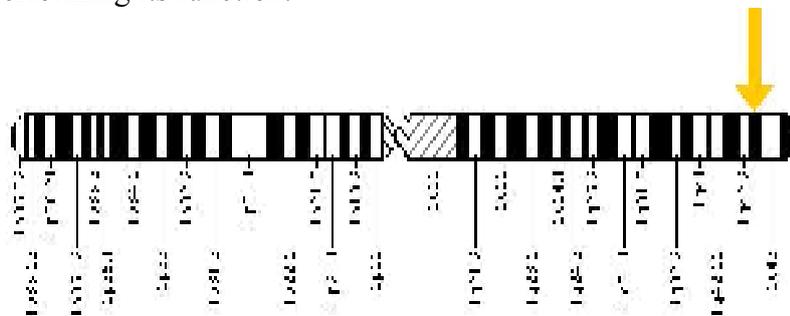


Fig 3: site of location of EDARADD gene

Table 1: Hypohidrotic Ectodermal Dysplasia: Genes and Databases

Gene Symbol	Chromosomal Locus	Protein Name
<i>EDA</i>	Xq12-q13.1	Ectodysplasin-A
<i>EDAR</i>	2q11-q13	Tumor necrosis factor receptor superfamily member EDAR
<i>EDARADD</i>	1q42.2-q43	Ectodysplasin-A receptor-associated adapter protein

The mutations in these genes responsible for the ectodermal dysplasia. 95% of this disorder caused by mutation in *EDA* gene and 5% is caused by *EDAR* & *EDARADD* genes.

Pathological changes:

Ectodermal dysplasia results from the abnormal morphogenesis of cutaneous or oral embryonal ectoderm (ie, hair, nails, teeth, eccrine glands). Note the following:

- Hair defects: A reduction in the number of hair follicles in conjunction with structural hair shaft abnormalities may be seen. Structural hair shaft abnormalities may result from aberrations in hair bulb formation and include longitudinal grooving, hair shaft torsion, and cuticle ruffling. Hair bulbs may be distorted, bifid, or small.
- Eccrine defects: Eccrine sweat glands may be absent or sparse and rudimentary, particularly in patients with hypohidrotic ectodermal dysplasia [28,29].
- Other secretory gland defects: Hypoplasia of the salivary and lacrimal glands may occur. In some patients, mucous glands may be absent in the upper respiratory tract and in the bronchi, esophagus, and duodenum.
- Dental defects: Abnormal morphogenesis or absence of teeth may occur [30].
- Nail dystrophy: Abnormal nail plate formation may result in brittle, thin, ridged, or grossly deformed nails.

Clinical features

EDA is characterized by the triad of signs comprising sparse hair (atrachosis or hypotrichosis), abnormal or missing teeth (anodontia or hypodontia) and inability to sweat due to lack of sweat glands (anhidrosis or hypohidrosis). The lack of teeth and the special appearance were reported to be major concerns. Most patients with EDA have a normal life expectancy and normal intelligence. However, the lack of sweat glands may lead to hyperthermia, followed by brain damage or death in early infancy, if unrecognized. Thus an early diagnosis is important. Families with EDA should therefore be offered genetic counseling.

Craniofacial structures

Considering how much osseous and dental tissue is missing, these patients have surprisingly normal facial structures. Already in 1936, Tannhauser stated that the characteristic deformity of the

cranial bones of all affected patients is such that the resemblance among the patients is bigger than when compared with their own unaffected sib [31].

Clinically, the forehead appears square,(fig 2) with frontal bossing, and there is a prominent supra-orbital ridge. The nose has a depressed nasal bridge and is called a saddle nose.(fig 1) The midface is depressed and hypoplastic, giving it a “dished-in” appearance. The cheekbones are high and broad, although they appear flat and depressed as well. The chin may be pointed and the lips everted and protuberant [32]. (fig 3)

In non-treated patients with EDA, craniofacial deviations from the norm increased with advancing age [33] with a tendency toward a Class III pattern with anterior growth rotation [34]. Cephalometric analysis and anthropometry studies have been performed. The quantitative findings show reduced facial dimensions, decreased lower facial height, variable pattern in facial widths, the maxilla has been relatively more retruded than the mandible, the nasal alar width and mouth width were significantly smaller [35].

This remarkable variability in facial dimensions and harmony found in patients with ED probably corresponds to the different kinds of dysplasia, with different expression of the interested genes [36].



Fig 3:abnormality in nose Fig 4:abnormality in forehead Fig 5: abnormality in lips

Oral structures

Missing teeth or the delay in teething often starts to worry the parents and leads to the diagnosis of EDA in the second year of life [37]. A dentist should not hesitate to radiographically examine a patient whose teeth have not erupted by the appropriate age in order

to exclude EDA. The screening limit for the first tooth to erupt is 15 months. Besides the delay in teething, the teeth appear radiographically abnormal in shape and structure.

The enamel layer is thin and the cervical area of the tooth is constricted. Enamel is rarely hypoplastic. If at that stage aplasia of several teeth is seen, the patient should be referred to a geneticist in a pediatric unit with a suspicion of EDA diagnosis. Tooth crowns are small and abnormal in shape. Upper incisors and cuspids are always conical or pointed.

Taurodontism, frequently on the second deciduous molars, is a common feature. Not only the shape is abnormal, but also the number. A severe hypodontia is a universal feature amongst affected individuals. All lacked some deciduous teeth and permanent teeth. The number varies from four to twenty. A few patients have congenital anodontia. There are generally more teeth in the maxilla than in the mandible, although both jaws can be toothless [38]. Most often the lower incisors and premolars are missing, followed by the upper premolars and incisors. The upper cuspids and first upper and lower molars are formed.

The edentulous EDA patients do not have any alveolar processes either [39]. In those patients with some natural teeth, there is a striking difference in the intra-oral height and breadth of the bone.

In areas where no teeth have developed, the alveolar bone is missing and the bone ridge is very thin in contrast to the normal alveolus surrounding an occasional tooth.

Many patients complain of dry mucous membranes in mouth and nose. Reduced salivary secretion has been spotted in some EDA patients. The oral mucous glands should be missing in the lips. Autopsy has also shown absence of mucous glands in the pharynx, larynx, trachea and bronchi. This is in agreement with the susceptibility to respiratory infections. The other salivary glands are not described in literature. Analysis of the saliva has revealed a reduced buffer capacity and an increased number of bacterial cultures. Most affected individuals were susceptible to dental caries.(fig 4&5)



Fig 6: abnormality in teeth



Fig 7: abnormality in teeth

Hair, nails, skin and skintags

Abnormalities of hair are present in all affected individuals. Most individuals have sparse, fine, slowly growing scalp hair (fig 6). Some individuals are completely bald by their middle teens, whereas other individuals have normal amounts of scalp hair, though it may exhibit an abnormal texture. Sparse eyebrows and eyelashes were always found. Most individuals show decreased body hair, pubic hair, and/or axillary hair, but these features are more variable. However, beard and moustache hair are normal. Electron microscopy of hairs from affected and unaffected individuals showed no abnormalities.

About half of the affected individuals exhibit mild fingernail abnormalities and nail dystrophy. Slow nail growth and split nails are most often reported. A few individuals had a longitudinal ridging, thinning and superficial peeling. Nail problems occur more frequently in older individuals. This suggests that the nail beds are more susceptible to progressive injury with age. Toenails were generally normal (fig 7).

Most individuals report dry skin. Affected individuals have a smooth, almost velvety skin texture. The skin of patients also seems to be “thinner” than expected for age. Some infants may have a premature look because of the thin skin. Scaling in the neonate may form a clue to diagnosis (fig 8).

Almost all affected relatives have decreased sweating, and many show heat intolerance. Some individuals only sweat in certain

areas on their body. Common sites of sweating include palms, soles and axillae. Because of the reduced number of sweat glands, there is a danger of hyperthermia. In this way EDA has been associated with sudden infant death. The hyperthermia may also lead to brain damage, and is probably the cause of the rare cases of EDA reported with mental retardation. Subcutaneous fat is often diminished and over one third of the boys have abnormalities of the breast, including absent or accessory nipples [40]. Episodes of hyperpyrexia and severe respiratory infections are life-threatening components in EDA. The delay in teething often leads to the diagnosis in childhood. After the first critical years of life the patients experience a general improvement in health. The lack of teeth is the most important factor in determining the quality of life in these patients, particularly in later life. They all suffer greatly from their abnormal facial and dental appearance.



Fig 8: abnormality in hair



Fig 9: abnormality in nails



Fig 10: abnormality in skin

Clinical diagnosis

Hypohidrotic ectodermal dysplasia (HED) can be diagnosed after infancy in most affected individuals by the presence of three cardinal features:

- **Hypotrichosis** (sparseness of scalp and body hair). In addition, the scalp hair has thin shafts and is lightly pigmented. Note: Although hair shafts can be brittle and twisted (pili torti) or have other anomalies on microscopic analysis, these findings are not sufficiently sensitive to be of diagnostic benefit [41]. Secondary sexual hair (beard and pubic hair) is normal.
- **Hypohidrosis** (reduced ability to sweat). Reduced ability to sweat in response to heat leads to hyperthermia:

- The function of sweat glands may be assessed by bringing the skin into contact with an iodine solution and raising ambient temperatures to induce sweating. The iodine solution turns color when exposed to sweat and can be used to determine the amount and location of sweating.
- The number and distribution of sweat pores can be determined by coating parts of the body (usually the hypothenar eminences of the palms) with impression materials commonly used by dentists.
- While skin biopsies have been used to determine the distribution and morphology of sweat glands, noninvasive techniques are equally effective.
- **Hypodontia** (congenital absence of teeth):
- An average of nine permanent teeth develop, typically the canines and first molars [42].
- Teeth are smaller than average and often have conical crowns.
- Dental radiographs are essential to determine the extent of hypodontia and are useful in the diagnosis of mildly affected individuals.

Note: Anthropometric variations (measurements of facial form and tooth size) in HED are subtle and have not proven clinically useful.

Carrier detection for X-linked HED

- Because carriers for X-linked HED show mosaic patterns of sweat pore function and distribution, use of an iodine solution to assess sweat gland function or impression materials to assess number and distribution of sweat pores is particularly useful.
- Carriers frequently will also display some degree of hypodontia [43].

Molecular Genetic Testing

Genes

- *EDA* is the only gene known to be associated with X-linked HED. Ninety-five percent of individuals with HED have the X-linked form.
- The genes *EDAR* and *EDARADD* are known to be associated with both autosomal dominant and autosomal recessive forms of HED. Mutations in these genes account for 5% of HED.

Clinical testing:

- **Sequence analysis**
- **EDA.** In males with X-linked HED, direct sequencing of the eight exons with flanking intron sequences of *EDA* identifies approximately 95% of mutations, including missense and nonsense mutations and smaller deletions.
- **EDAR.** Sequence analysis of the *EDAR* coding region is available on a clinical basis.
- **EDARADD.** Sequence analysis of the *EDARADD* coding and flanking intronic regions is available on a clinical basis.

- **Duplication/deletion testing.** Sequence analysis of *EDA* cannot detect exonic, multiexonic or whole gene deletions in females, and additional testing using methods that detect deletions is required.

Table 1. Summary of Molecular Genetic Testing Used in Hypohidrotic Ectodermal Dysplasia

Gene Symbol	% of HED Attributed to Mutations in This Gene	Test Method	Mutations Detected	Mutation Detection Frequency by Gene and Test Method
<i>EDA</i>	95%	Sequence analysis	Sequence variants	~95%
		Duplication/deletion analysis	Partial or whole <i>EDA</i> deletions	Unknown
<i>EDAR</i>	5%	Sequence analysis	Sequence variants	Unknown
<i>EDARADD</i>		Sequence analysis	Sequence variants	Unknown

1. For males affected with X-linked HED, mutations detected include intragenic deletions, since lack of amplification by PCR prior to sequence analysis can suggest a putative exonic or whole gene deletion on the X chromosome in affected males. Confirmation requires deletion analysis.
2. Sequence analysis of genomic DNA cannot detect deletion of an exon (s) or a whole gene on an X chromosome of carrier females.

3. Deletion analysis is used to detect exonic deletions in females and to confirm exonic deletions in affected males
4. Testing that detects deletions/duplications not readily detectable by sequence analysis of genomic DNA; a variety of methods including quantitative PCR, real-time PCR, multiplex ligation-dependent probe amplification (MLPA), or array GH may be used.

Testing Strategy:

Confirming the diagnosis in a proband:

- If the proband's findings are classic and are consistent with X-linked inheritance (i.e., males generally more severely affected than females, no male-to-male transmission), initial testing should be for *EDA* mutations:
 - If the affected individual is male, sequence analysis is sufficient as it detects both sequence variants and deletions.
 - If the affected individual is female, sequence analysis should be performed first; if no mutation is identified, deletion testing should be performed next.
- If the proband's findings are classic and consistent with autosomal recessive inheritance, or mild and consistent with autosomal dominant inheritance, testing should be done for *EDAR* and *EDARADD* mutations.

Carrier testing for relatives at risk for X-linked HED or autosomal recessive HED requires prior identification of the disease-causing mutation(s) in the family.

Prenatal Diagnosis

Prenatal diagnosis of EDA has occasionally been reported. The diagnosis has been made on fetal skin biopsy, obtained by fetoscopy by 20 weeks gestation after determination of the sex of the fetus. By histological analysis they demonstrate of either complete lack of, or reduction in, the number of pilosebaceous follicles and by the lack of sweat glands primordia in multiple skin biopsies. The interpretation of the biopsies can be difficult if one does not appreciate the normal regional variability of the distribution of skin appendages of fetal skin, and that sweat gland primordia only begin to develop at around 20 week gestation. This procedure is complicated and implies a considerable risk to the pregnancy.

The use of linked markers on DNA from chorionic villi has greatly improved the safety of prenatal diagnosis of X-linked EDA. This new method of prenatal diagnosis has major advantages as well as disadvantages. It permits the diagnosis to be made in the first trimester of pregnancy prior to the development of the affected structures, thereby allowing an early determination of an affected pregnancy. It is technically simpler and may present a lower risk to the pregnancy than the fetoscopy and multiple skin biopsies. Disadvantages to a linkage based indirect analysis include the need for the sampling of previously affected individuals. The counseling of families is more complex since one is dealing with the probabilities of an affected fetus, rather than a more definitive diagnosis based on direct observation. However, these statistical concepts are difficult for many families to comprehend fully.

The identification of mutations in the family will further improve the accuracy of prenatal diagnosis [44]. However, EDA is a disorder which in most cases is associated with a normal life expectancy and a normal intelligence. Prenatal diagnosis will therefore probably not be an option in most families with EDA.

The diagnostic procedure in ectodermal dysplasia patient is explained by showing a case report.

Case report

A male newborn with 10 days of life from the city of Caxias do Sul, state of Rio Grande do Sul, southern Brazil, was admitted to the Neonatal ICU of the Teaching Hospital at the Universidade de Caxias do Sul (UCS).

On August 20th, 1998. Patient presented with history of episodes of persistent hyperthermia since the first days of life. At physical examination, ES presented with dry mucous membranes, dry and desquamative skin, hyperthermia (39°C), and umbilical granuloma.

In order to investigate the origin of the fever we carried out chest X-ray, hemogram, hemoculture, urinalysis, urine culture, and liquor examination. The exams presented no alterations. Next, an umbilical stump culture was collected for suspected diagnosis of

omphalitis, which also presented negative. We started empiric therapy with oxacillin and gentamicin despite patient presenting normal for the examinations carried out.

On August 25th, 1998 patient peak temperatures persisted and the above examinations were carried out for a second time; once more, results were negative. We replaced oxacillin and gentamicin with vancomycin, amikacin, and cefotaxime.

On the 14th day of hospital stay the patient still did not present any improvement of clinical status. Consequently, we carried out exams to rule out HIV and congenital neonatal infection (STORCH). Again, patient presented negative for both exams. He also presented normal for ultra sonography examination of the abdomen.

Only on September 9th of that same year we suspected that the patient had anhidrotic ectodermal dysplasia. Biopsy of a specimen taken from the dorsum of the patient and histopathological report confirmed the diagnosis. Specimen submitted to anatomopathological exam indicated absence of eccrine and sebaceous gland structures and hypoplasia of follicular structures.

Patient was discharged from the hospital on September 12th, 1998. The mother was instructed regarding procedures for control of temperature and use of emollient for dry skin.

One year later, the clinical signs of anhidrotic ectodermal dysplasia were more evident. At physical examination, patient presented typical facies with frontal boss, small nose, lip protrusion, erythematous malar region rash, and rhinorrhea. Patient also presented hypotrichosis; thin and sparse hair; depigmentation of the hair; and sparse eyebrow hair. The skin was dry, pale, thin, and with protruding vessels.

Patient was submitted to an X-ray of the teeth that indicated total anodontia of deciduous teeth (maxillary and mandibular). The maxilla presented all permanent teeth germs, according to age; the lateral incisors, however, presented conoid characteristic and were in an advanced stage of development in relation to central incisors. In

relation to the mandible, we only found tooth germs of the first molar teeth (partial anodontia). Currently, the patient is being followed-up at the outpatient Dermatology and Pediatric clinic of the Teaching Hospital at UCS [45].

Treatment

There is no specific treatment for this disorder.

Medical Care

The care of affected patients depends on which ectodermal structures are involved. Note the following:

- For patients with anhidrosis/hypohidrosis, advise air conditioning for home, school, and work. Encourage frequent consumption of cool liquids to maintain adequate hydration and thermoregulation. Finally, advise patients to wear cool clothing.
- For patients with dental defects, advise early dental evaluation and intervention and encourage routine dental hygiene. Dentures may be indicated as early as age 2 years. Multiple replacements may be needed as the child grows, and dental implants may eventually be required [46,47,48,49,50]. Advise orthodontic treatment for cosmetic reasons and to ensure adequate nutritional intake.
- Patients with xerosis or eczematous dermatitis may benefit from the use of topical emollients.
- Patients with severe alopecia can wear wigs to improve their appearance.
- Patients with scalp erosions should be treated with topical and systemic antibiotics as needed. General scalp care may involve the use of weekly dilute bleach baths or acetic acid soaks to minimize bacterial colonization of the scalp. Application of special scalp dressings may be helpful.
- Use artificial tears to prevent damage to the cornea in patients with reduced lacrimation.
- Protect nasal mucosa with saline sprays followed by the application of petrolatum.
- Patients with ectodermal dysplasia with immunodeficiency should be monitored for infection and treated with therapeutic and/or prophylactic antibiotics when appropriate.

- Allogeneic stem cell transplantation has been performed in a small number of patients with autosomal dominant ectodermal dysplasia with immunodeficiency (EDA-ID); poor engraftment and post-transplant complications were common [51, 52].

Surgical Care

Early repair of cleft lip or palate may lessen facial deformities and improve speech. Other mid facial defects or hand/foot deformities may be surgically corrected in order to improve function and reduce physical disfigurement.

Conclusion

Ectodermal dysplasia is a genetic disorder. There is no pharmacological treatment for ectodermal dysplasia it is necessary to develop the researches for the development of drug therapy for ectodermal dysplasia. This review represents that it is mandatory to develop the awareness to the research scientists for developing the drug for ED.

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