Clouston Syndrome with Palmoplantar Keratoderma

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ABSTRACT

Clouston syndrome (hidrotic ectodermal dysplasia) is characterized by the clinical triad of nail dystrophy, alopecia and palmoplantar hyperkeratosis. Clouston syndrome is transmitted as an autosomal dominant trait and caused by mutations in the GJB6 gene (13q12), encoding the gap junction protein connexin 30 (C × 30). At present, there is no treatment for the disease and management is purely supportive. The life span, patients is normal. In this report, a case of 9-year-old boy is presented who had few set of primary dentition, but surprisingly complete absence of permanent dentition which observed radiographically. In this case, anodontia of permanent dentition was present and no alopecia which is a rare finding.

Keywords: Trichodysplasias, Onychodysplasias, Dyshidrosis.

INTRODUCTION

The ectodermal dysplasias (EDs) are congenital, diffuse and nonprogressive 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). They are classified as either group A disorders having at least two of the four classic ectodermal structures defect with or without other defects and group B disorders having one classic ectodermal structure defect with a defect in other ectodermal structures, i.e. ears, lips, dermatoglyphics; the four defects being trichodysplasias, dental abnormalities, onychodysplasias and dyshidrosis.

Thurnam published the first report of patient with ectodermal dysplasia in 1848, but the term ectodermal dysplasia was not coined until Weech termed it as so in 1929. In 1984, Friere-Maia proposed the first classification with updates in 1994 and 2001. With recent identification of the causative genetic defect for a number of the EDs, newer classification systems have been devised. In 2003, Lamartine reclassified the EDs into the following four functional groups based on the underlying pathophysiologic defect: (1) Cell to cell communication and signaling, (2) adhesion, (3) development and (4) others.

Similarly in 2005, Priolo and Lagana reclassified EDs into two main functional groups: (1) Defect in developmental regulation/epithelial-mesenchymal interaction and (2) defect in cytoskeleton maintenance and cell stability. The most common type of ED is X-linked recessive anhidrotic ED (Christ-Siemens-Touraine syndrome). It has full expression only in males, although female carriers outnumber affected men but show little or no sign of the condition. The typical facies is characterized by frontal bossing, sunken cheeks, saddle nose, thick everted lips, wrinkled hyper pigmented periorbital skin and large low set ears. Dental manifestations include conical or pegged teeth, hypodontia or complete anodontia and delayed eruption of permanent teeth. Fine, sparse, lusterless fair hair over scalp is seen in most of the patients. Onychodystrophy may be seen but is not common. Extensive scaling of the skin and unexplained pyrexia and heat intolerance due to anhidrosis occurs. Intelligence is normal. Palmoplantar keratoderma is a component of hidrotic ED but has been reported in anhidrotic ED. Patients may have chronic nasal infections with foul smelling discharge and increased lung infections. Clinical recognition of ED varies from birth to childhood depending on the severity of symptoms and the recognition of associated complications. Dental, hair and nail anomalies usually become evident during infancy or childhood. A family history of similar clinical features is helpful.

The disease was first described in the French-Canadian population (in which it is associated with a founder effect), but has since been identified in several other ethnic groups.
The exact prevalence is unknown and the syndrome is likely to be underdiagnosed. Disease penetrance is complete, but expression is quite variable even between affected individuals from the same family. Nail abnormalities are the most consistent feature and frequently manifest at birth or in early infancy. The nails are thickened, slow growing, brittle, often hyperconvex and discolored with striation. Additional reported features include micronychia, onycholysis and recurrent paronychial infections leading to nail loss. Hair involvement manifests at birth or later during infancy or childhood and ranges from total to partial, often progressive alopecia. Residual scalp hair is slow growing, sparse, fine and brittle.\(^9\)

Eyebrows and eyelashes are also frequently sparse and axillary, pubic and body hair can be affected. Palmoplantar hyperkeratosis is not a constant finding. When present, it usually begins in childhood and tends to worsen with age; some patients also develop hyperkeratosis and hyperpigmentation over the joints and bony prominences. Diagnosis may be suspected on the basis of the clinical triad of nail dystrophy, hypotrichosis and hyperkeratosis of the palms and soles. The diagnosis can be confirmed by molecular analysis of the GJB6 gene. The differential diagnosis should include pachyonychia congenita and other forms of ectodermal dysplasia. Prenatal testing is possible in families where the disease-causing mutation has been identified. At present, there is no treatment for the disease and management is purely supportive. The life span of patients is normal.\(^9\)

**CASE REPORT**

A 9-year-old boy reported to our clinic with a chief complaint of missing teeth (Fig. 1). His medical history was noncontributory and family history revealed that he was born to nonconsanguineous marriage with normal delivery and mother did not suffer from any disease during pregnancy and other siblings were not affected with the same problem. Detail history also revealed that there was no history of decrease or absence of sweating. On general physical examination, his weight was 18 kg, height 3 feet 11 inches and there was dystrophy of nails and hypermelanin pigmentation along with hyperkeratosis of palms and soles (Fig. 2). On extraoral examination, he had a concave profile with retrognathic mandible along with mild frontal bossing, there was sparse eyebrows present (Fig. 3). On intraoral examination, he had knife-edge pattern of the ridge in upper maxillary front region and lower incisors were conical in shape. Teeth present were 53, 54, 63, 64, 71, 72, 73, 74, 75, 81, 82, 83, 84 and 85.

Radiographic examination (OPG) revealed erupted set of primary teeth with altered morphology of lower mandibular teeth, presence of wide pulp canals and increase crown to root ratio favoring taurodontism (Fig. 4). A provisional diagnosis of nonsyndromic partial anodontia was given with differential diagnosis of ectodermal dysplasia hidrotic variety, Rieger syndrome and Witkop syndrome.

Pediatric and dermatologic consultation was taken regarding general health status of the child. Complete set of investigations were done which included radiographic examination of chest as well as phalanges, routine examination of blood including serum calcium, alkaline phosphate, TSH, T3, T4. The findings of these investigations were normal. Final diagnosis of hidrotic ectodermal dysplasia was made. Full mouth rehabilitation was planned along with endodontic therapy.

**DISCUSSION**

Hidrotic ectodermal dysplasia 2 or Clouston syndrome (referred to as HED2 throughout this entry) is characterized by partial or total alopecia, dystrophy of the nails, hyperpigmentation of the skin (especially over the joints) and clubbing of the fingers. Sparse scalp hair and dysplastic nails are seen early in life. In infancy, scalp hair is wiry, brittle, patchy and pale; progressive hair loss may lead to total alopecia by puberty. The nails may be milky white in early childhood; they gradually become dystrophic, thick and distally separated from the nail bed. Palmoplantar keratoderma may develop during childhood and increases in severity with age. The clinical manifestations are highly variable even within the same family.
Diagnosis/testing: HED2 is suspected after infancy on the basis of physical features in most affected individuals. GJB6 is the only gene known to be associated with HED2. Targeted mutation analysis for the four most common GJB6 mutations is available on a clinical basis and detects mutations in approximately 100% of affected individuals. Sequence analysis is also available on a clinical basis for those in whom none of the four known mutations is identified.

Genetic counseling: HED2 is inherited in an autosomal dominant manner. Most individuals with HED2 have an affected parent; de novo gene mutations have also been reported. Offspring of affected individuals have a 50% chance of inheriting the mutation and being affected. Prenatal testing for pregnancies at increased risk is possible if the disease-causing mutation in an affected family member is known; however, requests for prenatal testing for conditions, such as HED2, are not common.10

Management of patients with this condition usually includes a removable and/or fixed partial denture, complete denture prosthesis, and an implant-retained prosthesis, when indicated. These treatment approaches can be used individually or in combination to provide an optimal result. Sequencing treatment appropriately is important for achieving the desired functional and esthetic results. Because of the early age at intervention and the need to easily modify the intraoral prosthesis during rapid growth periods, a removable partial denture or complete denture prosthesis is indicated initially. A retained prosthesis can be implanted once the growth is complete. Treatment of manifestations: Special hair care products to help manage dry and sparse hair, wigs, artificial nails, emollients to relieve palmoplantar hyperkeratosis.10

Hypodontia is associated with lack of development of the alveolar ridge and results in less volume of bone available to support a conventional prosthesis. The placement of endosseous implants in locations favorable for subsequent restorations may be difficult, as this requires bone grafting. Placing implants in growing children is not recommended as a routine practice.11 In the present case, due to the boy’s young age, ongoing development of his jaws and insufficient alveolar bone support, multiple implant placements were not possible. The bone height and width were not sufficient for implant insertion without using an advanced surgical approach. Application of removable dentures may be the only restorative option for this patient. When he has finished growing, treatment planning may include an implant-retained prosthesis. Medical management of the boy’s condition has also been planned in consultation with a pediatrician and dermatologist.

CONCLUSION

Early recognition of this condition is important to enable better management of anodontia or hypodontia for both physiological and psychosocial reasons. Oral rehabilitation is an important part of the treatment protocol from esthetic, functional and psychological perspectives. It involves a number of challenges as the treatment procedures are complicated by growth and development of the child, variation in tooth development and eruption, type of prosthesis, planning and timing of treatment. Moreover, successful treatment depends on good cooperation and communication between the dental team, the patient, and his parents. Optimal management requires a multidisciplinary approach involving the pedodontist, orthodontist, prosthodontist, endodontist, pediatrician, dermatologist and psychologist.

REFERENCES

2. Thurnam J. Two cases in which the skin, hair and teeth were very imperfectly developed. Proc RM Chir Soc 1848;31: 71-82.