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Hypohidrotic Ectodermal Dysplasia: a rare inherited multisystem disorder

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Hypohidrotic ectodermal dysplasia (HED), also known as Christ-Siemens-Touraine syndrome, is a rare X-linked genetic disorder characterized by the faulty development of the ectodermal structures, resulting in most notably anhydrosis/ hypohidrosis, hypotrichosis and hypodontia. Here, we report clinical presentation of a HED case. A female child aged 8 years was brought with complaints of high grade fever along with upper respiratory tract illness symptoms. She also had recurrent episodes of unexplained hyperpyrexia and thirst. Physical examination revealed characteristic appearance which aided in arriving at a diagnosis. Diagnosing this disorder in early life prevents mortality which is high especially during neonatal period. Therefore, it is essential for the treating clinician to have basic knowledge on the clinical presentations as well as complications of this specific genetic disease so that it is not missed. It is rare to see a classical case of hypohidrotic ectodermal dysplasia in female children with typical phenotypic features hence, this case report is presented.

Keywords: Christ-siemens-touraine syndrome, Hyperpyrexia, Hypodontia, Hypohidrosis, Hypotrichosis

Christ-siemens-touraine syndrome, also known as hypohidrotic (or anhidrotic) ectodermal dysplasia (HED) occurs in 1 in 1,00,000 births which affects development of two or more ectodermally derived structures. Clinical triad of hypohidrosis, hypotrichosis and hypo/ anodontia is seen typically in this condition. It is the most common form of Ectodermal dysplasia(ED) which affects males more commonly. Females are usually carriers and less severely affected but they exhibit high phenotypic variability[1]. It is characterized by reduction in the amount of hair (hypotrichosis), absence of sebaceous glands (asteatosis) and absence of sweat glands (anhidrosis). Patients often show these manifestations in their appearance: prominent supraorbital ridges, protuberant lips, sunken cheeks, depressed nasal bridge and wrinkled hyperpigmented skin around the eyes and mouth. Dental manifestations include malformed conical or peg-shaped teeth, hypodontia or complete anodontia in both deciduous and permanent dentition, generalized spacing, delayed eruption of permanent teeth, underdeveloped alveolar ridges, and high arched palate or cleft palate[2,3]. It also affects major salivary glands as well as accessory glands which result in xerostomia and dry cracked lips. Ocular manifestations are also reported in the form of sparse and thin lashes, trichiasis, pseudodistichiasis in many children[4].

Case report

Here we report a case of 8 years old female child who presented with complaints of high grade fever along with symptoms of upper respiratory illness. Mandatory procedure of informed consent was obtained from the parents and institutional ethics committee approval was obtained prior to clinical observation and presentation. Child was first born to non-consanguineous marriage by full term normal delivery and developmentally normal with good scholastic performance. Her mother stated that child had recurrent episodes of unexplained hyperpyrexia with history of recurrent respiratory tract infections since birth. On examination child had frontal bossing, alopecia, sparse eyebrows and eyelashes, depressed nasal bridge (Fig. 1A) with hyperpigmentation of skin over the scalp. Intraoral examination revealed the complete absence of primary and permanent teeth (Fig. 1B). She had no nail dystrophy and normal

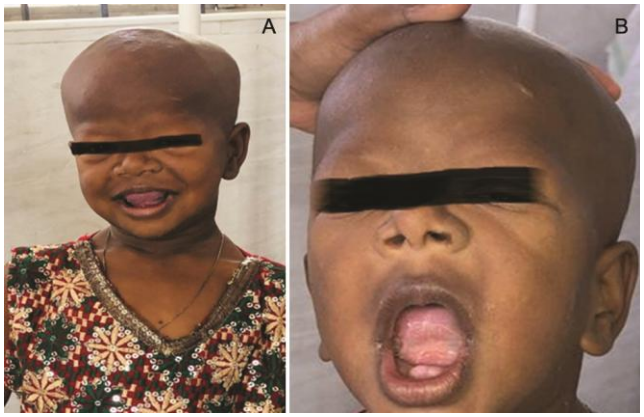

Fig. 1 — (A) 1Hypohidrotic Ectodermal Dysplasia; and (B) Anodontia

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systemic examination. There was no history of similar features in the family members. Child's complete blood count and urine analysis reports were normal. Based on the history, clinical features and examination, the child was diagnosed as a case of hypohidrotic ectodermal dysplasia. Diagnosis was based on clinical grounds as genetic testing could not be performed[5]. Skin biopsy showed reduced number of eccrine sweat glands in the dermis. Panoramic radiograph and skull x-ray was taken to assess the development of jaw bones for further dental reconstruction and prosthesis.

Discussion

Christ-Siemens-Touraine syndrome is caused by mutation in novel transmembrane protein ectodysplasin A located on Xq12-q13.1 with extremely rare incidence at birth, and mortality rate of 28% in males up to 3 years of age[6]. In rare instances, many members of the same family are reported to have varied forms of ectodermal dysplasias[7,8]. To date, more than 192 distinct disorders have been described. Among ectodermal dysplasias (ED), there are several examples of overlapping phenotypes from various distinct diseases posing diagnostic challenge in exact identification of that syndrome. Depending upon the severity, it can be classified as either hypohidrotic or anhidrotic ectodermal dysplasia. The clinical presentation of our patient was consistent with a case of hypohidrotic ectodermal dysplasias (HED).

Infants often present with high fever and feeding difficulties in which 6% of the affected children experience febrile seizures. They are more prone to develop recurrent respiratory tract infection like pneumonia. Adolescents present with features of heat exhaustion[9] and sometimes with mild mental retardation. Neurological impairments can occur due to repeated exposure of brain to higher temperature[10]. Females being carriers, rarely present with the signs of this condition and their clinical identification is difficult. Contrary to this, our case, a female child exhibited many clinical signs including agenesis of temporary teeth. Spontaneous gene mutation is possible and may occur without any previous history of the syndrome in family[11]. Early diagnosis of this disorder may help to prevent dangerous hyperthermia episodes in infancy and allow timely intervention so that mortality is greatly reduced during neonatal period. Prenatal diagnosis with DNA based mutation analysis from DNA sample collected by chorionic villous biopsy is now a confirmatory diagnosis. Fetal skin mapping is not reliable since there will be lack of hair and sweat glands primordia in normal fetus at early stages also. Latest method in prenatal diagnosis is tooth germ sonography in first trimester of gestation[12]. There is no specific treatment for this condition. Management includes multidisciplinary approach including psychological counselling; use of wigs and dental prosthetics[13] may improve child's cosmetic appearance. Consultation with speech therapist and otolaryngologist is warranted if abnormalities in phonetics and word articulation are detected. Prenatal diagnosis and correction with in utero recombinant protein which have receptor binding domain of EDA are being tried now with good outcome[14].

Conclusion

The female child presenting with all the clinical signs of hypohidrotic ectodermal dysplasia (HED) as reported here is rare. Though genetic testing would be the appropriate method of diagnosis, at times due to the situation, the diagnosis has to depend upon other secondary methods as described above. Timely diagnosis prevents morbidity and mortality. Being a recessive disorder, genetic counselling plays an important role in preventing recurrence in future pregnancy.

Conflict of interest

Authors declare no competing interests

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