ISSN: 2754-494X

Journal of Dermatology Research Reviews & Reports

SCIENTIFIC Research and Community

Case Report

Open Access

A Case of Hypohidrotic Ectodermal Dysplasia in a 1-Year Old Filipino Male

Maria Criselda C Valerio*, Janella Cristin S Mercado-Garcia, Athena Emmanuelle M Parro-Mallari, Kyla Janika M Nerva, Erika Gayle C Ty and Maria Franchesca S Quinio-Calayag

Department of Dermatology, East Avenue Medical Center, East Avenue, Diliman, Quezon City, 1100 Metro Manila, Philippines

ABSTRACT

Introduction: Hypohidrotic Ectodermal Dysplasia (HED) is the most common Ectodermal Dysplasia, a group of rare, inherited multisystemic disorders exhibiting developmental aberrations in ectodermal structures including the hair, teeth, nails, and sebaceous and sweat glands. HED is commonly X-linked, presenting with abnormalities of the hair and teeth accompanied by inability to sweat. This case report aims to present a case of X-linked HED in a 1-year-old Filipino male.

Case Report: A 1-year-old Filipino male presented with reduced sweating since birth and heat intolerance. He had scalp and facial papules, slowly growing, sparse eyebrow and scalp hair, periorbital wrinkling with hyperpigmentation, everted lips, frontal bossing, absent tooth, and negative palmoplantar starch-iodine test. Maternal male relatives had similar symptoms while females had little to no symptoms. He was diagnosed with HED. Skin punch biopsy with immunohistochemistry showed absence of eccrine glands on the plantar skin, which strengthened the diagnosis. Management of symptoms was mainly supportive and involved multidisciplinary collaboration with Pediatrics, Otorhinolaryngology, Dentistry, and Nutrition and Dietetics.

Conclusion: This report underscores the critical role of Dermatologists in identifying key clinical signs of HED, which primarily relies on clinical assessment. A high level of suspicion is warranted when abnormalities in hair, teeth, and sweating are evident. It is crucial to consider other potential features in patients with symptoms of hypotrichosis, hypodontia and hypohidrosis, due to the varied manifestations of the disease. Early detection, comprehensive supportive treatment, and patient education are vital for improving the quality of life for those affected by HED.

***Corresponding author**
Maria Criselda C Valerio, Department of Dermatology, East Avenue Medical Center, East Avenue, Diliman, Quezon City, 1100 Metro Manila, Philippines. Tel: +63 995 724 6831.

Received: April 12, 2024; **Accepted:** April 15, 2024; **Published:** April 24, 2024

Keywords: Hypohidrotic Ectodermal Dysplasia, Ectodermal Dysplasia, Hypohidrosis, Hypotrichosis, Hypodontia

Introduction

Ectodermal Dysplasia is a group of uncommon, diverse disorder exhibiting alterations affecting the ectoderm-derived structures such as hair, nails, teeth and sweat glands. Hypohidrotic Ectodermal Dysplasia (HED), the most common phenotype with X-linked inheritance, has a frequency of one per 17,000 live births in the general population. Genetic mutations from EDA1, EDAR, EDARADD genes are associated with different forms of HED. This skin condition demonstrates reduced ability to absent sweating (hypohidrosis, anhidrosis), few to absent teeth (hypodontia, anodontia), and sparse hair (hypotrichosis). No gene therapy has been established to date and treatment is limited, involving some general measures such as avoidance of overheating, proper skin and oral care, and monitoring for complications. This case report aims to describe a case of X-linked HED in a 1-year-old Filipino male [1,2].

Case Report

The patient is a 1-year-old Filipino male who came in to the Dermatology out-patient clinic due to reduced sweating since birth. Whenever exposed to a hot environment, the patient's skin becomes warm to touch and is associated with intermittent, few, erythematous papules on the scalp and face. Symptoms are relieved by transfer to a cooler environment. He also had slowly growing, sparse hair on his scalp and eyebrows. This prompted consultation with a pediatrician who gave Desonide cream for the erythematous papules, applied twice a day on affected areas and Cetirizine 2.5mg per mL oral solution, 1mL given once at night, which relieved the lesions.

1 month prior to consultation, on follow-up with the pediatrician, the patient was advised to be seen by a pediatric neurologist for evaluation of the apparently increasing head circumference. He was brought to a pediatric hospital, seen by a pediatric neurologist, and was advised to have cranial ultrasound, which yielded unremarkable results. He was then cleared of any neurologic problems at the time of examination and was referred to a dermatologist, hence this consultation.

Review of systems revealed the presence of intermittent fever, absence of tears, ear or nasal discharge and prominent salivation, absence of cervical lymphadenopathy, absence of seizures or decrease in sensorium. The patient had a previous history of

impacted cerumen at 8 months of age but did not experience frequent upper respiratory tract infections. A relevant family history finding was that his mother and his mother's maternal male cousins had similar symptoms of almost-none to sparse scalp hair, few peg-shaped permanent teeth, periorbital wrinkling and hyperpigmentation, and everted lips.

The patient was born full-term to a 39-year-old G2P1 (1001) mother via cesarean section secondary to Oligohydramnios, appropriate for gestational age, no collodion membrane or marked scaling noted after birth. Patient was treated for Neonatal Pneumonia, completed 7 days of Ampicillin 310mg IV and Cefotaxime 155mg IV prior to discharge. The Otoacoustic Test and Newborn Screening results were normal. The patient's mother had regular pre-natal check-ups starting 2 months age of gestation with unremarkable course. He was breastfed during the first month of life but was subsequently bottle-fed. The patient is able to tolerate fortified infant cereals but not mashed vegetables. The patient was at par with age in all domains of development during the time of diagnosis.

Pertinent general physical examination findings in the initial consultation were: low weight-for-height, normal body temperature, frontal bossing, and absence of nasoaural discharge. Cutaneous examination revealed sparse, fine, lightly pigmented scalp hair, periorbital wrinkling with some hyperpigmentation, absent eyebrow hairs, several, well-defined, skin colored to erythematous, round papules on the scalp and cheeks, everted lips, absence of teeth, hypoplastic nipples, normal nail findings, negative Starch Iodine Test on the palms and soles (Figure 1). The patient's mother and older sister also underwent cutaneous examination. His mother had thin, sparse eyebrows and a few peg-shaped teeth. The patient's 5-year-old sister did not have any significant cutaneous findings.

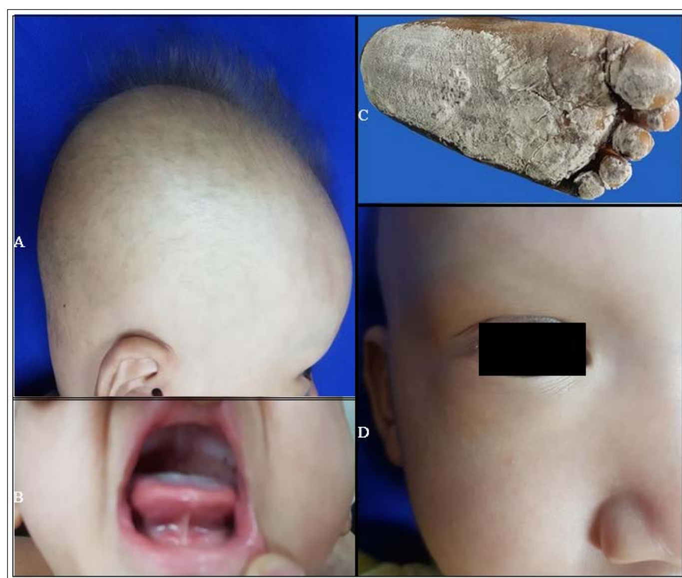

Figure 1: Clinical features of the patient. A. Sparse, thin, lightly pigmented scalp hair and frontal bossing. B. Absence of primary tooth at 15 months of age. C. Negative starch-iodine test on plantar skin. D. Absent eyebrow hairs, periorbital wrinkling with hyperpigmentation, few skin colored to pinkish papules on the face

The skin punch biopsy on the plantar aspect of the left foot revealed marked decrease to absence of eccrine glands. Immunohistochemical staining of Epithelial-membrane Antigen (EMA) showed mild positive staining of sparse immature or rudimentary eccrine glands in the reticular dermis. This immune histomorphologic staining pattern is supportive of a diagnosis of Ectodermal Dysplasia. The final diagnosis, Hypohidrotic Ectodermal Dysplasia, was explained to the patient's mother and caretakers. On follow-up, the patient was noted to have recurrence of papules on the scalp triggered by heat and recurrence of fever, intermittent cough with thick dry nasal secretions and yellowish green ear discharge. They were educated regarding avoidance of triggers, the importance of maintaining a cool ambient temperature for the patient, close monitoring for hyperthermia and recurrent infections, use of gentle cleansers for hair and skin, and oral hygiene with clean gauze and toothpaste on gums and oral mucosal surfaces.

The patient was also referred to other medical specialties for comprehensive management: Pediatrics and Otorhinolaryngology for the systemic symptoms and nasoaural discharge, Dentistry for regular oral examination and intervention for hypodontia, Nutrition service for nutritional build-up, and Speech Therapy for supportive management of complications from hypodontia and dry oral mucosa. A genetic consultation may be recommended to the patient prior to his childbearing years so that he can better understand his own reproductive risk.

Discussion

This paper presents a case of HED in a 1-year-old Filipino male presenting with reduced sweating since birth, heat intolerance, papules on the scalp and face, slowly growing, lightly pigmented, fine, sparse hair on the eyebrows and scalp, periorbital wrinkling and hyperpigmentation, everted lips, hypoplastic nipples, frontal bossing, absent tooth and absence of sweating documented by negative Starch-Iodine test on palms and soles (Figure 1). Maternal male relatives of the patient had similar symptoms while female family members presented with little to no symptoms at all. Signs and symptoms pointing to HED were further supported by the skin punch biopsy and immunohistochemistry results showing the absence of eccrine glands on the plantar skin. Management of symptoms was mainly supportive and involved a multidisciplinary collaboration with Pediatrics, Otorhinolaryngology (ENT), Dentistry and Nutrition and Dietetics.

Hypohidrosis, hypotrichosis, and hypodontia, the three classic characteristics present in X-linked HED, were seen in this patient. This classic triad of X-linked HED was documented by the study of. Hypohidrosis manifested with intermittent fever due to the patient's reduced sweating ability, causing overheating in warm environments and a negative starch iodine test. The absence of collodion membrane, intense scaling similar to ichthyosis, and history of frequent hospitalization due to high fever and seizures during infancy that are seen in documented cases of X-linked HED shows the variable expressivity of the disease. These observations could also signify that the patient has less severe thermoregulation problems and may suggest a favorable prognosis. Hypotrichosis of the patient manifested with thin, sparse and light-colored hairs on the scalp and eyebrows. Lastly, the hypodontia of the patient manifested with the absence of any primary tooth at 15 months of age. In addition to the presence of classic features of HED, the male predominance of similar symptoms among the patient's family members and little to absent manifestation in female family members strongly suggest an X-linked pattern of inheritance [2-4].

Other dysmorphic features of HED such as prominent forehead or frontal bossing, everted lips, periorbital wrinkling and hyperpigmentation, thin, pale and dry skin were also seen in the

patient. The absence of tears and prominent salivation, dry thick nasal secretions, impacted cerumen, and his inability to tolerate semisolid foods are possible indicators of defective development of exocrine glands that further support the diagnosis of HED in this patient [2].

HED is a genetically heterogenous group of disorders caused by different gene mutations involved in encoding the ectodysplasin A (EDA) signaling pathway, a tumor necrosis factor α (TNF-α) signaling pathway that is important in the connection of the ectoderm to the mesenchyme, thereby affecting the development of skin appendages. Despite the advances in the genetic basis of disease, the establishment of HED diagnosis remains clinical. Molecular genetic testing to identify mutations in EDA, EDAR, EDARADD or WNT10A genes may confirm the diagnosis, and at the same time, identify carriers in the family that is needed for genetic counseling. Histologic evaluation of the skin is usually not mandatory but can help in proving the paucity or absence of the eccrine glands. The said histopathologic finding was well documented in this patient who underwent skin punch biopsy with EMA stain. Interestingly, in a journal by Rouse, et al. (2004) on further characterization of hair and sweat Glands in families with HED, their findings suggested that a scalp biopsy should be preferred for individuals suspected of having HED because it is an easier site for obtaining a specimen, carries a lower risk of problematic scarring, and was found to be more sensitive than palmar biopsy. Additionally, non-invasive trichograms and sweat testing with starch-iodide, despite being not sensitive or highly specific, are simple, inexpensive tests that can support the diagnosis of HED.Starch-iodide testing was done on the patient prior to skin biopsy which revealed negative results. This became congruent to the subsequent histopathologic findings of decreased to absent eccrine glands on skin punch biopsy [2,5-8].

Management of HED remains challenging due to the lack of established guidelines given the disease rarity and varying symptom severity. Treatment is mainly supportive with a goal of alleviating the associated symptoms through avoidance of overheating, maintenance of proper skin and oral health, addressing eczematous rashes, and recognizing and managing subsequent infections. A multidisciplinary approach aiming to improve the patient's general health and overall quality of life is essential. This was exemplified by this case wherein referrals to different medical specialties were facilitated to address the non- cutaneous signs and symptoms of HED. Pediatric, Pulmonological and ENT consultations are necessary for the early intervention of possible recurrent infections due to dry mucosal passages. Dental management of HED entails education on proper oral care and dental prosthesis as deemed necessary for underdeveloped teeth that could impair speech, feeding and nutrition. Supportive counseling for both the patient and family members could help them cope with living with this rare genetic condition. Genetic counseling is also beneficial to both the patient and the family in providing information about the inheritance pattern and reproductive risks [6].

Conclusion

This case report highlights the vital role of a Dermatologist in recognizing key clinical features of HED as the diagnosis remains clinically-based. A high index of suspicion of HED is warranted given the presence of abnormalities in hair, teeth and sweating. It is also important to remember that there are other features to look for in patients presenting with hypohidrosis, hypotrichosis and hypodontia due to the diverse involvement of the disease. Early detection, holistic supportive care, and patient education are crucial in optimizing the quality of life of patients living with HED.

References

1. Majmundar VD, Baxi K (2021) Ectodermal Dysplasia [Internet]. PubMed. Treasure Island (FL): Stat Pearls Publishing https://www.ncbi.nlm.nih.gov/books/NBK563130/.
2. Reyes Reali J, Mendoza Ramos MI, Garrido Guerrero E, Méndez Catalá CF, Méndez-Cruz AR, et al. (2018) Hypohidrotic ectodermal dysplasia: clinical and molecular review. International Journal of Dermatology 57: 965-972.
3. Anbouba GM, Carmany EP, Natoli JL (2020) The characterization of hypodontia, hypohidrosis, and hypotrichosis associated with X-linked hypohidrotic ectodermal dysplasia: A systematic review. American Journal of Medical Genetics 182: 831-841.
4. Fete M, Hermann J, Behrens J, Huttner KM (2014) X-linked hypohidrotic ectodermal dysplasia (XLHED): Clinical and diagnostic insights from an international patient registry. American Journal of Medical Genetics Part A 164: 2437-2442.
5. Kang S, Amagai M, Bruckner AL, Enk AH, Margolis DJ, et al. (2019) Fitzpatrick's Dermatology. 9th ed. Mc-Grawhill Education https://accessmedicine.mhmedical.com/content.aspx?bookid=2570§ionid=21041330.
6. Aftab H, Escudero IA, Sahhar F, Aftab H, Escudero IA, et al. (2023) X-Linked Hypohidrotic Ectodermal Dysplasia (XLHED): A Case Report and Overview of the Diagnosis and Multidisciplinary Modality Treatments. Cureus https://www.cureus.com/articles/161149-x-linked-hypohidrotic-ectodermal-dysplasia-xlhed-a-case- report-and-overview-of-the-diagnosis-and-multidisciplinary-modality-treatments#.
7. Sanpreet Singh Sachdev, Padawe D, Ankita Khade, Vilas Takate, Kishore Dighe (2023) Hypohidrotic hereditary ectodermal dysplasia: A case report. IP international journal of medical paediatrics and oncology 8: 165-169.
8. Rouse C, Siegfried EC, Breer WA, Nahass GT (2004) Hair and Sweat Glands in Families with Hypohidrotic Ectodermal Dysplasia. Archives of Dermatology 140: 850-855.

Copyright: ©2024 Maria Criselda C Valerio. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.