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Case Report

X-linked ichthyosis associated with Hypohidrotic ectodermal dysplasia

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Abstract

X-linked ichthyosis is a genetic disorder characterized by a generalized scaling of the skin with large, polygonal, dark brown scales, more prominent on the extensor aspects of the limbs. Only males manifest the disease, while female carriers do not present it. Since 1978 it has been known that a deficit in steroid sulphatase enzyme (STS) is responsible for the abnormal cutaneous scaling, although the exact physiological mechanism remains uncertain. On the other hand, Hypohidrotic ectodermal dysplasia (HED) is a rare genetic disorder characterized by the faulty development of the ectodermal structure, resulting in most notably anhydrosis/hypohydrosis, hypotrichosis and hypodontia. The condition is usually an X-linked recessive disorder affecting predominantly males. But X-linked ichthyosis asociated with Hypohidrotic ectodermal dysplasia is a rare presentation. In this article we are reporting a rare case of X-linked ichthyosis associated with hypohidrotic ectodermal dysplasia.

Introduction

X-linked ichthyosis is a genetic disorder, X-linked, recessive pattern affecting approximately 1 in 6000 males,[1] with no significant racial or geographical differences. As seen in all diseases with a sex-linked recessive hereditary trait, X-linked ichthyosis is transmitted by women and affects males almost exclusively.[2]

Although Cockayne[3] was the first author to report the existence of clinical forms of ichthyosis affecting only males, X-linked ichthyosis was definitely separated from the rest of the ichthyoses as a distinct entity by Wells and Kerr[4] in 1965. That same year, France and Liggins[5] observed the absence of the enzyme STS in the placenta of some male foetuses and, in 1976, Jo¨bsis et a.[6] suggested that this deficiency could also be related to X-linked ichthyosis. In 1978, Koppe et al.[7] and Shapiro et al.[8] identified the STS enzyme deficiency in skin fibroblasts from patients with X-linked ichthyosis. These early reports were followed by others confirming that the deficit was widely distributed, involving other tissues such as the epidermis,[9] leucocytes[10] and stratum corneum.[11]

X-linked ichthyosis is characterized by the presence of dark brown, polygonal scales on different parts of the body surface. The lesions are usually distributed symmetrically and are generally more evident on the extensor aspects of the limbs, particularly on the lower extremities.[12] Scale size varies individually but in general the scales are larger on the extensor areas of the lower limbs than on the upper part of the trunk. The face is usually free of scales, except in the preauricular areas, which according to some authors is a pathognomonic feature.[13] Often, but not always, the flexures are affected (Fig. 1),[14] as are the neck and scalp, where pityriasiform desquamation is observed. The palms and soles are very rarely involved, although such involvement does not exclude a diagnosis of X-linked ichthyosis.[15] The hair and nails are normal.[16]

X-linked ichthyosis (XLI) may occur solely as a skin disorder or may be associated with other physical findings such as corneal opacities, cryptorchidism, chondrodysplasia punctata, and nephrotic syndrome.[17] Deletions encompassing STS have been reported to be associated with multiple behavioral, cognitive, and neurological phenotypes notably: mental retardation, developmental conditions including autism spectrum disorders (ASDs), attention deficit hyperactivity disorder (ADHD), and seizures.[18]

X-linked ichthyosis is rarely associated with Hypohidrotic ectodermal dysplasia (HED). Ectodermal dysplasias are a group of inherited disorders that share common developmental defects involving at least two of the major structures classically hold to derive from

the embryogenic ectoderms – hair, teeth, nails and sweat glands. HED is characterized by partial or complete absence of sweat glands, hypotrichosis, and hypodontia. The X-linked HED, otherwise called Christ–Siemens–Touraine Syndrome, was first described in 1848 by Thurnam. The incidence at birth is 1 in 100,000 males.[19]

HED can present with peeling skin similar to "post-mature" babies. Eccrine function (sweating), although present, is greatly deficient, leading to episodes of hyperthermia. More often, diagnosis is delayed until the teeth fail to erupt at the expected age (6- 9 months) or the teeth that erupt are peg-shaped, conical, or knife-edge in shape, which may affect the ability to eat and speech. Patients also have a peculiar facies, characterized by periorbital hyperpigmentation, depressed nasal bridge (saddle nose deformity), pointed chin, frontal bossing, everted lips, midface hypoplasia. They tend to have sparse scalp and body hair (hypotrichosis) that is often light-coloured and slow-growing; eyebrows and eyelashes are sparse or totally absent.[20] Abnormalities in function of the mucous membrane leads to frequent respiratory tract infections and changes in nasal secretions from concretions (solidified secretions in the nasal and aural passages) in early infancy to large mucous clots.[21] The epidermis is xerotic, with patches of hyperkeratosis and/or eczematous. Common otorhinolaryngological manifestations include chronic infections such as rhinitis, pharyngitis, otitis media, hearing loss, epistaxis, and dysphonia. As a consequence of gastroenteric glands hypoplasia, HED patients can also suffer from dysphagy and constipation.[22] Physical growth and psychomotor development are otherwise within normal limits. In HED males are affected but female carriers may manifest milder features: congenital tooth agenesis and misshapen teeth, sparse and thin hair and some problems with sweat glands function.[23] National Foundation for Ectodermal Dysplasias (NFED) has created a database for patients which allowed to determine the most frequent clinical characteristics in a large group of patients, based on this, the most reported feature in patients with HED is hypohidrosis, followed by hypotrichosis and hypodonthia equally represented among patients. Other complications described mainly in male patients are nasal congestion with bad odor interfering with feeding, eczema and recurrent sinusitis.[24]

Case Report

A 12 years old student hailing from Gazipur visited on 7 December 2018 at OPD of Dermatology and Venereology, BSMMU with the complaint of generalized dark, large scales for 12 years. This boy was brought to the hospital by his parents repeatedly due to decreased sweating, dry skin, recurrent episode of high-grade fever, and delayed eruption of abnormally shaped teeth.

Initially his parents noticed that erythema over abdomen which later developed dark, large scales on erythematous site. After some times scaling spreaded over different parts of the body but spare face, flexures, palm and sole. The elbow and knee flexures were relatively spared. Scales were dark, large and more prominent on extensor surface of the extremities and the trunk. Patient's conditions does not improve with age.

On integumentary system examination dark, Large, prominent Scales involving all over the body but more prominent in extensor surface of limbs and sparing the face, flexures, palm, sole. Mucous membrane and nail detect no abnormality. Other general & systemic examination reveal no abnormality.

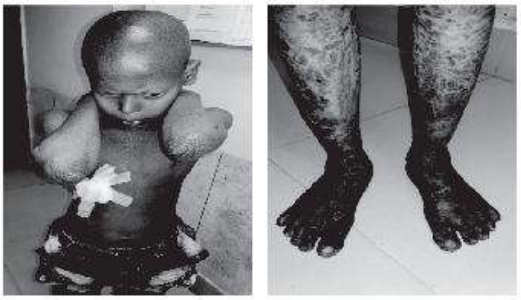

Fig-I: X linked ichthyosis showing prominent scales on extensor surface and abdomen

The boy was born via caesarian section. His mother noticed that absence of hair all over the body since birth. None of his family members was affected with this kind of illness. Based on the history, clinical features, and examination, the child was provisionally diagnosed as a case of X linked ichthyosis. This diagnosis has been confirmed by skin biopsy. Microscopic examination revealed mild hyperkeratosis with preserved granular layer in epidermis. The dermis showed mild perivascular infiltration of chronic inflammatory cells which was compatible with X linked ichthyosis.

His parents also gave the history of decreased sweating, dry skin, recurrent episode of high-grade fever, and delayed eruption of abnormally shaped teeth. The parents revealed that the child had intermittent episodes of fever in the past, associated with physical activity. Such episodes used to occur more frequently in hot climate, but no definite cause had been diagnosed for the same. There was a history of reduced sweating and heat intolerance. None of the family members was involved in a similar manner in previous generations. There was no history of consanguinous marriage of parents.

On examination, patient's vitals and systemic examination were normal. Intraoral examination revealed the child had mandibular and maxillary hypodontia with two peg-shaped incisors. There was loss of eyebrows and eyelashes. His skin was dry, warm, and sensitive.The nasal bridge was depressed and frontal bossing was present. The oral mucosa, palate, nails were normal. No other sibling had similar cutaneous features.

The systemic examination including otorhinolaryngological examination was normal. The physical development including external genitalia and mental development was normal. The routine biochemical tests were within normal limits. Patient's complete blood count, comprehensive metabolic panel, and urine analysis reports were normal. Based on the history, clinical features, and examination, the child was diagnosed as a case of hypohidrotic ED.

Discussion

X-linked ichthyosis (XLI) is a skin condition caused by the hereditary deficiency of the steroid sulfatase (STS) enzyme that affects 1 in 2000 to 1 in 6000 males.X-linked ichthyosis manifests with dry, scaly skin and is due to deletions[25] or mutations[26] in the STS gene.

Clinically, X-linked ichthyosis is characterized by a generalized scaling of the skin, with large, polygonal, dark brown scales, more prominent on the extensor aspects of the limbs. Only males manifest the disease, while female carriers do not present it. The lesions are usually distributed symmetrically and are generally more evident on the extensor aspects of the limbs, particularly on the lower extremities.[12]Scale size varies individually but in general the scales are larger on the extensor areas of the lower limbs than on the upper part of the trunk. The face is usually free of scales, except in the preauricular areas, which according to some authors is a pathognomonic feature. The palms and soles are very rarely involved, although such involvement does not exclude a diagnosis of X-linked ichthyosis.[15] The hair and nails are normal.[21]

Inherited ichthyoses are usually apparent during the first year of life, often at birth, and continue to affect a person throughout life.[27]

In our case, a 12 years old boy presented with generalized dark, large scales for 12 years. These dark, large, prominent scales involved all over the body but more prominent in extensor surface of limbs and sparing the face, flexures, palm, sole. Mucous membrane and Nail detect no abnormality. Hair is absent all over the body. Patient's conditions does not improve with age . All these features including skin manifestation consistened with typical features of X-linked ichthyosis.

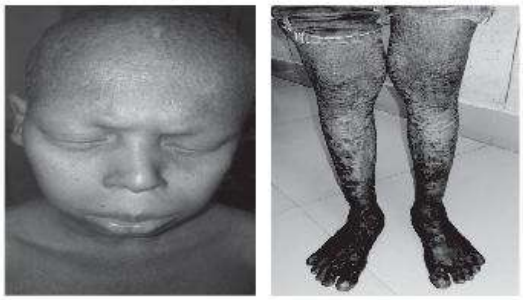

Fig-II: Hypohidrotic ectodermal dysplasia showing loss of eyebrows, eyelashes, scalp hair and dry skin involving lower limbs.

X-linked ichthyosis is usually associated with some extracutaneous manifestations like corneal opacity and cryptorchidism. Some authors have found corneal opacity to be more frequent during the second and third decades of life.[28] The incidence of cryptorchidism is higher in patients with X-linked ichthyosis than that expected in the general population,[29] Some neurological findings observed in patients with X-linked ichthyosis are epileptic seizures[14] and reactive psychological disorders.[30] But our case having no such type of extracutaneous manifestations or any neuological or psychological disorders.

Hypohidrotic ectodermal dysplasia (HED) is a rare genetic disorder characterized by the faulty development of the ectodermal structure, resulting in most notably anhydrosis/hypohydrosis, hypotrichosis and hypodontia. This condition is usually an X-linked recessive disorder affecting predominantly males.[31]

In our case, a 12 years old boy presented with decreased sweating, dry skin, recurrent episode of high-grade fever, and delayed eruption of abnormally shaped teeth.

Clinically, HED is characterized by sparse or absent eccrine glands as well as by hypotrichosis and oligodontia with peg-shaped teeth.The conical and pointed teeth are key features of the syndrome and may be the only obvious abnormality.[32] Same features were present in our case.

Because of their severely diminished ability to sweat, patients with HED have a propensity to develop hyperthermia with physical exertion or exposure to a warm environment, and affected infants often present with recurrent high fevers.[32]

In our case, the child had intermittent episodes of fever in the past, associated with physical activity. Such episodes used to occur more frequently in hot climate, but no definite cause had been diagnosed for the same. There was a history of reduced sweating and heat intolerance.

In HED, The scalp hair, eyebrows, and eyelashes are sparse, fine, and oftentimes lightly pigmented. Our patient had loss of eyebrows, eyelashes and scalp hair. In contrast to several other types of ectodermal dysplasia, nails were normal. HED patients have a characteristic facies with frontal bossing, a saddle nose, and full, everted lips.[33] Same findings were found in our case.

Conclusion

To the best of our knowledge, this is the first rare case report of X-linked ichthyosis associated with hypohidrotic ectodermal dysplasia in our country. When a clinician will face a case of X-linked ichthyosis, association of Hypohidrotic ectodermal dysplasia should not be overlooked. A multidisciplinary teams consisting of physicians from several clinical modalities is required to provide comprehensive medical care to children suffering from X-linked ichthyosis associated with hypohidrotic ectodermal dysplasia. As X-linked ichthyosis is caused by a gene mutation or deletion, there is no "cure." One of the aims of treatment is to reduce scaling by removing the excess, flaky scales, and keep the skin hydrated. This can be achieved using a variety of topical creams. The pediatrician should manage acute complications of ectodermal dysplasia such as hyperpyrexia and respiratory infections symptomatically. The pediatric dentist should use dentures, prosthetics etc. Consultation with a child psychologist, dermatologist, otolaryngologist, and speech-therapist should be needed for symptomatic treatment and psychosocial well-being of the child.

Declaration of patient consent

These authors certify that they have obtained all appropriate patient consent forms. In the form, the legal guardian has given his consent for images and other clinical information to be reported in the journal. The guardian understands that names and initials will not be published and due efforts will be made to conceal patient identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

Acknowledgement

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