

# H Syndrome: A Case Report

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## Abstract

H Syndrome is one of the rarest diseases in the world. It is an autosomal recessive (AR) disorder that occurs due to mutations in the solute carrier family 29.

H Syndrome is characterized by cutaneous hyperpigmentation, hearing loss, hypertrichosis, hypothyroidism, hepatomegaly, flexion contracture of the fingers and toes, short stature, hypertriglyceridemia, diabetes mellitus type one, and hypogonadism.

It was named H syndrome considering the fact that most of the clinical features start with the letter "H."

**Key words:** H Syndrome, SLC29A3 gene, hypertrichosis.

## Introduction

H Syndrome is an autosomal recessive disease (ARD) with systemic manifestations and pathognomonic skin lesions (1). It is due to mutations in the solute carrier family 29 (nucleoside transporter) member 3 (SLC29A3 gene), encoding human equilibrative nucleoside transporter hENT3, and leading to mononuclear cell skin infiltration and cutaneous manifestations(2). The first cases of this extremely rare syndrome were reported in consanguineous families of Arab and Bulgarian descent and described in 2008 by Molho-Pessach et al (3). The described disorders are characterized by hearing loss, hypertrichosis, hypothyroidism, hepatosplenomegaly, short stature, flexion contracture of the fingers and toes, hypertriglyceridemia, diabetes mellitus type one, and hypogonadism (4).

This report describes the case of an eight-year-old girl with H syndrome due to a SLC29A3 mutation identified utilizing a whole-exome sequencing approach. There are approximately 100 patients diagnosed with the disorder worldwide (5).

## Case history

An eight-year-old girl, a product of consanguineous marriage and normal vaginal delivery, birth weight 2760-gram, uneventful pregnancy, presented to our pediatric endocrinology and diabetes clinic at Queen Rania Al-Abdullah Hospital for Children (Amman -Jordan) with a complaint of short stature. On examination, her height and weight were 115 cm (−2.2 standard deviation [SD]) and 18 kg (−3 SD) respectively, and the sex-adjusted mid parental height was 157 cm. On physical examination she had dilated vein on her face, was pale, wore hearing aids, had bilateral enlargement of cervical and inguinal lymph nodes, Pectus carinatum, hyperpigmented skin lesion on the abdomen, (Figure 1) and the upper half of both thighs, and hypertrichotic lesions mainly involving the extremities (Figure 2). Tanner's staging of the breasts was Prepubertal (stage 1), with stage 2 pubic hair. See table (1) for clinical examination findings.

Laboratory test results showed an elevated ESR value of 45, the CBC showed mild microcytic anemia, thyroid function tests showed hypothyroidism and abdominal ultrasound scan found mild hepatosplenomegaly.

Liver function tests, renal function tests, serum electrolytes, urine analysis, HbA1c, tissue Transglutaminase antibodies (IgG, IgA), chest x-ray, Echocardiography, and karyotype were normal.

Because of all of these clinical findings, our patient described here was suspected to have H Syndrome. Whole-exome sequencing confirmed the diagnosis

**Table 1: Findings on examination**

Examination	Findings
Anthropometric parameters	Weight, 17.7 kg; height, 117 cm; BMI, <17.7.
Skin	Hyperpigmented patches with overlying hypertrichosis, involving the right side of the abdominal and medial aspects of the thighs and extending to the anterior aspects of the legs. There is facial telangiectasia.
Head	The face looks flat; ears are of abnormal shape and size.
Eyes	Mildly exophthalmos; Ophthalmoscopic examination showed bilateral swelling of the optic disc. Visual acuity is normal.
Hearing assessment	Severe hearing loss.
Heart	Normal.
Abdomen	Hepatosplenomegaly and central echogenic fat.
Lymph nodes	Mildly enlarged cervical and inguinal lymph nodes.
Genitourinary	Lack of secondary sexual signs.
Musculoskeletal	Pectus carinatum, flexion contracture of the fingers and toes.
Endocrine	Short stature, hypothyroidism.

**Figure 1: Hyperpigmented skin lesion****Figure 2: Hypertrichosis on the lower extremities**

## Discussion

We find ourselves in front of a large constellation of symptoms and signs related to different pediatric branches, including endocrinology, dermatology, gastrointestinal, ophthalmology, cardiology, and genetic diseases; so, we find that most patients are either not diagnosed or are diagnosed late by tracking and examining their history.

This syndrome is newly identified so most doctors are unaware of this syndrome, however, the pathognomonic features of H syndrome are typically the cutaneous hyperpigmentation and hypertrichosis.

In addition to the pathognomonic clinical features of H syndrome, the diagnosis should ideally be confirmed by mutation analysis of SLC29A3. Our patient had characteristic findings, including hyperpigmentation, hypertrichosis, short stature, hearing loss, hepatomegaly, hypothyroidism, and flexion contracture of the fingers and toes. Insulin-dependent diabetes mellitus and cardiac anomalies were absent in our case. We confirmed the diagnosis by whole-exome sequencing.

Molho-Pessach reported lymphadenopathy in 24% of patients with H syndrome (6). Inguinal, cervical, and axillary nodes, which were also present in our patient, are usually the most commonly affected lymph nodes. Elevated ESR, mild microcytic anemia, and bilateral optic disc swelling were present in our patient, which was also reported by Al-Hamdi KI et al (7).

Many cases reported around the world are of Arab consanguineous families with the main features of H syndrome (8).

No definitive treatment of this rare disorder exists which makes it crucial to recognize its presence, and thereby, avoid unnecessary interventions for treating cutaneous manifestations.

Genetic counseling may play an important role in management.

## Conclusion

H syndrome, which seems to be more common among persons of Arab descent, has been described worldwide and should be included in the differential diagnosis of patients with short stature and systemic inflammation, particularly when accompanied by the characteristic cutaneous findings.

Despite this rare case, the cutaneous hyperpigmentation and hypertrichosis (pathognomonic feature) which are typical in H syndrome are still the key features to differentiate a multisystemic disease from others.

Moreover, recognition of the other clinical features (hypothyroidism, hepatosplenomegaly, short stature, hypertriglyceridemia, diabetes mellitus type one) of H syndrome is important for diagnosis.

Regardless, the genetic study is important not only for the diagnosis but also for genetic counseling.

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## Conclusion

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