CASE REPORT

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Autism Spectrum Disorder in a Child With Hunter Syndrome

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Abstract

Mucopolysaccharidoses (MPS) include a group of chronic and progressive lysosomal storage disorders (LSD) which are characterized by the absence or deficiency of specific lysosomal enzymes. MPS type II or Hunter syndrome (HS) is an X-linked recessive disease caused by deficiency of the lysosomal enzyme iduronate-2-sulphatase. Although the pathophysiology of Autism spectrum disorders (ASDs) is unclear, multifactorial causes are thought to play an important role in their development. Here, we report a case of HS presenting with autism-related symptoms such as restricted behaviors and lack of social interaction. To our best knowledge, this is the first report of ASD in a child with HS. In our case, the most prominent symptoms such as restricted social communicative behaviors and interest, poor eye contact, unresponsiveness to his name, repetetive behaviors, and declined enjoyment in interacting with the peers emerged were considered as autism-related which are also reported in the other types of MPS, particularly in Sanfilippo disease. Taking into account that his autistic symptoms occurred developmentally up to 3 years old, we suggested that ASD, particularly in the domains of speech, language, restricted communication, and interest, poor eye contact, and repetetive behaviors may develop concurrently in children with HS. The common genetic and biological pathways, and neural links between two disorders may undelie the development of ASD in HS cases. Clinicians should consider examining for HS, when autistic-like behaviors are observed alongside other physical or other developmental abnormalities.

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INTRODUCTION

Mucopolysaccharidoses (MPS) include a group of chronic and progressive lysosomal storage disorders (LSD) which are characterized by the absence or deficiency of specific lysosomal enzymes leading to the accumulation of undigested or partially digested macromolecules within lysosomes. MPS type II or Hunter syndrome (HS) is an X-linked recessive disease caused by deficiency of the lysosomal enzyme iduronate-2-sulphatase. The age at diagnosis is usually between 18 and 36 months. Systemic manifestations of HS include coarse face, skeletal anomalies and joint restriction, cardiac valve disease, and hepatosplenomegaly. The children with HS appear normal at birth, although they tend to be heavy, some have inguinal or umbilical hernias and there is an increased frequency of Mongolian blue spots [1]. Neurological findings of severe HS include progressive impairment of gross and fine motor abilities, epilepsy, sensorineural deafness with severe language disturbance and loss of verbal language, retinal degeneration, and sleep problems [2,3]. Volumetric magnetic resonance studies show extensive white matter changes as well as dilated perivascular spaces significant atrophic changes in brain in MPS II patients [4].

Although the pathophysiology of autism spectrum disorders (ASDs) is unclear, genetic defects and multifactorial causes are considered to play an important role in their development. Several studies have indicated that of the children with Sanfilippo disease (MPS III), 20% had autism-related symptoms such as poor eye contact, language delay, and impaired social communication [5].

Here, we report a case of HS presenting with autism-related symptoms such as restricted behaviors and lack of social interaction. To our best knowledge, this is the first report of ASD in a child with HS. Written informed consent was obtained from the parent of the patient for

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publication of the submitted article and the accompanying images.

CASE REPORT

A two and a half year-old boy was admitted to child and adolescent psychiatry department with the complaint of speech delay. At the age of one and a half, his social communication skills were not efficient for making contact and was not eager to start playing with peers. He also experienced a noticable crying and anger tantrums in social conditions. His mother stated that he had usually a limited eye contact and he did not react to people even when he was called out with his name. The mother also observed that he exhibited some restrictive patterns of behaviour presenting itself with repetetive, persistent and excessive use of pencils. Futhermore, he was getting agitated upon his pencils were taken.

In his initial psychiatric assessment, there was no meaningful word acquried in his verbal communication except a few syllables and having inappropriate gestures. He was unable to make eye contact and was uninterested in playing with toys. He was also not able to respond to commands. Moreover, a lack of joint attention was observed and he frequently tended to scribble the sheet during the interview. We did not record any additional stereotypic movements at the examination. His autism behavior checklist (ABC) score was 91. As well as these autism-related symptoms, his physical examination revealed that he had bone deformities including shortness of the distal joints especially in the hands and there were also dysmorfic facial features with an enlarged head, a protruding tongue and short neck. Additionally, he had mongolian blue spot at his back. In his neurological examination, some dismorphic features were observed. Based on these symptoms and signs, ASD diagnosis was made and the patient was consulted to pediatric neurology clinic with a possible diagnosis of a neurometabolic disease (Figure 1). His brain MRI scan indicated that there were a periventricular cyst, enlarged perivascular distance and sulcal dilatation compatible with a cortical atrophy. Audological examination revealed a mild hearing loss. These dysmorphic features and MRI findings were consistent with a possible diagnosis of MPS. The patient was diagnosed as HS with an elevated urinary GAG excretion, and a low iduronate 2-sulfatase activity. The case graudally became communicative, and started to use a few single words, and followed simple directions, within the six months of an enzyme replacement therapy, and special education.

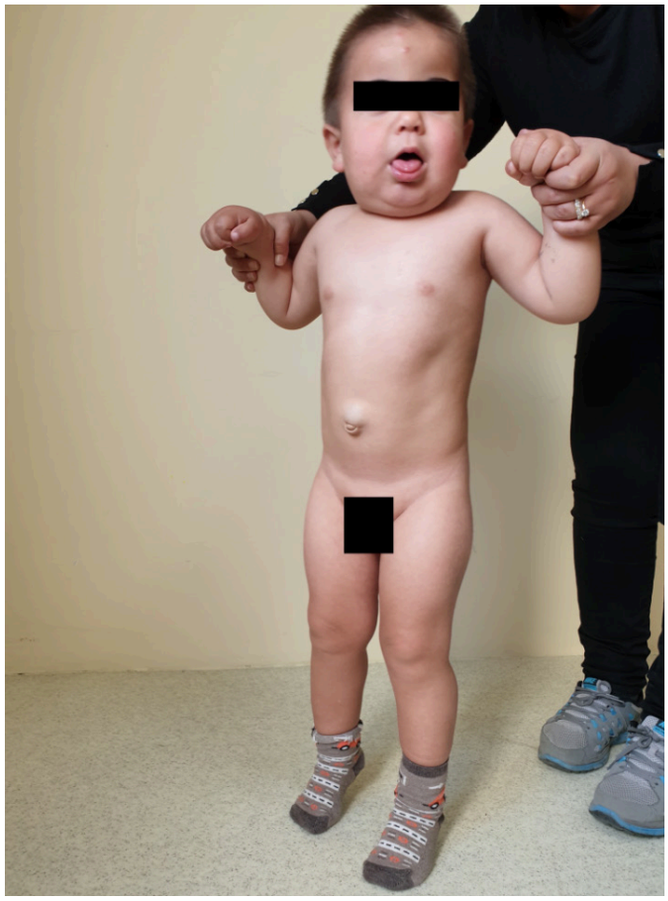

Figure 1. Physical appearance of the case

DISCUSSION

Although several psychological problems may occur in children with HS, autism-related symptoms were not previously reported in HS children. It is uncertain whether autistic-like symptoms in MPS emerge from normal developmental or behavioral background. In our case, the most prominent symptoms such as restricted social communicative behaviors and interest, poor eye contact, unresponsiveness to his name, repetetive behaviors, and declined enjoyment in interacting with the peers emerged were considered as autism-related which are also reported in the other types of MPS, particularly in Sanfilippo disease. Taking into account that his autistic symptoms occurred developmentally up to 3 years old, we suggested that our case might be qualified for a formal diagnosis of autism. Unlike children with MPS III [6], our case presented with restricted interests or repetitive behavior, like an idiopathic ASD.

Previous reports indicated that the emergence of new autistic-like symptoms in children with early onset Sanfilippo syndrome provides a model of ‘acquired’ autistic behaviors. The early onset ASD in our case may not enable to view HS as a model for acquisition of autistic-like symptoms. Instead, we may suggest that HS may play an

important role in the development of ASD [7]. The onset of autistic-like symptoms around 36 months may suggest that such symptoms are characteristic of disease progression in HS. Therefore, we supposed that an increase of autistic-like social behaviors in children with the early onset form of HS may occur within the first 3 years of life. The possible overlapping neural characteristics of both disorders is supported by the finding that the behavioral abnormalities in HS can be described as a Klüver-Bucy-like presentation that appears after the age of 2 or 3 years, with diminished fear, startle, poor social interaction, orality, and reduced emotional attachment and compliance with parents [8]. Similar to previous findings [9], brain changes associated with HS in our case were enlarged perivascular distance and sulcal dilatation indicating a cortical atrophy. Another neural link is demonstrated by the association of autistic behaviors with abnormalities in heparan sulfate metabolism in murine models, given the central role of heparan sulfate in Hunter syndrome [10].

Our case may demonstrate that ASD, particularly in the domains of speech, language, restricted communication, and interest, poor eye contact, and repetetive behaviors may develop concurrently in children with HS. The common genetic and biological pathways, and neural links between two disorders may underlie the development of ASD in HS cases. Clinicians should consider examining for HS, when autistic-like behaviors are observe alongside other physical or other developmental abnormalities.

Informed Consent: Parents gave verbal and written informed consent for publication.

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