HUNTER SYNDROME ASSOCIATED WITH AUTISM-CASE PRESENTATION

Andreea-Cristina Stanciu¹, Raluca Grozavescu², Andreea Musat¹, Magdalena Budisteanu³

1. University of Medicine and Pharmacy “Carol Davila”, Bucharest, Romania;
2. Pediatric Psychiatry Department, "Prof. Dr. Alexandru Obregia" Clinical Hospital of Psychiatry, Bucharest, Romania
3. Neuropsychiatry Department, Head of Psychiatry Research Laboratory, "Prof. Dr. Alexandru Obregia" Clinical Hospital of Psychiatry, Bucharest, Romania

1. INTRODUCTION

Mucopolysaccharidosis type II also known as Hunter Syndrome is a rare, X-linked lysosomal storage disease, affecting 1 in 100,000 to 1 in 170,000 primarily males. It is caused by a deficiency in the lysosomal enzyme iduronate-2-sulfatase(I2S), which is one of the enzymes responsible for the degradation of the glycosaminoglycans (GAGs) heparan sulphate and dermatan sulphate. The lack of this enzyme causes heparan sulfate and dermatan sulfate to accumulate in all body tissues. The IDS gene is located in Xq28, spans 24 kb and contains 9 exons. Although MPS II is associated with a broad spectrum of clinical severity, patients with the disease are usually classified as having the severe, intermediate or attenuated forms. The differences between the severe and attenuated forms are mainly due to the progressive development of neurodegeneration in the former one. The age at onset of symptoms and the presence/absence of behavioural disturbances are predictive factors of ultimate disease severity in very young patients. In the severe form, the clinical signs and symptoms appear between 2 and 4 years of age and the life expectancy is less than two decades mostly due to cardiopulmonary complications. In contrast, a milder form of Hunter syndrome is characterized by preservation of intelligence and survival into adulthood, but with obvious somatic involvement. The diagnosis is usually made between 4 and 8 years of age and in many cases the life expectancy is near normal. The symptoms of Hunter syndrome are generally not apparent at birth but, as the buildup of GAGs continues throughout the cells of the body, they become more and more visible. The symptoms usually debut with abdominal hernias, ear infections, runny noses, and colds. The physical appearances are characterised by a distinctive coarseness of the facial features, including a prominent forehead, a nose with a flattened bridge, and an enlarged tongue. The continued storage of GAGs causes abnormalities in multiple organ systems. These can lead to a thickening of the heart valves and walls and a thickening of the airway walls, resulting in a progressive decline in cardiac function and obstructive airway disease. These can also lead to joint stiffness and limited motion. The phenotypic expression of Hunter syndrome spans a wide spectrum of clinical manifestations. In a study conducted on 23 male Filipino patients with Hunter syndrome, it was recorded one case associated with autism.

2. CASE PRESENTATION

We report a case of a 30 months old boy with Hunter syndrome associated with autism. The boy experienced a normal natural birth with an Apgar Score of 10 and a normal postnatal adjustment. The family medical history was unremarkable, with the exception of the maternal aunt who presented epilepsy. His early development was normal, marked by babbling at 6 months and by walking alone at 14 months. However, at 18 months he stopped communicating completely. At the age of 20 months, the boy was admitted in the Department of Child Psychiatry for absent speech, lack of communication and social interaction difficulties. It was recommended an Autism Disorder Observation Schedule (ADOS) for diagnosing and assessing autism and an Autism Spectrum Disorder (ASD) was confirmed by a score of 12. He performed behaviour and speech therapy, showing some progress. The clinical evaluation showed coarse facies, hirsutism, joint stiffness both in upper and lower limbs, abdominal distension, speech delay, moderate intellectual disability, hyperkinesia. The boy also experienced frequent respiratory tract infections.

The dysmorphic features raised the suspicion of X-linked mucopolysaccharidosis, so the evaluation of the activity of iduronate-2-sulfatase and genetic test for Hunter syndrome were recommended. Analysis of urine glycosaminoglycans (GAGs) can be used to confirm the suspicion of Hunter syndrome. Excess urinary excretion of dermatan sulfate and heparan sulfate is characteristic of Hunter syndrome but not diagnostic as these GAGs can also be elevated in other types of mucopolysaccharidoses. Thus, measurement of iduronate-2-sulfatase enzyme activity is necessary to confirm the diagnosis. Absent or low I2S activity in males is diagnostic of Hunter syndrome but absolute enzyme activity cannot be used to predict the severity of the phenotype. In this case, the activity of iduronate-2-sulfatase was below its reference range. The genetic test showed a pathogenic mutation in the IDS gene.

Figure 1.

Figure 2.

Figure 3.

3.CONCLUSION

Mucopolysaccharidosis type II presents a complex phenotype in which the nervous, cardiovascular, respiratory and osteoarticular systems are affected. In the present case, the autistic behaviour was the most evident feature at the onset of Hunter syndrome. This raises the hypothesis that Hunter syndrome can facilitate the ground for the appearance of Autism Spectrum Disorders. An early diagnosis is tremendously important in order to establish an efficient personalized management plan.

4. KEYWORDS

Mucopolysaccharidosis type II; Iduronate-2-sulfatase; Heparan sulfate; Dermatan sulfate; Autism Spectrum Disorder;