Case Report

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A Girl with Farber Disease Treated with Bone Marrow Transplantation

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ABSTRACT

Background: Farber disease is a very rare autosomal recessive disease of lipid metabolism caused by deficient activity of lysosomal acid ceramidase. Symptoms can begin in the first year of life by a triad of painful and swollen joints and subcutaneous nodules, progressive hoarseness and variable central nervous system involvement.

Case Report: A 5 months old girl with subcutaneous nodules in limbs, pain and swelling in her fingers, Knees, elbow and hoarseness was referred to our clinic. She had neurodevelopment delay in walking and talking. Genetic analysis was reported homozygosity for a c.830C>A mutation in exon 11 of N-Acylsphingosine Amidohydrolase 1 (ASAH1) gene. She diagnosed with Farber disease and treated with bone marrow transplantation. After that her signs and symptoms were improved and she could to walk.

Conclusion: Farber disease is associated with characteristics including swollen joints, subcutaneous nodules, progressive hoarseness and variable CNS involvement. Moreover, bone marrow transplantation improved these symptoms.

Introduction

Farber disease, Etiology/pathophysiology: Farber disease was described and characterized in 1957 by Sidney Farber.[1] Farber disease as a very rare[2] autosomal recessive disorder[3, 4] of lipid metabolism is created by deficient activity of lysosomal acid ceramidase.[5] The enzyme participates in the normal deregulation and turnover of ceramide, an important precursor of gangliosides, myelin and membrane components. Ceramidase deficiency leads to abnormal accumulation of ceramide in lysosomes of multiple organs and tissues and causes progressive development of multiple ceramide-containing subcutaneous nodules (lipogranulomata). Granulomatous infiltrations could be seen in subcutaneous tissues and joints and in other sites including the larynx, liver, spleen, lung, heart and Central Nervous System.[3]

Clinical manifestation: Farber disease is clinically heterogeneous.[6] It has been classified into 7 subtypes.[7] Onset can be during infancy or much later, causing death within the first year or in some cases in adult age. Characteristic symptoms involve a Triad of painful, swollen joints, subcutaneous nodules and progressive hoarseness.[3] Nervous system involvement is seen in the majority of patients including psychomotor delay, diminished reflexes, hypotonia and seizures. Children with neurological involvement usually die early in infancy.[7]

Diagnosis: Reduced or absent lysosomal ceramidase activity in white blood cells, cultured skin fibroblasts and aminocytes the presence of farber bodies in biopsy samples DNA mutation.[3]

Treatment: No effective therapy currently exists for this disease. Bone marrow transplantation in few patients leads to resolution of somatic symptoms but without apparent effect on neurological features.[3]

Case report

The patient is a 3 years old girl. In 5 months old, she with subcutaneous nodules in limbs, pain and swelling in her fingers, Knees, elbow and hoarseness referred to Pediatric Endocrinology Clinic of Shahid Sadoughi hospital, Yazd, Iran. These symptoms were progressive. Her parents were relative. She had neurodevelopment delay in walking and talking. In neurologic examination, she had hypo reflexia. Farber disease was suspected for her and genetic study was done. Homozygous mutation (C.830 > A) in exon 11 was reported. Patient was treated with bone marrow transplantation, her symptoms were improved and the patient was able to walk.

In the Figures 1 and 2 the girl knees and vocal cord are shown.

Discussion

Farber disease is a very rare autosomal recessive disorder created by deficiency of lysosomal enzyme acid ceramidase and leads to accumulation of ceramide in various tissues, especially the joints.

Figure 1. The patents knees with swollen joints.

In this study, symptoms began in the first year of life with painful joint swelling and subcutaneous nodule formation.

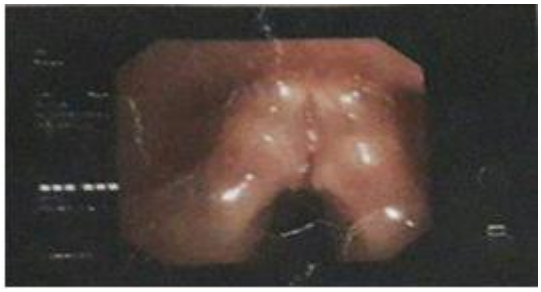

Figure 2. The patients vocal cord nodules.

The diagnosis of this disorder should be suspected in patients who have nodule formation over the joints but no other findings of rheumatoid arthritis.[8] We performed bone marrow transplantation for the child. Ahmad et al reported a two-and-a-half-year-old infant with progressive regression of milestones and swollen joints. The child lost weight during this period. Biopsy of subcutaneous swellings was performed and child was diagnosed by Farber disease.[4] Ehlert in 2007 reported that allogeneic hematopoietic stem cell transplantation can be a promising approach for Farber disease patients without neurological involvement.[9] Liuet al also obtained same result.[10]

Conclusion

Farber disease is associated with characteristics including swollen joints, subcutaneous nodules, progressive hoarseness and variable CNS involvement. Moreover, bone marrow transplantation improved these symptoms.

Informed Consent

Written informed consent for the publication of the photographs has been obtained by the patients respectively their parents.

Conflict of Interests

The authors declare that they have no competing interests.

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