CASE REPORT

Farber Disease: A Rare Neurodegenerative Disorder

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ABSTRACT

This is the case report of a two-and-a-half-year old male infant with Farber disease, which is a rare neurodegenerative mucolipidosis. The child presented with regression of milestones, laryngeal involvement and painful joints with swellings around the joints. Neuroimaging findings and the biopsy of the soft tissue swellings helped to reach the diagnosis.

Key words: *Neurodegeneration. Mucolipidosis. Joint swelling. Cerebral hypoplasia.*

INTRODUCTION

Farber disease is an autosomal recessive form of mucolipidosis developing soon after birth and characterized by swollen joints;[1] formation of nodules or granules in subcutaneous tissue, around joints, on vocal cords, and in the upper airway. It is a rare disorder and the true incidence is not known. There may be several variants, ranging from mild to severe forms. Farber disease is a progressive disease; it often leads to death during the first few years of life.

CASE REPORT

A two-and-a-half-year old infant presented with progressive regression of the milestones with swollen joints. He was born to cousin parents with one elder brother and one sister who are normal. The child also remained normal upto 5 months of age. He attained neck holding at 4 months of age and sitting with support at 5 months of age and then he gradually lost these milestones. The child developed multiple swellings on the body, which started from the scalp (Figure 1) and spread all over the body especially around the joints (Figure 2). The voice became hoarse and there were repeated chest infections during this time. He also developed difficulty in swallowing and choking episodes. The child lost weight markedly during this period. There was no history of fits, hearing or visual problems.

Examination revealed a young infant with multiple soft swellings of various sizes especially over scalp, dorsal aspects of joints and the spine. Movements of the joints were painful. The weight of the child was 6 kg (below 5th percentile) and the head circumference 46 cm (below-2 SD). Cranial nerves were intact. Tone, power and reflexes were diminished. There was no neck holding with intact hearing and vision. There was no cherry red spot in the retina. Patient did not have hepato-splenomegaly.

Blood counts and lipid profile were normal. Serology for rheumatoid factor was negative. CT scan and MRI of the brain revealed marked cerebral hypoplasia. Biopsy of the subcutaneous swellings showed granulomas with macrophages containing lipid cytoplasmic inclusions. Diagnosis of Farber disease was made on the basis of regression of the milestones, laryngeal involvement, multiple swellings over the joints and the biopsy findings.

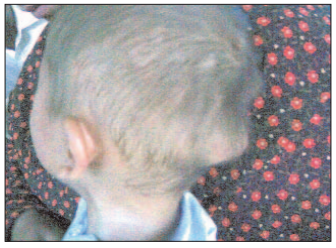

Figure 1: Multiple soft tissue swellings over the scalp.

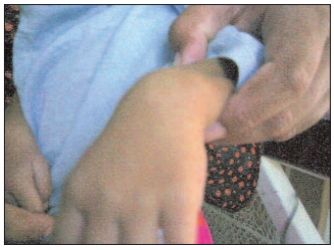

Figure 2: Painful swelling of the wrist joint.

DISCUSSION

Ceramidase deficiency (Farber lipogranulomatosis or Farber disease), first described as an inborn storage disease by Farber and co-workers,[1] leads to tissue accumulation of ceramide due to deficient activity of lysosomal ceramidase.

The clinical presentation of Farber Disease (FD) is characterized by the appearance of subcutaneous skin nodules, usually near the joints, most often inter-phalangeal, wrist, elbow and ankle joints, or over points of mechanical pressure. These manifestations are very painful and lead to progressive joint stiffness, limitation

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of motion by contractures and finally to immobilization and deformity of joints. As a major symptom, FD patients exhibit chronic destructive joint inflammation resembling rheumatoid arthritis. Indeed, increased CD95 receptor/ligand interaction has been implicated in the pathogenesis of inflammatory arthritis.[2,3] Also, a characteristic sign of FD, which was also found in this child, is the development of a progressive hoarseness due to laryngeal involvement.[4] Hepatomegaly or hepatosplenomegaly is present in 25% of the cases. It was not found in this case.

Beside these major manifestations, seven phenotypes have been described, which differ in severity and additional organ involvement, like the lungs, nervous system, heart and lymph nodes.[4] Dependent on residual lysosomal ceramidase turnover, patients have a variable degree of Central Nervous System (CNS) disease, leading to progressive neurologic deterioration. In most cases, the neuronal dysfunction rather than the general physical dystrophy seems to limit the duration of FD.[5] Patients with FD may die due to pulmonary disease with interstitial pneumonia.

In typical cases of FD, the clinical triad of subcutaneous nodules, joint and laryngeal involvement verifies the disease. When typical features are missing, diagnosis is confirmed by determination of acid ceramidase activity, which is less than 6% of control values, measured in cultured skin fibroblasts, white blood cells or amniocytes. Another diagnostic approach is the demonstration of typical histopathologic features on biopsy, showing granulomas with macrophages containing lipid cytoplasmic inclusions in subcutaneous nodules or other tissues. Determination of ceramide accumulation in tissues by chromatography or mass spectrometry is also an established diagnostic test for FD.[4] In this case, the diagnosis was established on clinical and biopsy findings as the facility for enzyme estimation was not available in the country.

Haematopoietic stem cell transfusion is an option of treatment in those patients having no CNS involvement.[6] As this patient was having CNS involvement, this was not a good option.

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