

Farber's Disease: A Case Report

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Introduction

Farber's disease (FD) is an inherited autosomal recessive lysosomal storage disorder due to deficiency of lysosomal acid ceramidase, which causes accumulation of fatty material ceramide within different tissue leading to abnormalities in the joints, throat, liver, CNS and other organs¹. Normally ceramidase is responsible for breaking down the fat. In Farber's disease there is mutation of the gene ASAHI-1 that encodes the acid ceramidase^{2,3}. FD is also known as "Fibrocystic dysmucopolysaccharidosis"³. It usually starts as early as two weeks of life with painful joint swelling and subcutaneous nodule formation. Joint deformity and hoarseness of voice with breathing difficulty are other common manifestations⁴. In some patients it manifests with hepatosplenomegaly, moderate to severe CNS, heart and lung involvement^{4,5}. Clinical phenotype depends on amount of acid ceramidase deficiency, that gives rise to mild, moderate to severe seven subtypes of Farber's disease^{6,7}. An important symptom of FD patients may exhibit is chronic destructive joint inflammation, joint swelling and deformity which may mimic the sign symptom of rheumatoid arthritis. In a typical case of FD the triad of subcutaneous nodules, joint and laryngeal involvement, is sufficient to make the diagnosis⁷. The typical histopathological findings of the subcutaneous nodules are foam cells in the early lesions and granulomas together with foam cells in advanced lesions^{5,8,9}. We are reporting a case of Farber's disease who was admitted in the department Paediatrics, Bangabandhu Sheikh Mujib Medical University (BSMMU) for the rarity of the problem and creating awareness to the physicians, not to diagnose and treat Farber's disease as rheumatoid arthritis.

Case report

"T" a 10-month old boy, only issue of his non consanguineous parents was admitted with the complaints of progressive development of palpable

nodules over the different parts of the body since 1 ½ month of his age. Initially there was a single nodule over the left great toe. Subsequently several nodules were developed over other areas, mostly around the joints (fig-1,2,3). Some of them were very painful causing restriction of movements of the involved joints. "T" also developed hoarseness of voice and difficulty in deglutition which was gradually increasing. There was no history of trauma, fever, skin rash, any bleeding manifestation, convulsion or unconsciousness. He was delivered at term and the perinatal period was uneventful. He had history of motor developmental delay (achieved neck control at the age of 8 months, could not sit without support till date and could not hold object properly). His vision and hearing was apparently normal. His weight falls on 25th centile, length above 25th centile and OFC 42 cm (Z score = -2.8). "T" had normal vital parameters but musculoskeletal system examination showed multiple soft to hard irregular tender nodules over the different joints, including hands, feet, elbow, shoulder and also in the scalp, pinna of ears and over the spine (fig-1,2,3,4). Restriction of movements of almost all the joints were present. There was mild hepato-splenomegaly. CNS findings were normal as far as examination could be done. "T" was diagnosed as a case of Juvenile Idiopathic Arthritis and treated with NSAIDs and other supportive treatment. But as there was no improvement, he was referred to BSMMU.

Investigations showed normal total and differential counts. X-ray of the chest, upper limbs and lower limbs were normal. Alkaline phosphatase, serum calcium and thyroid function tests were within normal limit. His vitamin C level was also normal.

Histopathology was done from a nodule on right elbow which showed dense collagen fibers and moderate infiltration of foamy histiocytes and lymphocyte. Ceramidase level estimation and genetic studies could not be done due to inavailability. Clinical presentation and investigations findings of "T" were consistent with disseminated lipogranulomatosis or Farber's disease. Consultation was done with Department of Orthopedic Surgery. With the opinion of orthopedic surgery his parents were counseled about the nature of the disease, its course and the possible treatment options and he was discharged with supportive treatment.

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Fig.-01: *Interphalangeal and metacarpal joint involvement (nodules).*

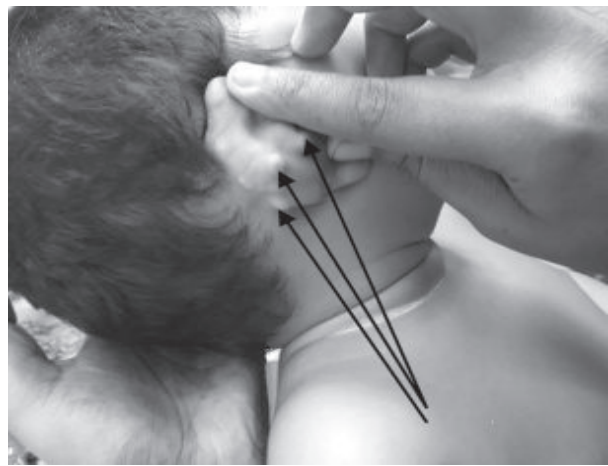


Fig.-02 : *Involvement of interphalangeal Joint of foot.*

Fig.-03: *showing multiple nodular swelling under surface of pinna.*

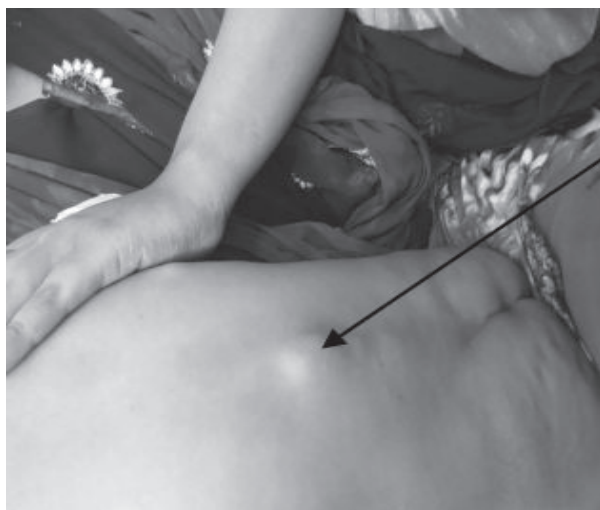


Fig.-04: *A subcutaneous swelling over the spine.*

Discussion

Farber disease (FD) also known as “Farber granulomatosis is a rare metabolic disorder. It was first described by Farber in 1957⁴. Sign symptoms of FD occurs due to deficiency in the enzyme ceramidase that leads to accumulation of fatty material sphingolipids in the tissue^{9,10}. So far 80 cases of Farber’s disease have been reported in the literature³. FD presents by three to five month of age and survive approximately up-to two year. In mild form, there is no neurologic component & they may live up-to 5-7 year of age^{10,11}. There are seven sub types of FD of different phenotypes^{11,12}. Type one is the classical form consists of joint pain and swelling along with development of subcutaneous

skin nodules, usually in the vicinity of or on the joints and over the points of mechanical pressures leading to joint stiffness. There is also hoarseness of voice and occasional organomegaly. Type two is the intermediate and type three is the mild form of disease with little neurological involvement. Type four is known as: "neonatal visceral form" of the disease and they present with hydrops fetalis and die at or before birth. Sub type five is referred to as "neurologic progressive" FD. Subtype six is associated with other syndrome and seven is another grave one^{12,13}. Our patient "T" presented at 1.5month and had all the three cardinal features including joint pain and swelling, subcutaneous nodules and hoarseness of voice and hepato-splenomegaly. Hepatomegaly or hepato-splenomegaly occurs in 25% of patients. Hoarseness of voice occurs due to laryngeal involvement¹¹. Beside the major manifestations other organs like lungs, liver, lymph nodes, heart and nervous system may also be involved^{12,13}. A typical case of FD presents with triad consisting of joints involvement, subcutaneous nodule near the joints, and laryngeal involvement^{3,13}. However, in an atypical case diagnosis can be confirmed by measuring the acid ceramidase level, also mass spectrometry and chromatography to measure ceramidase levels can be used for diagnosis³⁻⁵. But unfortunately, methods of measuring ceramidase level is not available in our country. Another approach is to look for the classical histopathological findings on biopsy from skin nodules. These findings include presence of granulomatous inflammation along with foam cells and a fibrovascularstroma^{6,13,14}.

Our patient "T" represented as the classical form of FD without CNS involvement. The histopathology report of our case had foams cells along with fibrovascular stroma. Absence of granuloma in our case could be due to the early stage of the disease.

Due to its rare occurrence and lack of awareness, many patients are misdiagnosed as juvenile idiopathic arthritis. "T" was also diagnosed as a case of JIA and received treatment accordingly. Hematopoietic stem cell transplantation is the probable treatment of Farber's disease without CNS involvement^{13,14}. This was also the preferred treatment in our case. Further work is still going on to come up with a definitive treatment of this rare entity, especially in those patients who have CNS involvement¹⁴.

Most of FD cases are still misdiagnosed. Very early onset of disease, extensive nodule formation around joints, nodular deposits of lipo-granuloma in other sites like conjunctiva, and hoarseness of voice due to laryngeal granuloma help to differentiate Farber's Disease from Juvenile Idiopathic Arthritis.

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