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Case Report

Chronic idiopathic thrombocytopenic purpura in a child with Sanfilippo type A

Karthik Prabhu Ramaraj*, Suresh Natarajan, Ravikumar KG

Department of Pediatrics, Kanchi Kamakoti Childs Trust Hospital, Chennai, Tamil Nadu, India

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***Correspondence:**
Dr. Karthik Prabhu Ramaraj,
E-mail: arkarthikpollachi@gmail.com

ABSTRACT

Mucopolysaccharidoses (MPS) are a group of storage disorders with an autosomal recessive inheritance. Sanfilippo disease is a type of MPS which occurs due to deficiency of lysosomal enzymes involved in the lysosomal degradation of heparan sulphate. They can be categorized into four different types based on the enzymes involved namely heparin N-sulfatase (type A), alpha-N-acetylglucosaminidase (type B), acetyl-CoA-glucosaminide acetyltransferase (type C) and N-acetylglucosamine-6-sulfatase (type D) respectively. In this case report we present a six years follow up of a child confirmed to have Sanfilippo type A disease, who developed chronic Idiopathic Thrombocytopenic Purpura (ITP).

Keywords: MPS, Sanfilippo type A, Idiopathic thrombocytopenic purpura

INTRODUCTION

Mucopolysaccharidoses (MPS) are a group of storage disorders with an autosomal recessive inheritance. Sanfilippo disease is a type of MPS which occurs due to deficiency of lysosomal enzymes involved in the lysosomal degradation of heparan sulphate. They can be categorized into four different types based on the enzymes involved namely heparin N-sulfatase (type A), alpha-N-acetylglucosaminidase (type B), acetyl-CoA-glucosaminide acetyltransferase (type C) and N-acetylglucosamine-6-sulfatase (type D) respectively. In this case report we present a six years follow up of a child confirmed to have Sanfilippo type A disease, who developed chronic Idiopathic thrombocytopenic purpura (ITP).

Occurrence of chronic ITP in Sanfilippo is quite rare and not described in literature to the best of our knowledge. PUB MED search revealed no previous association of ITP with Sanfilippo disease.

CASE REPORT

We report a 9 year old female child born to consanguineous parents who was noted to have coarse facial features at birth. Child was delivered by elective LSCS for oligo-hydramnios. The child was apparently well till 3 year of age when she was able to say a few words. However, she lost her language skills gradually afterwards but her motor development remained normal. The parents noted abdominal distension and brought her for evaluation at 4 years. Clinical examination showed coarse facies with low anterior hair line, frontal bossing, broad and thick eye brows, widely spaced eyes depressed nasal bridge, thick vermillion of upper lip (Figure 1). Mild hepatomegaly and bilateral bitots spots with no corneal clouding were noted. Her speech and language milestones were delayed with normal gross and fine motor development. X-ray spine, pelvis and hands with wrist (Figure 2) revealed dysostosis multiplex suggestive of mucopolysaccharidoses. A CT scan of head revealed diffuse cerebral atrophy. Brainstem auditory evoked

potential test showed left auditory pathway dysfunction. Urine Cetyl Pyridinium Chloride (CPC) citrate turbidity test for heparan sulphate was positive. Urinary Glycosaminoglycan (GAG) quantitation using Dimethyl methylene blue dye binding showed 10 fold increase in levels (119 mg/mM creatinine, normal values: 5.2 to 11.6). Leukocyte enzyme activity assay (method: artificial fluorogenic substrates) for heparan sulphate sulphaminidase showed undetectable levels, confirming MPS IIIA (Sanfilippo A).

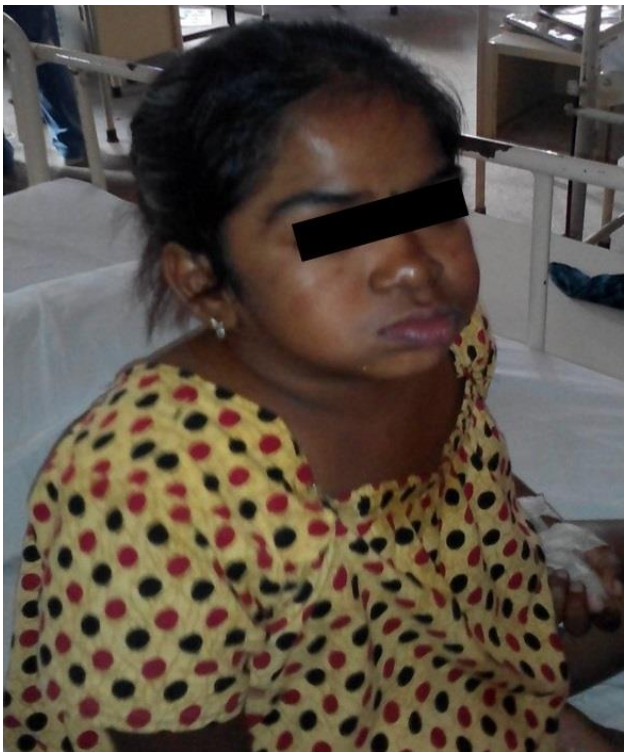

Figure 1: Child with Sanfilippo type A.

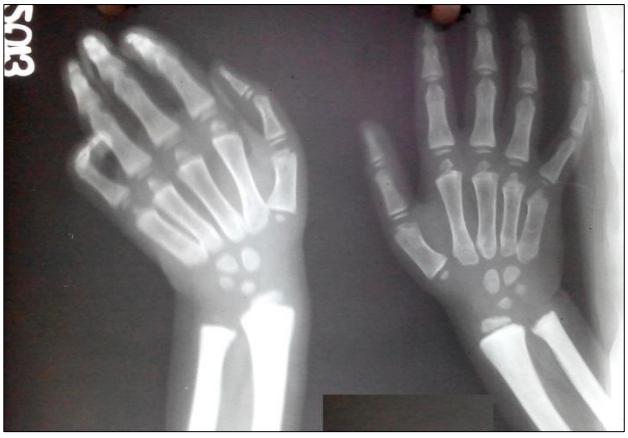

Figure 2: X-ray-wrist showing dysostosis.

The child was admitted again at 6 years of age for a prolonged viral illness during which the platelet count was noted to be low (30000 per cubic millimeter). Ecchymotic patches were seen over the lower limbs and left eyelid. In view of persistent thrombocytopenia, a bone marrow aspiration was done 6 months later and it showed reactive marrow morphology with adequate megakaryocytes in varying stages of maturation suggestive of Idiopathic Thrombocytopenic Purpura (ITP). She was treated with corticosteroids after which the platelet count improved up to 90000 per cubic millimeter. Subsequently, the platelet counts dropped several times requiring intermittent oral steroid courses for the next three years. During this time, her platelet count was always found to be below 100000 per cubic millimeter. Further treatment options such as immunoglobulins and rituximab could not be started due to cost constraints. At present, she was also found to have behavioral disturbances, hyperactivity and proximal muscle weakness.

DISCUSSION

Sanfilippo disease takes its name from Dr. Sylvester Sanfilippo, who described the condition in 1963. Among all types of mucopolysaccharidoses, Sanfilippo disease (MPS type III) is the most common entity.[1] Speech delay was the most frequent clinical symptom before diagnosis[2-4] and coarse facial features were present before diagnosis in 78% of MPS III patients.[5] Unlike Hurler syndrome (MPS I) or Hunter syndrome (MPS II), patients with Sanfilippo disease often have early very mild coarse facial features.[6,7] Neurological disturbance is the dominant clinical feature. MPS III is a progressive disease with three phases that begin after a period of apparently normal development. In the first phase between the ages of 1 and 3 years, a slowing of cognitive development occurs, speech is more affected than other cognitive functions.[2] Motor development progresses normally during the first phase.

The second phase starts usually at 3-4 years of age and is characterized by progressive cognitive deterioration and sleep disturbances and behavioural difficulties. The third phase begins in the teenage years, characterized by severe dementia and decline of motor function. Behavioral problems slowly disappear as patients lose locomotion. Spasticity and swallowing difficulties appear. Eventually, a fully bedridden state ensues, and patients usually die at the end of the second or beginning of the third decade of life. Our patient had language delay with no motor involvement as described in the literature.

Urinary GAG assay is the usual first step in making a biochemical diagnosis. Enzyme activity assay is the gold standard to confirm the diagnosis and to determine the subtype. Enzyme activity can be measured in leucocytes or cultured fibroblasts. In our patient, leukocyte activity of heparan sulphate sulphaminidase was not detected confirming the diagnosis of Sanfilippo type A.

Current treatment options are limited to supportive care. Hematopoietic Stem Cell Transplantation (HSCT) with bone marrow cells has been attempted in this population

based upon positive outcomes in patients with MPS I, MPS VI and MPS VII,[8-10] but it failed to prevent the neurological deterioration and cognitive decline even when performed early in the disease course.[11] Our patient's platelet count remained low for 3 years with bone marrow showing features of ITP and hence this child was diagnosed as chronic ITP.

We have described a child with confirmed Sanfilippo disease, which is an inherited storage disorder. High suspicion, clinical correlation and appropriate laboratory investigations will help in diagnosing this rare entity. The occurrence of thrombocytopenia in Sanfilippo disease has not been previously described.

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