Case Report

# Sanfilippo syndrome may go un diagnosed if not picked up during well health visit

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**Abstract**

Sanfilippo syndrome type B (Mucopolysaccharidosis IIIB) is a lysosomal storage disease resulting from deficiency of N-acetyl-glucosaminidase activity. A 12-month-old Saudi boy was presented to outpatient department in Assir Central Hospital, Saudi Arabia, with history of regression of milestone. Sanfilippo syndrome is a rare genetic disorder and can be missed easily during the routine health visit and it should be considered in the differential diagnosis of developmental delay or milestone regression and hence considering the subsequent investigation.

**KEY WORDS:** Lysosomal storage disease, Sanfilippo syndrome type B, N-acetyl-glucosaminidase (NAGLU) activity

## Introduction

Mucopolysaccharidosis IIIB (MPS IIIB) is a lysosomal storage disease which results from a deficiency in N-acetyl-glucosaminidase activity and manifests around 3–5 years of age. Clinical signs include hyperactivity, loss of social interaction, and progressive mental degeneration, which eventually results in severe impairment of neurocognitive ability and loss of motor function.[1,2] Patients may remain in this state for years, after which there is a regression in the patient behavior. This is associated with a progressive and severe loss of intellectual processes (such as speech) and motor functions (including walking and swallowing). MPS III patients ultimately regress to a vegetative state until death, which can occur anywhere between the early teens in the most severe scenarios, to as late as the sixth decade in attenuated forms.[3] The incidence of MPS III (all four types combined) is estimated to be 1 in 70,000 births.[4] Type A is the most common one in Northwestern Europe, type B in Southeastern Europe, and types C and D are rare everywhere.[3] In this case report, we had a child who presented in January 2015 with regression of milestone that diagnosed to have MPS III-B. The rationale of the report is to alert health workers and pediatricians generally about the importance of well-baby visit in particular developmental assessment.

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## Case Report

A 12-month-old Saudi boy was presented to outpatient department at Assir Central Hospital (a tertiary care hospital at southwest province of Saudi Arabia) with history of milestone regression. He was healthy till the age of 6 months when the parents noticed that their baby started to lose his milestone in form of loss of head control and inability to sit with support which he was able to do before. Family also noticed that the patient has hearing impairment but there was no concern regarding his vision. No history of convulsion or fever. Other systemic reviews were unremarkable. Past medical and surgical histories were also unremarkable. There was no previous hospitalization or surgical procedure. His developmental history was appropriate till age of 6 months, after that he started to deteriorate. Perinatal follow-up is unremarkable. He is fully vaccinated and his nutrition is acceptable. Family history revealed five members related to the child as direct paternal ankles suffered from an undiagnosed developmental delay and mental retardation, all of them died at early age with unclear diagnosis or even follow-up. The last one died around 8 years back. The parents are first-degree cousins, this patient is the only child for them, no deaths or abortion. Parents are healthy apart from the father who has hearing impairment for which he is using hearing device. On examination he

was conscious, alert, good body built, looks well with coarse facial features [Figure 1]. His head circumference corresponding to 97th percentile. Vital signs were within normal range. Chest and cardiovascular examinations were normal. Abdominal examination revealed hepato-splenomegaly with liver and spleen edge palpable 6 and 3 cm below costal margin, respectively. Central nervous system examinations were significant for large head and normal cranial examination apart of mild hearing impairment, power, and tone in upper limbs are normal, but increased in lower limb, his reflexes were brisky all over. Fundus examination showed normal macula, normal disk with no papilledema. Musculo-skeletal examinations were unremarkable, skin exam revealed two large Mongolian spots in the lower back. The initial investigation of this patient showed a complete blood count, serum electrolyte, renal function test, and liver function test all within normal limits. Acyl carnitine and amino acid were unremarkable, urine for mucopolysaccharide was 44 mg/mmol ($R$ = ≤31.0 mg/mmol). Magnetic resonance imaging of brain and spine was done and the finding was prominent perivascular space along the corpus callosum due to hypo intensity of the bilateral thalami and posterior limb of internal capsule, peritrigonal hypomyelination, dysplastic changes of the dense process of C2 with small sinus reaction articulating with anterior C1 ring, abnormal peaking of the upper lumbar vertebrae [Figure 2]. Ultrasound of the abdomen showed moderate hepato-splenomegaly with no focal echogenicity [Figure 3]. Molecular study showed that the patient was homozygous for the mutation p.R297X.

**Future Plan**

We will refer patient's father to genetic center for further screening regarding possibility that father might have a milder form of his son's disease. We are also planning to collect all cases of Sanfilippo syndrome in our area to lock for its prevalence and also to address the importance of prenatal investigation for purpose of early intervention. Other plans include health education, premarital counseling, prenatal diagnosis, and newborn screening of suspected baby.

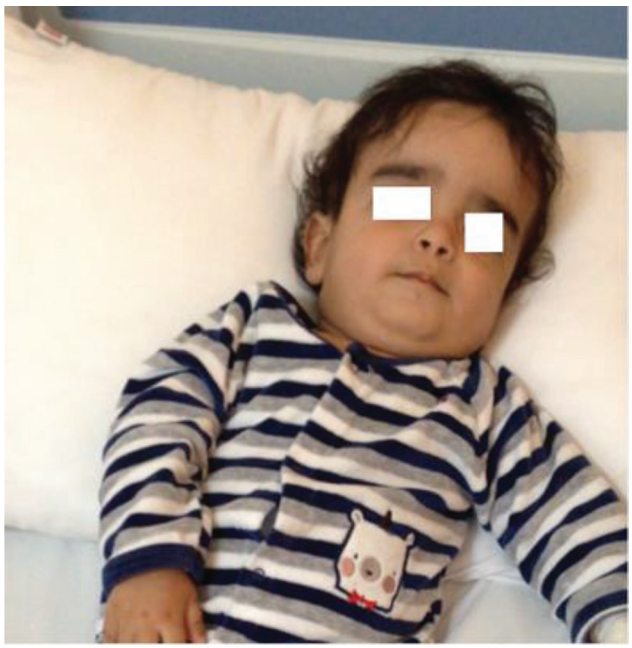

**Figure 1:** Facial features of the case.

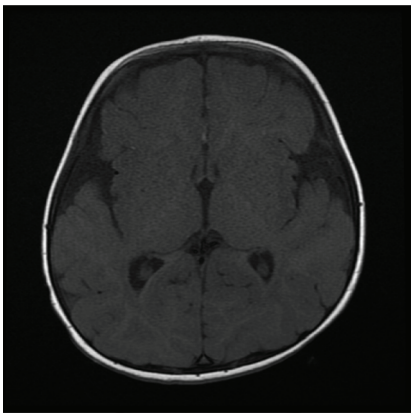

**Figure 2:** MRI picture of the case.

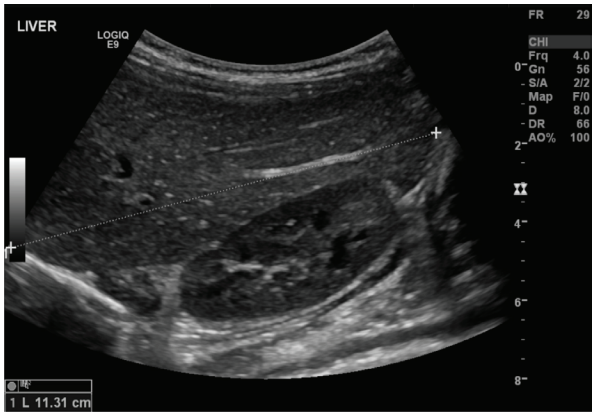


**Figure 3:** Abdominal ultrasound of the case.

## Discussion

Although Sanfilippo syndrome is a rare genetic disorder but has a usual presentation. It is usually present with developmental delay in the initial phase, later on they start to have abnormal behaviors for years and end in last phase by sever motor and mental retardation.[5] As far as we know, there is no published data regarding the prevalence of MPS type 3 in our region but because of high prevalence of consanguineous marriage in our community we expect the prevalence of this disease is higher than the international prevalence.[6] Unfortunately till now the lysosomal storage diseases including Sanfilippo syndrome are not included in the national newborn screening program, hence the importance of postnatal follow-up and through assessment of any suspected patient.

## Conclusion

Sanfilippo syndrome is a rare genetic disorder and can be missed easily during the routine health visit and it should be considered in the differential diagnosis of developmental delay or milestone regression and hence considering the subsequent investigation.

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