



Case Studies from the Child Development Center

Toddler with delayed speech, language development

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CB was nearly 4 years old when he was referred to the Child Development Center for evaluation of delayed speech and language skills. He began speech and language intervention at age 2 through a birth-to-3 program. A mild-to-moderate hearing loss was noted at about 36 months of age, and he was fitted for hearing aides. He continued speech therapy services through an early childhood program and also received supplemental speech therapy through a local hospital. At the time of his evaluation at the Child Development Center, he was using about 100 single words and occasional two- or three-word phrases. His mother reported hearing some "true words" mixed into language-like utterances (gibberish). Overall, the parents estimated that CB's communication skills were at a 2-year-old level.

In other respects too, CB seemed developmentally delayed. He was not toilet-trained, could not button or snap his clothing and could not make recognizable drawings. He seemed to be well coordinated and could pedal a tricycle. He liked to be "helpful" around the house and imitated sweeping and vacuuming. He pretended to feed a doll. CB was "slow-to-warm-up" around other children but would join in with active physical activities.

Past medical history included hospitalization during infancy for bronchiolitis. He had three insertions of ear tubes for recurrent ear infections. In addition, CB experienced recurrent sinus infections. Despite removal of his adenoids and tonsils, snoring and night terrors disrupted CB's sleep. He was noted to have severe myopia and was wearing corrective lenses. A congenital trigger thumb was repaired when he was 2 years old.

His mother's pregnancy was uncomplicated. CB was born at term weighing 9 pounds, 8 ounces. He did not require any special care in the nursery and was discharged home on the second day of life. Developmentally, he sat alone at 7 months and walked alone at 12 months. He waved goodbye at age 1 and started to say single words at 18 months.

The immediate family history was negative for individuals with speech, language or learning disorders. There was no history of consanguinity.

The primary care pediatrician noted macrocephaly and ordered an MRI scan of the brain, but it was normal. Complete blood count with differential, thyroid function studies (T4 and TSH) and chromosome karyotype with fragile X syndrome tests were also normal.

Physical examination identified a large boy: height, weight and head circumference were at or above the 98th percentile. His mother's head circumference was at the 95th percentile, and his father's head circumference was at the 98th percentile. CB's facial features were somewhat coarse in appearance, and he had slight contracture of the elbows and knees bilaterally, but his tongue did not appear enlarged. There was no corneal clouding. Chest and heart examinations were normal. Muscle bulk, tone and strength also were normal. The neurological examination was within normal limits. CB generally was cooperative and social. He tried to speak on several occasions, but I was unable to understand most of what he said.

The history and physical examination suggested the likelihood of a metabolic storage disease. X-rays of CB's spine revealed mild, oval-shaped configurations of the thoracic and upper-lumbar vertebral bodies. A urine test for mucopolysaccharides was positive, and lysosomal enzyme analysis confirmed the diagnosis of Sanfilippo syndrome (MPS III-type B).

Sanfilippo syndrome

Sylvester Sanfilippo, MD, first described this syndrome in 1963. It is a relatively rare, autosomal recessive disorder with an estimated prevalence of one in 70,000 births. The subtypes of Sanfilippo syndrome result from deficiencies in four different enzymes necessary to breakdown heparan sulfate, part of a sugar-amino-sugar polymer compound, also known as glycosaminoglycans or mucopolysaccharides, found in bones, cartilage, skin, tendons and other body structures. The accumulation of heparan sulfate in the brain is responsible for progressive deterioration of function.

Of the seven known types of mucopolysaccharidoses, Sanfilippo syndrome produces the mildest physical abnormalities. For this reason, diagnosis often is delayed during early childhood.

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The disorder is said to have three distinct clinical stages. During preschool years, the child may have general developmental delays without obvious abnormal physical features. In the second phase, children with this disorder may have extreme hyperactivity, restlessness and difficult-to-manage behaviors. Sleep problems also are very common. Language and cognitive development may begin to deteriorate with loss of previously acquired skills. In the third phase, affected children may lose the ability to walk and become severely developmentally disabled.

All of the mucopolysaccharidoses share common features and affect multiple organ systems. For example, thickened facial bones and mucosal lining may cause airway obstruction resulting in chronic ear and sinus infections. Enlarged tonsils and adenoids may block the airway and result in sleep apnea. Recurrent or chronic respiratory problems are common. Deafness frequently occurs, both conductive and sensorineural forms. Retinal changes may lead to loss of peripheral vision and night blindness. Heart valves may be affected by accumulation of glycosaminoglycans and lead to valvular obstruction or incompetence. There may be liver and spleen enlargement, and this may result in umbilical herniation. Joint stiffness and limitation of movements eventually may cause pain and loss of function. Hips may become dislocated and tight heel cords may impair walking. Autonomic dysfunction may lead to cold hands and feet. Seizures are frequent in the later stage of the disorder and often are responsive to conventional antiepileptic medications.

Unfortunately, there are no known treatments to correct the underlying metabolic defect in this disorder. Life expectancy in Sanfilippo syndrome is extremely varied. Many individuals live into their teenage years, and some mildly affected individuals have lived into their 30s or 40s.

Once a definitive diagnosis was made, CB's parents were counseled with the help of the Children's Hospital of Wisconsin genetics counselors and clinical social worker. We were able to help coordinate the variety of health care visits he required and assist the family in managing his care. CB will be followed on an annual basis to monitor his developmental and behavioral progress. The parents also expressed an interest in having more children. Currently, molecular sequencing of the Sanfilippo type B gene has a 96 percent detection rate for identifying mutations on both alleles, to differentiate heterozygote/carrier from homozygote/affected status. They were offered further genetic screening services through the Children's Hospital of Wisconsin Genetics Center to assist with their family planning decisions.

Reference

A Guide to Understanding Sanfilippo Syndrome: Mucopolysaccharidosis (MPS) III. The National MPS Society, Inc.; 2000.

Case Studies from the Child Development Center is a limited edition newsletter to help inform referring physicians and other professionals on the depth and breadth of pediatric communication and behavioral issues diagnosed and treated in the Child Development Center at Children's Hospital of Wisconsin.

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It also is available online at www.chw.org, Child Development Center, Related Links.

Questions and suggestions can be forwarded to:

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