



Case Studies from the Child Development Center

Severe behavior problem leads to genetic diagnosis

Mark Simms, MD, medical director, Child Development Center, Children's Hospital of Wisconsin; professor, Pediatrics, Medical College of Wisconsin.

CG was a 5-year 3-month-old boy referred to the Child Development Center for evaluation and treatment of severe behavior problems. His mother was concerned about frequent head banging, destructive tantrums, nail biting and obsessive behaviors. Head banging seemed triggered by frustration and occurred up to 10 times each day, mostly in the afternoons. He had a history of breaking windows and mirrors with this behavior. There were many things that CG wanted to be "just right." For example, he would make up rules or create roles for people at home and became very upset when they were not followed. He was preoccupied with the family pet gerbils and constantly wanted to see what they were doing. He also became fascinated with a yellow jacket nest in the backyard. CG was able to speak in words and phrases, but could not form full sentences. He was a socially aware and affectionate child.

Sleep disturbance was a long-standing problem. After having a bath and reading a story, his parents placed him in his own room at approximately 9:30 each evening. He generally fell asleep between 10 p.m. and 11 p.m. and woke at 5:30 a.m. or 6 a.m. CG napped every day from 2:30 p.m. until 6 p.m., again in his own bed.

The pregnancy history was uneventful, and CG was a full-term infant who weighed 6 pounds 8 ounces. He was hypotonic following birth and had difficulty gaining weight. Additional problems during the preschool years included gastroesophageal reflux and frequent otitis with chronic rhinorrhea.

Developmental milestones were delayed. CG sat at 15 months and began walking at 19 months. He waved bye-bye at 2 years old and said single words at about 30 months.

The family history was unremarkable. No other family members had developmental disabilities or birth defects.

On physical examination, CG was at the 50th percentile for height and the 25th percentile for weight. His head circumference was at the 5th percentile. Dysmorphic features were present including a round face with brachycephaly, flat

mid-facial features and upslanting of the palpebral fissures. Neurological examination was normal. His speech was limited for his age and his voice was husky. He was generally cooperative during the examination, but he behaved in an immature manner. At one point, CG became frustrated and began to bang his head repeatedly on the wall.

Arrangements were made for further psychological evaluation, and chromosome tests were drawn. Zoloft was started in an attempt to reduce his frustration and obsessive behaviors. The chromosome tests revealed a deletion at 17p11.2, consistent with the diagnosis of Smith-Magenis syndrome (SMS). Zoloft 20 mg resulted in some attenuation of the obsessive behaviors, but tantrums, head banging and sleep problems persisted.

Shortly after making the genetic diagnosis, his mother attended a national conference on SMS and became aware of a novel treatment approach for the sleep disorder associated with this syndrome. After reviewing the published literature, CG was treated with remarkable improvement in his sleep pattern and dramatic reduction in his tantrums.

Discussion

Smith-Magenis syndrome is a relatively uncommon disorder, affecting approximately 1:25,000 individuals. Almost all cases appear de novo and there is a very low recurrence risk within a family. A specific FISH probe is available to identify cases that are not diagnosed with high-resolution chromosomal karyotyping. Typically, newborns and infants with this syndrome are lethargic following birth, have very poor sleep patterns and fail to gain weight. By 18 months of age, stereotypic behaviors and tantrums appear. Sixty to 80 percent of children display maladaptive, stereotypic and self-abusive behaviors. Several behaviors appear to be unique to SMS, forming a "behavioral phenotype" typical for this disorder. These include hand-licking and page flipping seen in 51 percent, spasmodic upper body squeezing ("self-hug") in 46 percent, onychotillomania (nail yanking) in 29 percent and polyembolokoilamania (bodily insertions) in 25 percent.

Sleep disturbance is universal in SMS. In infancy, hypersomnolence is most common. This is followed by fragmented and short sleep

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Smith-Magenis syndrome cont.

cycles, prolonged nocturnal awakening and excessive daytime sleepiness/napping. In 2003, De Leersnyder¹ described an inversion of the circadian rhythm of melatonin in virtually every person with SMS that was studied. They noted that tantrums and tiredness occurred when melatonin peaks between mid-day and evening hours. By administering a selective beta-1 adrenergic antagonist (acebutalol) in the morning to suppress endogenous release of melatonin, followed by a single dose of slow release melatonin in the evening, sleep was converted to a normal pattern. Night awakenings and afternoon "sleep attacks" disappeared. The total amount of sleep was observed to increase to a mean of approximately nine hours. This treatment also resulted in a significant improvement in inappropriate behaviors, reduction in tantrums and increased ability to concentrate. No complications were noted in this group of 10 children aged 4-18 years followed over the course of a 12-month study. Using this treatment approach, we successfully have treated the three children with Smith-Magenis syndrome seen at the Child Development Center over the past 12 years. Each child has shown a dramatic improvement in their sleep pattern with a significant improvement in overall behavior during the day.

This case illustrates the importance of pursuing a specific genetic diagnosis in children with developmental disabilities. Unfortunately, currently available technology does not result in a specific etiologic diagnosis for most developmentally disabled children. Clinicians therefore usually rely on a fairly generic approach to treat behavioral problems. Although SMS is a relatively rare disorder, positive identification of

this syndrome may lead to a very successful treatment approach for extremely disruptive symptoms.

References

¹De Leersnyder H, Bresson JL, de Blois MC, et al. Beta-1-adrenergic antagonist and melatonin reset the clock and restore sleep in a circadian disorder, Smith-Magenis syndrome. *J Med Genet* 2003;40:74-78.

Smith ACM, Gropman A. Smith-Magenis syndrome (chapter 22). In: Cassidy SB, Allanson JE. (Eds.), *Management of Genetic Syndromes*. 2001: New York, Wiley-Liss.

School Performance Program offers range of services

Ken Grizzle, PhD, child psychologist, Child Development Center, Children's Hospital of Wisconsin.

The School Performance Program in the Child Development Center offers a range of services for children with learning and attention problems. Diagnostic evaluation includes psychoeducational, language and pediatric neurodevelopmental assessments. Treatment approaches coordinate behavioral and medication therapy for both the core symptoms of ADHD and the co-morbid/co-occurring disorders such as anxiety, mood disorders, social difficulties and parent-child conflict.

A six-week socialization group is available for children with ADHD, language and/or learning difficulties. Behavior management groups also are available to parents of children with ADHD and/or Oppositional Defiant Disorder.

For more information about the School Performance Program, contact Kenneth Grizzle, PhD, at (414) 266-2928.


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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Questions and suggestions can be forwarded to:

Mark Simms, MD, Child Development Center, MS744,
Children's Hospital of Wisconsin, PO Box 1997, Milwaukee, WI 53201-1997
or call (414) 266-2928.

Child Development Center, MS 744
PO Box 1997
Milwaukee, WI 53201-1997

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