Published in final edited form as:

Pediatr Ann. 2018 March 01; 47(3): e130–e134. doi:10.3928/19382359-20180223-01.

Behavioral Outbursts in a Child with a Deletion Syndrome, Generalized Epilepsy, Global Developmental Delay, and Failure to Thrive

Adam H. Lewis, BS [Research Assistant],

Section of Developmental and Behavioral Pediatrics, The University of Chicago

Ankur Chugh, MD [Assistant Professor],

Medical College of Wisconsin

Sarah A. Sobotka, MD, MSCP [Instructor]

Section of Developmental and Behavioral Pediatrics, The University of Chicago

Abstract

A 7-year-old girl with 20q13.33 deletion and a history of generalized convulsive epilepsy presented to the Developmental and Behavioral Pediatrics Clinic due to concerns about her behavioral outbursts in the context of overall delayed development. Evaluation by the Developmental and Behavioral and Gastroenterology teams revealed failure to thrive (FTT) as the primary cause of the behavioral outbursts and developed a high-calorie, high-fat, high-protein nutritional counseling plan. Children who have FTT and a genetic disorder are often thought to not thrive because of their underlying genetic disorder; however, feeding skills and nutritional intake need to be thoroughly investigated before determining an etiology for FTT. Motoric, communicative, and developmental skills in children with genetic disorders may impede appropriate feeding mechanisms, inducing or exaggerating FTT in these children with developmental disabilities due to genetic etiologies.

Feeding challenges are abundant in children with genetic disorders and developmental disabilities. When these obstacles become dramatic enough to impair appropriate nutrition and growth, the result often leads to failure to thrive (FTT). Unfortunately, families and providers may overlook concerns about growth due to the underlying genetic disorder, and as a result, nutritive interventions can be delayed or missed.

ILLUSTRATIVE CASE

The patient was a 7-year-old girl with 20q13.33 deletion and a history of generalized convulsive epilepsy who presented to the Developmental and Behavioral Pediatrics Clinic due to parental concerns about frequent crying and screaming spells in the context of overall delayed development. These episodes began 10 months prior to her presentation and

Address correspondence to Sarah A. Sobotka, MD, MSCP, Section of Developmental and Behavioral Pediatrics, The University of Chicago, 950 East 61st Street, Suite 207, Chicago, IL 60637; ssobotka@peds.bsd.uchicago.edu.

Disclosure: The authors have no relevant financial relationships to disclose.

occurred 2 to 3 times per week, typically lasting 20 minutes, with some spells lasting up to 5 hours. The patient would stiffen and kick her legs in a nonrhythmic fashion during episodes and occasionally bite herself or others. Her mother noticed that episodes frequently occurred approximately 20 minutes after eating but not on a consistent basis. The episodes had intensified since their onset, although eating, drinking, or listening to music would sometimes help to calm her down.

Three months prior to this presentation the patient saw her neurologist who performed a video electroencephalogram (EEG) to evaluate seizure activity as a potential cause. The spells were not found to correlate with any abnormal EEG activity, but she was continued on her prior anticonvulsant therapy due to her history of multiple seizures and abnormal prior EEG studies.

Developmental History

The patient's parents were first concerned about her development when she was age 4 months. In infancy, the patient was referred to a Developmental and Behavioral Pediatrician who diagnosed global developmental delay and recommended genetic testing. A chromosomal microarray revealed 20q13.33 deletion.

The patient's developmental trajectory remained delayed throughout early childhood. She learned to crawl at age 2 years and to stand at age 3 years. At age 7 years, the patient demonstrated an ability to take steps with assistance but relied on a wheelchair for longer distances.

The patient communicated with eye gaze and directing attention but did not speak. Her mother estimated that her daughter functioned at approximately the level of an 18-month-old child. She received special educational services from her public school and used insurance to obtain physical therapy and hippotherapy services outside of school.

Physical Examination

On presentation the patient was a thin-appearing, nondysmorphic child. Her height was 114 cm (2nd percentile, z-score -2.07), weight was 16.9 kg (<1st percentile, z-score -2.78), body mass index (BMI) was 13 kg/m^2 (<5th percentile, z-score -2.15) (Figure 1), and her head circumference was 46 cm (<3rd percentile). She was afebrile, breathing comfortably, and in no apparent distress during the visit. She had conjugate gaze, making eye contact with the examiner. Her mucous membranes were moist and she was able to protrude her tongue. No drooling was noted. Her heart and lung examination were unremarkable. Her abdominal examination was notable for a thin abdomen, without discomfort on examination. She was able to sit without support and demonstrate a few independent steps with wide-based gait and minimal assistance. She had low tone overall and thin extremities with diminished strength. The patient frequently placed her hands in her mouth throughout the visit.

On review, the Developmental and Behavioral Pediatrician became concerned about the patient's FTT and discussed it further with her mother. Her mother described the patient's appetite as voracious, despite her continued low weight over time. As a result, the patient was referred to Pediatric Gastroenterology to evaluate for FTT.

At the initial consultation with Pediatric Gastroenterology, the mother described crying spells that she thought could be related to abdominal discomfort, given their temporal relationship to eating. She also noted excessive eructation. Previous evaluation included an upper gastrointestinal X-ray that did not show reflux or other abnormalities. Additionally, the patient had a trial of a proton pump inhibitor for many months that was unsuccessful. The gastroenterologist determined that a differential diagnosis for the patient's symptom included pancreatitis, eosinophilic gastroenteritis, gastritis, peptic ulcers, celiac disease, and malabsorption syndromes. Laboratory and stool testing were done to evaluate the suspected etiologies and were unremarkable. A diagnostic upper endoscopy was then performed, which was grossly normal with normal biopsies. Given the history of excessive gas and symptom persistence, Gastroenterology prescribed simethicone for gas and an empiric trial of rifaximin for small intestinal bacterial overgrowth. With the trial not yielding an improvement in her behavior, Developmental and Behavioral Pediatrics and Gastroenterology chose to focus on her nutrition.

Diagnosis

During the course of the next 3 months, the Developmental and Behavioral and Gastroenterology teams provided feeding and nutritional counseling focused on providing the patient with efficient high-calorie, high-fat, and high-protein supplementation. Because of the patient's overall motor delays she generally took longer to eat, thus appearing to consume a great deal of food despite her insufficient caloric intake. With the recommended interventions, the patient's mother focused on adding olive oil and peanut butter to preferred foods. When the patient returned to clinic 4 months later she had gained 7 pounds, placing her weight in the 15th percentile (z-score, -1.05), and her BMI at 15.64 kg/m^2 , which was in the 44th percentile for girls her age (z-score -0.15). The mother reported that the patient's behavioral outbursts had almost completely resolved. Additionally, her endurance for long-distance ambulation and school activities increased. The team, together with her mother, concluded that the behavioral outbursts were likely the result of the patient's frequent hunger. Due to challenges with fine motor skills and coordinating oral muscle movements for eating, the patient was often unable to take in enough calories to support growth and development. She also struggled to communicate her discomfort due to a reduced level of neurodevelopmental functioning (in the moderate to severe intellectual disability range) with no verbal and minimal nonverbal communication skills. A prolonged lack of sufficient nutrition and FTT contributed to the patient's poor endurance during longer walking distances and long school days, and potentially hindered her ability to function at full capacity in school, home, and community settings.

DISCUSSION

Genetic disorders and associated developmental disabilities often lead to challenges with feeding. When substantial enough to impair appropriate nutrition and growth, these feeding challenges often lead to FTT. In some instances, children respond to dietary modifications that stress efficient high-nutrient/caloric intake. Other children require dietary supplementations such as nutritional drinks or meal replacement drinks. A minority of

children are ultimately unable to orally feed themselves sufficient calories for growth and require supplementation by gastrostomy tube.

FTT is a physical sign of malnutrition leading to inadequate growth, weight gain, and development in children.^{1,2} Monitoring for growth is particularly important in children with neurodevelopmental disability because of their increased risk of poor nutrition. The medical home is best positioned to plot a child's growth over a series of visits to observe the clearest trend of growth over time.¹⁻⁴ Children who are not gaining weight between appointments or children who are below the 5th percentile in their growth parameters should be monitored closely, and z-scores (measures of standard deviations) should be used.

Genetic disorders are often coupled with FTT, and patients with microdeletion syndromes present with FTT approximately 25% of the time.⁴ However, the mechanisms surrounding FTT can most often be attributed to delays and disabilities with the oral motor skills required for eating. Children with developmental disabilities, particularly those that affect oral motor skills, can require supplementation because of the impact of their disabilities on oral nutritional intake. Although some genetic disorders may cause short stature, few directly cause failure to gain weight. A common presumption is that children who have FTT and have a genetic disorder are failing to thrive due to their underlying genetic disorder, yet nutrition needs to be thoroughly evaluated before an etiology for FTT is determined.

Growth below average for gestation, corrected age, sex, genetic potential or underlying medical condition, or as compared to other children in a peer group can indicate FTT.¹ Medical consensus suggests weight-for-age decline across two major centiles and weight-for-length of less than 80% of normal weight are the two primary indicators for a FTT diagnosis.¹⁻⁴ Limitations to this definition reside within normal variations of children's growth patterns.²

Previous definitions of FTT divided diagnoses into two categories, organic and nonorganic, indicating the presence of an underlying medical condition or not, respectively. Of course, FTT can be influenced by an array of factors not exclusively bound to organic or nonorganic sources, so perhaps FTT is better understood from a multifactorial perspective.^{2, 4} A variety of high-risk factors may compound and exacerbate the potential for FTT, especially when operating in concert with a high-risk medical or social condition. Underlying medical conditions such as prematurity, congenital abnormalities, neurodevelopmental disorders, and genetic disorders predispose children to the risks surrounding FTT.¹ Social conditions that may predispose to FTT include poverty, domestic violence, parental intellectual disability, and parental substance abuse.¹

Children with genetic disorders are at high risk for FTT, which is often under-recognized by parents, as well as providers. In children with developmental disabilities, 23% of parents did not recognize growth concerns, especially for underweight and overweight categories. Up to 80% of children with developmental disabilities have been found to be at risk for feeding disorders (compared to an estimated 25%-45% of typically developing children), with one-half at moderate or high risk.⁵ In addition, the mental, physical, and emotional challenges of caring for a child with special needs may hinder a parent's ability to provide appropriate

nutrition to their child and/or family. Parents may also expect that a thin or malnourished appearance is normal for a child with a genetic disorder and subsequently forgo medical attention for growth concerns.

A clear understanding of the particular mechanisms driving FTT in children with genetic conditions helps establish the proper course of nutritional treatment. Although there are typically psychosocial factors at play, at the biological level FTT is caused by a lack of usable nutrition available to promote sufficient growth in a child.^{1,3,4} These insufficiencies can be categorized as inadequate calorie intake, inability to absorb and/or retain calories, increased metabolism, defective nutrition utilization, and neglect.^{1,3,4} Cases of chromosomal disorders and syndromes are most often connected to caloric intake inadequacies and higher metabolic demands.^{1,2} A detailed evaluation of the child's medical history is critical for establishing an FTT diagnosis and should cover the following areas: prenatal, postnatal, and past medical history; feeding history; developmental history; family history; psychosocial history; and information from other health professionals.^{1,3} Ultimately, management of FTT via a multidisciplinary team of health care workers (such as a pediatrician, nutritionist, and social worker) yields the most promising outcomes.^{1,4}

The consequence of poor nutrition has varying impact based on the period of child development, as well as duration and degree of malnutrition. In children younger than age 3 years, inadequate nutrition can lead to a high risk of reduced cognitive and executive functioning later in life.⁶ It has been reported that children who were formerly diagnosed with FTT struggle with language development, reading skills, social maturity, and have a higher prevalence of behavioral problems than in children without FTT from similar sociodemographic circumstances.⁷ As one might imagine, in a child already predisposed to cognitive disability because of a genetic disorder, the neurodevelopmental impact of nutritional deficiencies may be underestimated.

The Agency for Healthcare Research and Quality performed a systematic review of the connection between children with FTT and concurrent or future behavioral problems.⁸ The study found children with FTT had concurrent behavioral problems with greater frequency than those with neurological or other organic damage or disease, and compared to control groups developed significantly more family problems, psychological impairments, or behavioral deficits.⁸ An inverse relationship between total risk factors and cognitive functioning has been identified in children with FTT and shown to remain years after diagnosis.⁹ It has also been reported that children who were formerly diagnosed with FTT are smaller than children without FTT, with 48% of children formerly diagnosed with FTT in the bottom 20th percentile for weight, 60% in the bottom 20th percentile for height, and 20% in the bottom 5th percentile for BMI. This same study reported 30% of children with a history of FTT had clinically significant aggression factors compared to 6% of the control group.⁶

CONCLUSION

FTT affects many children with genetic disorders due to the motor, communicative, and developmental skills required for appropriate feeding. Nutrition is critical for growth and development, and therefore deficiencies must be promptly identified and addressed.

Acknowledgment:

The authors thank the patient and her family for their support of sharing their story through this article..

Grant: S. A. S. is funded by grant K12 HS023007 from The University of Chicago Patient Centered Outcomes Research K12 Training Program, and the T73 Leadership Education in Neurodevelopmental and Related Disorders Training Program.

REFERENCES

1. Scholler I, Nittur S. Understanding failure to thrive. *Paediatr Child Health*. 2012;22:10:438–442. doi:10.1016/j.paed.2012.02.007.
2. Jaffe AC. Failure to thrive: current clinical concepts. *Pediatr Rev*. 2011;32:100–107. doi:10.1542/pir.32-3-100. [PubMed: 21364013]
3. Cole SZ, Lanham JS. Failure to thrive: an update. *Am Fam Physician*. 2011;83(7):829–834. [PubMed: 21524049]
4. Rabago J, Marra K, Allmendinger N, Shur N. The clinical geneticist and the evaluation of failure to thrive versus failure to feed. *Am J Med Genet Part C Semin Med Gent*. 2015;169(4):337–348. doi:10.1002/ajmg.c.31465.
5. Malone C, Sharif F, Glennon-Slaterry C. Growth and nutritional risk in children with developmental delay. *Ir J Med Sci*. 2016;185:839–846. doi:10.1007/s11845-015-1377-3. [PubMed: 26573207]
6. Dykman RA, Casey PH, Ackerman PT, McPherson WB. Behavioral and cognitive status in school-aged children with a history of failure to thrive during early childhood. *Clin Pediatr (Phila)*. 2001;40:63–70. doi:10.1177/000992280104000201. [PubMed: 11261452]
7. Oates RK, Peacock A, Forrest D. Long-term effects of nonorganic failure to thrive. *Pediatrics*. 1985;7(1):36–40.
8. Perrin EC, Cole CH, Frank DA, et al. Criteria for determining disability in infants and children: failure to thrive: summary. <https://www.ncbi.nlm.nih.gov/books/NBK11940/>. Accessed March 1, 2018.
9. Mackner LM, Starr RH Jr, Black MM. The cumulative effect of neglect and failure to thrive on cognitive functioning. *Child Abuse Negl*. 1997;21(7):691–700. [PubMed: 9238552]
10. Centers for Disease Control and Prevention. Clinical growth charts. <https://www.cdc.gov/growthcharts/data/set2clinical/cj411074.pdf>. Accessed March 1, 2018.

Figure 1.

BMI-for-age growth chart. BMI, body mass index. From the Centers for Disease Control and Prevention¹⁰ (in the public domain; permission is not required).