A 12-Month-Old Boy with Failure to Gain Weight

Robert Listernick, MD

A 12-month-old boy was transferred for evaluation of failure to gain weight. He was growing and developing appropriately and meeting his milestones up until age 8 months, at which point he had significant drop-off in his weight, resulting in three hospitalizations elsewhere. He drank a cow’s milk-based formula during his first 6 months. He started receiving a variety of solid foods at age 6 months. At age 8 months he started refusing to eat. His mother thought that he had “sensory issues” because he would start gagging with most foods. He would turn his head away from the bottle. His doctor was concerned about the weight loss and admitted him to a local hospital. There were stressors in the home at this time, including his father’s new job that left the mother alone for long periods of time.

During the first admission, the child had a nasogastric tube inserted but he developed significant gagging, choking, and vomiting due to what was thought to be the sensation of the tube in his throat. He gained weight over 2 days and was discharged home with no changes in his diet other than an increase in the formula’s caloric density.

Two months later he was hospitalized for 12 days with similar complaints. Once again, insertion of a nasogastric tube led to frequent vomiting. He was changed to an elemental formula, which he tolerated better. He had a large diagnostic work-up that was unrevealing, including barium upper gastrointestinal series and upper intestinal endoscopy. He did well at home for a few weeks after discharge. He was able to eat some solid food and he drank 2 to 3 ounces of the elemental formula every 3 hours around the clock.

Another 2 months later, he had a third admission after failing to meet his weight goal at the doctor’s office. Additionally, there was some concern that he had some developmental regression; whereas previously he had been crawling, pulling to stand, and taking steps with assistance, he was “too tired” or unable to do so. He slept a large part of the day, and when he was awake he was crabby and irritable. He was transferred for “consideration of placement of either gastrostomy or central venous access for total parenteral nutrition” (TPN) given his inability to tolerate oral and nasogastric feeds.

On review of systems, his parents noted that he had developed occasional right eye twitching and “staring off into space.” During the previous hospitalization, it was noted that he had episodes of several seconds of staring during which he seemed to respond; an electroencephalogram was reportedly normal.

On social history, the father and grandparents expressed concern that the mother had had second thoughts about having the baby and that she was not taking her prescribed medicine despite a diagnosis of postpartum depression. They felt that the mother didn’t spend enough time feeding him or dressing him warmly enough.

The father is currently living with the child and the mother in the maternal grandmother’s house, but he feels that the child worsens in his absence. The local hospital had reported the family to the Department of Child and Family Services for maternal neglect, which was the transfer diagnosis.

The family history was remarkable in that the father recently had a recent parathyroid adenoma resected.

On examination in our hospital, the child was able to sit independently. He

continued on page 262
was previously able to crawl, pull to stand, and take steps with assistance, none of which he would do now. He could speak five single words and had an age appropriate receptive vocabulary. There was no language regression.

His birth history was unremarkable save for having been born via cesarean delivery.

On examination, he was a thin, emaciated, and lethargic boy. Vital signs were unremarkable. His weight was below the 5th percentile, length was in the 25th percentile, and head circumference was greater than the 95th percentile. HEENT (head, eyes, ears, nose, and throat) examination was normal. Anterior fontanel was closed. No nystagmus was noted. Red reflexes were normal. Extraocular movements were intact. Heart, lungs, and abdomen were unremarkable. He had decreased muscle mass with loose skin. On neurologic exam, he had slighty diminished axial tone with normal tone in the extremities. However, cranial nerves, strength, and deep tendon reflexes were all normal with downgoing Babinski reflexes.

**Robert Listerick, MD, moderator:** Comments?

**Valeria Cohran, MD, pediatric gastroenterologist:** Indications for TPN include intestinal failure, ileus, or intestinal obstruction, none of which he has. Enteral feeding can promote intestinal healing and is strongly preferred over TPN unless the former can’t be performed effectively or safely. In addition to its significant cost, risks associated with TPN include infection and thrombosis of the central venous access.

**Dr. Listerick:** Obviously there’s something serious going on here, but can you comment on the purported diagnosis of “sensory issues”?

**Dr. Cohran:** There are certainly many children who have sensory integration disorders in whom certain textures or consistency provoke food refusal. However, this child started refusing both the bottle and solids that he had previously eaten for a long time. This is not particularly consistent with the diagnosis. In addition, the developmental regression was obviously a major red flag that something more serious was occurring.

**Dr. Listerick:** What about his symptoms when the nasogastric tube was put down?

**Dr. Cohran:** Those were unusual and not expected. Although babies may gag, choke, and vomit during the tube’s placement, it’s very unusual for these symptoms to continue once it has been placed successfully. He had already had a barium study, which was reviewed here and did not show evidence of a malrotation or other anatomic abnormalities.

**Dr. Listerick:** Moving forward, it’s no surprise that his macrocephaly was a huge red flag. When we obtained his growth chart, despite a paucity of points, it was clear that he did have progressive macrocephaly with his head circumference crossing many quintile lines until presently being greater than the 95th percentile. Shall we look at the neuroimaging shortly after he arrived here?

**Arthur DiPatri, MD, pediatric neurosurgeon:** It’s not subtle. There is a large suprasellar mass distorting the brainstem. The third ventricle is obliterated by the mass. There’s either a cystic or necrotic component as well. In addition, he has impressive hydrocephalus due to obstruction of cerebrospinal fluid flow from the third ventricle.

**Dr. Listerick:** Differential diagnosis?

**Dr. DiPatri:** The most common suprasellar tumor in children is a craniopharyngioma, although this does not have the radiographic characteristics. Nor does this appear to be a pituitary macroadenoma, as it’s so large. Most likely it’s a low-grade glioma based on imaging characteristics.

**Rishi Lulla, MD, pediatric neurooncologist:** It’s seems pretty apparent from the history that this child had a central nervous system neoplasm. The combination of failure to gain weight, vomiting, lethargy, regression of developmental milestones, and the rapidly increasing head circumference makes this diagnosis obvious.

**Dr. Cohran:** I agree. Although we see many children with emesis and poor weight gain for a variety of gastrointestinal reasons, we don’t see developmental regression to this degree in any of our diseases.

**Dr. Listerick:** In addition, I know that this child’s head circumferences were never plotted on a standard growth chart prior to arrival here.

**Natasha Pillay Smiley, DO, pediatric neurooncologist:** This child has diencephalic syndrome. We see many children with brain tumors who have vomiting and weight loss. However, the child with classic diencephalic syndrome has a hypothalamic tumor and develops severe emaciation despite normal caloric intake and normal linear growth. Classically, they eat normally, or even voraciously, but lose weight. In addition, they are often described as “happy” or “hyperalert.”

**Dr. DiPatri:** Often these children start out as having characteristic symptoms of diencephalic syndrome but then develop hydrocephalus that leads to the lethargy that this child had. In addition, he had the classically described appearance of “pseudohydrocephalus,” which is a big head on a small, emaciated body.

**Dr. Pillay Smiley:** It’s not been fully elucidated yet, but the hormone leptin may play a role in the poor weight gain. It’s interesting that you can give these children TPN but they won’t gain weight until chemotherapy is started. At the other end of the spectrum are the children who have hypothalamic obesity and insatiable appetites who have hypothalamic tumors.

**Dr. Listerick:** Let me ask you about macrocephaly. I see children who have neurofibromatosis type 1, many of
whom have macrocephaly. Their heads don’t start out big; rather they’re normal at birth and cross percentiles during the first year at life. Yet, I don’t obtain neuroimaging on most of them.

Dr. DiPatri: That’s a good point. We see lots of kids who are referred for macrocephaly whose head circumferences are crossing percentiles. The difference between those children and the children who have brain tumors is that the former are acting normally, they’re developmentally appropriate, and they have flat fontanels. Often, they have familial macrocephaly so we also measure the parents’ head circumferences.

Dr. Listerick: Let’s start talking about treatment.

Dr. DiPatri: We first had to deal with his increased intracranial pressure. On careful examination of the magnetic resonance imaging scan, we noticed that his lateral ventricles are each individually obstructed at the level of the third ventricle. Draining one lateral ventricle will not decompress the contralateral one. We initially created a fenestration through the septum pellucidum, creating a connection between the two lateral ventricles, and we left in an extraventricular drain to decompress this newly formed “monoventricle.” Several days later, we operated on him, placing a ventriculoperitoneal shunt and performing a biopsy of the tumor.

Dr. Listerick: What about removal of the tumor?

Dr. DiPatri: These tumors are usually low-grade pilocytic astrocytomas, which are difficult to remove in their entirety. Often, there are a number of penetrating arteries coming off the anterior and middle cerebral arteries going right through the tumor. Any mistake could lead to a neurologic catastrophe. In the past, we often tried to debulk the tumor by opening up the ventricle so as to get a better exposure, but recently we have been trying to avoid doing that.

Dr. Listerick: Can we see the biopsy?

Nitin Wadhwani, MD, pediatric neuropathologist: Let me take you through our thought process. First, we looked at the histology and saw glomeruloid vessels and spindled glial cells. We used special stains to tell us that these are neoplastic glial cells. Next, we used other special stains to help us determine the proliferative index (ie, how aggressive the tumor is). Unfortunately, the biopsy specimens were so small that we had limited ability to be definitive. The best we could say in this case was that our results favored a low-grade glioma.

Dr. Listerick: How did you proceed with these results?

Dr. Pillay Smiley: I’m treating him as a low-grade glioma patient and using a combination of carboplatin and vincristine. This regimen is very well tolerated with minimal side effects. The goal of chemotherapy in the treatment of low-grade gliomas is to stabilize the tumor and prevent it from getting any bigger. As a rule, one-third of the tumors will get smaller, one-third will remain the same size, and one-third unfortunately will grow. In this latter group, we have alternate chemotherapeutic regimens that we can use with the goal of trying to avoid radiotherapy and all its inherent side effects.

Dr. Listerick: What about his poor weight gain and the diencephalic syndrome?

Dr. Pillay Smiley: As long as the tumor doesn’t progress, it’s been shown that most children will start gaining weight by 6 months into treatment and will be back on their curve after 1 year.

Dr. Listerick: What about mortality?

Dr. Pillay Smiley: The overall survival for children with low-grade gliomas is excellent. However, we don’t have good survival data for those children who present with diencephalic syndrome.

Jason Fangusaro, MD, pediatric neurooncologist: The whole paradigm for low-grade glioma treatment has changed over the past 15 years. In the past, we felt we needed to “cure” the child and make the tumor disappear with radiotherapy. Now we understand that children can live with the tumor much like they do with other chronic diseases.
such as diabetes or asthma with excellent very long-term survival.

**Dr. Listernick:** Children with suprasellar/hypothalamic tumors may develop endocrinologic problems.

**Laura Torchen, MD, pediatric endocrinologist:** They’re at high risk for developing any combination of pituitary hormone deficiencies. We generally assess free thyroxine, thyroid-stimulating hormone, insulin-like growth factor-1, insulin-like growth factor binding protein-3, and first morning cortisol looking for adrenocorticotropic hormone deficiency. On admission, he had no signs of diabetes insipidus. A 12-month-old child who doesn’t have access to free water should be hypernatremic if he has diabetes insipidus. His initial serum sodium was normal.

**Dr. Listernick:** Several days into his admission, it was noted that his serum sodium was starting to decline.

**Dr. Torchen:** This prompted us to wonder whether he had the syndrome of inappropriate secretion of antidiuretic hormone (SIADH), or alternatively cerebral salt wasting. These may be difficult to distinguish. Children with SIADH should be euvolemic or mildly hypervolemic, whereas those with cerebral salt wasting should be a bit hypovolemic. We look for signs of volume status such as tachycardia, orthostatic blood pressure, and urine output. Admittedly, it was quite difficult to know in this child. The treatment of SIADH is fluid restriction, whereas the treatment of cerebral salt wasting is sodium supplementation. We tried both when he developed significant hyponatremia and had a seizure when his serum sodium was 121 mEq/L. He was treated with 3% normal saline in an attempt to correct his serum sodium. It was initially difficult to control so we considered treatment with a vasopressin II receptor antagonist, thinking there was a component of SIADH contributing to his hyponatremia. Ultimately, his hyponatremia stabilized and he tolerated his first round of carboplatin without clinically significant worsening of the hyponatremia.

**Dr. Pillay Smiley:** At the moment, I’m treating him solely with carboplatin. I withheld the vincristine on the assumption that it might aggravate the SIADH. He’s tolerating the treatment well.

**Dr. Listernick:** Thank you, everyone.

---

**Key Learning Points**

1. Enteral feeding promotes intestinal healing and is strongly preferred over total parenteral nutrition unless the former cannot be performed effectively or safely.
2. The child with classic diencephalic syndrome has a hypothalamic tumor and develops severe emaciation despite normal caloric intake and normal linear growth. Classically, these children eat normally, or even voraciously, but lose weight. In addition, they are often described as “happy” or “hyperalert.”
3. Children who have familial macrocephaly act normally, are developmentally appropriate, and have flat fontanels.
4. The overall survival for children with low-grade gliomas is excellent. With therapy, children live with these tumors much like they do with other chronic diseases, such as diabetes or asthma, with excellent long-term survival.