A 7-month-old Boy with Failure to Thrive

Robert Listernick, MD

This 7-month-old boy was evaluated for failure to gain weight. He was the 7-lb., 7-oz. product of a full-term pregnancy to a 31-year-old gravida 2 para 2 woman. It was a precipitous vaginal delivery, but there were no perinatal problems. His mother initially nursed him every 3 hours for 20 minutes on each breast. Recently, he had been feeding once during the night. He had three normal bowel movements each day without diarrhea or vomiting. If his mother pumped, she expressed a total of 4 oz. from the combination of the two breasts. Although his parents have tried to give him solid foods, he will not eat from a spoon. He drinks pumped breast milk from a bottle, although he prefers nursing. When he drinks from a bottle, he can take 3 oz. in about 30 minutes. There is no history of choking, sputtering, or tachypnea with feeds.

His past history is remarkable for a skin rash that started at 4 months. The rash was described as pruritic, red, and scaly over his entire body. He was treated with Eucerin without effect and was switched to EpiCeram. He has had no significant infections, other than one episode of otitis media. Development is normal. The family history is unremarkable.

On physical exam, he was a thin, uncomfortable boy who was constantly scratching. Weight, length, and head circumference were all less than the 5th percentile; they had all been in the 25th percentile at birth. He had diffuse erythroderma involving the skin folds. There were patches of flaky dermatitis on his extremities and scalp. He had sparse scalp hair with normal eyebrows. Lungs were clear. S1 and S2 were normal without murmurs. Abdomen was soft. Liver was palpable 3 cm below the right costal margin without splenomegaly.

Neurologic exam was normal save for mildly decreased truncal tone. The remainder of the physical examination was unremarkable.

Robert Listernick, MD, moderator: One of the first things to decide is whether this child’s poor weight gain is the result of inadequate breastfeeding. How can we go about doing that?

Sandra Sanguino, MD, general academic pediatrician: There’s a great deal of information that needs to be gleaned. Does the mother feel engorged breasts? Does she feel a let-down reflex? Does she hear the baby sucking and swallowing? If she pumps, how much milk gets expressed at feeding time? This can be deceptive because often a woman won’t express as much milk while pumping as she would deliver to a nursing infant. Sometimes you can get a sense as to the adequacy of nursing by offering the infant a bottle after a presumably successful feeding; if he drinks 4 oz. readily, then he probably didn’t get much during the nursing.

Dr. Listernick: What’s your gestalt here?

Dr. Sanguino: My sense is that the mother is producing enough breast milk; 4 oz. of pumped breast milk is not a large amount but...
would probably be sufficient if the baby was normal. At a minimum, he won’t eat from a spoon, which perhaps indicates a degree of oral motor dysfunction. In addition, drinking 3 oz. in 30 minutes is abnormally slow. Finally, he appears to have hepatomegaly, which suggests a more significant problem than a feeding disorder.

Dr. Listernick: When I first met this child, the combination of the poor weight gain and rash brought to mind the possibility of immunodeficiency.

Sarah Chamlin, MD, pediatric dermatologist: He had a not particularly severe generalized dermatitis. Basically, he had erythroderma with fine white scales. Important clues are that his diaper area is spared and that his skin was normal at birth.

Dr. Listernick: Can you easily decide that the rash is not simply severe atopic dermatitis?

Dr. Chamlin: I would perform a thorough history and physical exam; if there weren’t any red flags, such as a history of recurrent infections or hepatosplenomegaly, I might treat the child as if he has atopic dermatitis and see if he improves and gains weight.

Dr. Listernick: What rashes are associated with immunodeficiency syndromes?

Dr. Chamlin: Omenn syndrome is characterized by exfoliative erythroderma at birth or shortly thereafter. It is an autosomal, recessive form of severe combined immunodeficiency characterized by rash, diffuse alopecia, recurrent infections, lymphadenopathy, and hepatosplenomegaly. Laboratory features may include leukocytosis with eosinophilia, increased T cells, decreased B cells, and hypogammaglobulinemia. Graft versus host reaction in infants with T cell immunodeficiency syndromes may have similar erythroderma. Netherton syndrome has a classic triad of generalized exfoliative dermatitis, sparse hair with abnormal hair shafts (trichorrhexis invaginata), and atopic skin disease. The immunologic abnormalities in Netherton’s syndrome are variable and generally not severe.

Dr. Listernick: What was your “dermatologic gestalt”?

Dr. Chamlin: We examined the eyebrows, which are the best place to find trichorrhexis invaginata; they were normal. He had mild erythroderma and alopecia; I initially thought he might have Netherton syndrome or another immunodeficiency syndrome.

Dr. Listernick: What about the possibility of food allergies leading to severe atopic dermatitis and failure to thrive? The pediatrician suspected this.

Ramsey Fuleihan, MD, pediatric immunologist: In a minority of cases, severe atopic dermatitis in infancy might be the result of food allergy. Failure to thrive would be unusual unless he was receiving a significantly hypocaloric diet.

Dr. Chamlin: During the first year of life, I will often aggressively treat the atopic dermatitis. If it doesn’t respond to therapy, I’ll consider the possibility of food allergy.

Dr. Fuleihan: That’s a reasonable approach if the skin disease is getting better and the baby is gaining weight. This child more likely has a systemic disease, given the failure to thrive. Occasionally, I’ll perform a series of RAST IgE antibodies to a variety of food allergens. The higher the level, the more likely it’s a true food allergy. Ultimately, the sensitivity and specificity are not perfect, and you need to resort to eliminating individual foods to see if the eczema improves.

Dr. Listernick: What is EpiCeram?

Dr. Chamlin: Ceramide is a fatty acid found in normal skin that’s decreased in children with atopic dermatitis. EpiCeram is an emollient that may help replace the missing fatty acid. It’s touted as being as good as low- to mid-potency topical corticosteroid in treating atopic dermatitis.

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Maria Greene, MD, pediatric gastroenterologist: Another diagnosis to consider in a 7-month-old with severe eczema, failure to thrive, and feeding difficulties
Robert Liem, MD, pediatric hematologist: If his only problem were neutropenia, he could certainly have autoimmune neutropenia. However, we really need to consider the neutropenia in the context of significant failure to thrive. Various nutritional deficiencies can lead to neutropenia, including vitamin B12 and folate deficiency, even in the absence of a macrocytic anemia. However, one diagnosis leaps to the forefront — Shwachman-Diamond syndrome (SDS). He had genetic testing, which confirmed this diagnosis.

Dr. Listernick: Let’s talk about SDS.

Dr. Greene: SDS is an autosomal, recessive, multisystem disease whose primary manifestations include exocrine pancreatic insufficiency, bone marrow failure, skeletal abnormalities, immunologic abnormalities, and a predisposition to the development of myelodysplasia and malignancy.

Dr. Listernick: How can you determine pancreatic insufficiency in suspected SDS?

Dr. Greene: Whether steatorrhea is present or not, the best initial test is measurement of fecal elastase. A value less than 15 mcg/g of stool is very specific for exocrine pancreatic insufficiency. However, the gold standard for the diagnosis of pancreatic insufficiency remains the 72-hour stool collection done together with a food record for calculation of the coefficient of fat absorption. A more direct (but more invasive) method to diagnose pancreatic insufficiency is quantitative pancreatic stimulation test, which can be done during endoscopy. The finding of low fat-soluble vitamin levels also supports the diagnosis of pancreatic insufficiency. Ultrason sound or computed tomography (CT) in patients with SDS will show pancreatic lipomatosis. Of note, pancreatic function often improves with age in SDS.

Dr. Listernick: What are the immunologic abnormalities?

Dr. Fuleihan: Neutropenia and neutrophil chemotaxis defects predispose these patients to recurrent otitis media, sinusitis, and invasive bacterial infections. There are variable degrees of hypogammaglobulinemia and deficits in cell-mediated immunity.

Dr. Listernick: What are the hematologic abnormalities?

Dr. Liem: Approximately one-third of patients have chronic neutropenia, and the remainder has intermittent neutropenia. The presence of anemia and thrombocytopenia is highly variable. Patients with SDS are at risk for the development of aplastic anemia, myelodysplasia, and a variety of hematologic malignancies, most commonly acute myelogenous leukemia. We should also mention that a variety of skeletal abnormalities have been reported, most commonly metaphyseal dysplasia. We always evaluate children for SDS when they have bone marrow failure syndrome without a clear etiology.

It’s also worth mentioning the possibility of Pearson syndrome, a mitochondrial disorder characterized by exocrine pancreatic insufficiency, sideroblastic anemia, renal Fanconi syndrome, and insulin-dependent diabetes.

Dr. Listernick: What about his skin disease?
Dr. Fuleihan: Eczema has been reported with SDS. In addition, he had specific IgE against cow’s milk protein, which might have been a contributing factor.

Dr. Listerick: What are the molecular genetics of SDS?

Dr. Liem: About 90% of individuals with SDS have mutations in the SBDS gene. Although its function is not known, it’s thought to be involved in the regulation of ribosomal biogenesis. Unfortunately, there’s no clear genotype-phenotype correlation.

Dr. Listernick: Let’s talk treatment.

Dr. Greene: These patients require meticulous attention to their nutritional status. To optimize growth, we give them high-caloric density formula or fortified breast milk, pancreatic enzyme replacement, and fat-soluble vitamin supplementation. As far as his serum transaminase elevation is concerned, this is likely a result of malnutrition and fatty infiltration of the liver associated with SDS. Elevated serum transaminases are seen frequently in SDS, regress with age, and appear to have no long-term sequelae.

Dr. Liem: We follow these children’s blood counts carefully. At times, if they are having recurrent infections, we administer granulocyte colony stimulating factor in an attempt to increase the neutrophil count. We’re also monitoring for the development of incipient bone marrow failure.

Dr. Listernick: What’s the role of bone marrow transplantation (BMT)?

Reggie Duerst, MD, pediatric oncologist: BMT is appropriate once these patients display significant symptomatic bone marrow dysfunction. Of course, if the transplant succeeds, it still doesn’t correct their pancreatic or skeletal abnormalities. There’s a suggestion in the literature that these patients have poorer outcomes than other BMT patients, which is perhaps related to poor bone marrow stroma or increased sensitivity to chemotherapy and radiation because of the underlying genetic defect.

Dr. Listernick: Thank you, everybody.

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### Key Learning Points

1. Omenn syndrome is an autosomal, recessive form of severe combined immunodeficiency syndrome characterized by exfoliative erythroderma, alopecia, hepatosplenomegaly, and recurrent infections.

2. Acrodermatitis enteropathica is a zinc deficiency syndrome that produces an erosive rash around the mouth and diaper area.

3. The presence of pancreatic insufficiency can usually be determined by either very low fecal elastase, or decreased coefficient of fat absorption obtained from a 72-hour fecal and dietary fat collection.

4. Shwachman-Diamond syndrome (SDS) is an autosomal recessive multisystem disease whose primary manifestations include exocrine pancreatic insufficiency, bone marrow failure, skeletal abnormalities, immunologic abnormalities, and a predisposition to the development of myelodyplasia and malignancy.