2 Diaper Rash and Feeding Difficulty in a 5-week-old Boy

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PRESENTATION

A 5-week-old boy presents to his pediatrician's office with a 10-day history of diaper rash and difficulty feeding. His parents describe the rash as red, firm, and spreading despite consistent use of barrier creams and antibiotic ointment. The rash involved only the buttocks at onset, but it has spread to the thighs and lower back. He is exclusively breastfed and often falls asleep at the breast or begins to arch his back, grimace, and pull away mid-feed. Trials with ranitidine and formula supplementation after breastfeeding have been attempted without improvement. He continues to void and stool appropriately. There is no history of fever, excessive spitting up, increased work of breathing or diaphoresis with feeds, or other systemic symptoms. His perinatal history is significant for term gestation and terminal meconium without aspiration. Apgar scores were 2 at 1 minute and 8 at 5 minutes. He was admitted to the special care nursery for hypoglycemia management. The mother took levothyroxine during pregnancy for hypothyroidism.

On examination, the patient is well appearing. His vital signs are normal for his age. Weight is 3,420 g (<5th percentile). Birth weight was 3,660 g (73rd percentile). Length is 21.65 in (55 cm) (38th percentile), and head circumference is 14.57 in (37 cm) (27th percentile). Firm, reddish, subcutaneous nodules are present over the buttocks and posterior thighs, with extension into the lower back bilaterally. Nodules are warm to the touch and without fluctuance, tenderness, or drainage. All other physical examination findings are normal.

Complete blood cell count, liver enzyme levels including alkaline phosphatase, and results of urinalysis are normal. A renal function panel reveals a total calcium level of 20.4 mg/dL (5.10 mmol/L). Ionized calcium level is greater than 7.90 mg/dL (>1.98 mmol/L) (reference range, 4.60–5.28 mg/dL [1.15–1.32 mmol/L]).

The Case Discussion and Suggested Readings appear with the online version of this article at http://pedsinreview.aappublications.org/content/38/3/140.

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DISCUSSION

Further evaluation was performed to determine the etiology of our patient's severe hypercalcemia. Parathyroid hormone level was less than 6 pg/mL (<6 ng/L) (reference range, 15–65 pg/mL [15–65 ng/L]). 25-Hydroxyvitamin D level was 22 ng/mL (55 nmol/L) (reference range, 20-50 ng/mL [50–125 nmol/L]), and 1,25 dihydroxyvitamin D_3 level was 96 pg/mL (250 pmol/L) (reference range, 24–86 pg/mL [62–224 pmol/L]). Random urine calcium level was 22.5 mg/dL (5.63 mmol/L), with urine creatinine level of 13.4 mg/dL (1,185 μmol/L). Thyroid study results and morning cortisol level were normal. Renal ultrasound revealed bilateral medullary nephrocalcinosis. Electrocardiogram revealed normal sinus rhythm, with QTc of 360 to 410 milliseconds without ST segment elevation. Echocardiographic findings were normal.

Hypercalcemia has many potential causes; however, our patient also had suppression of his parathyroid hormone level, with an elevated 1,25 dihydroxyvitamin D_3 level, a normal 25-hydroxyvitamin D level, and a normal alkaline phosphatase level, suggesting ectopic production of calcium (Fig).

The Condition

Subcutaneous fat necrosis (SCFN) of the newborn is an uncommon and self-limiting panniculitis often presenting by 2 to 4 weeks of life in term and postterm infants. It presents with red to purple nodules on sites of pressure or trauma, such as the buttocks, back, thighs, cheeks, and arms. The condition generally occurs in the setting of a complicated perinatal course, such as birth asphyxia, meconium aspiration, birth trauma, maternal preeclampsia, gestational diabetes, or therapeutic cooling (for hypoxic ischemic encephalopathy or cardiac interventions). Patients are typically healthy appearing but may be lethargic or irritable or may fail to thrive, particularly if their course is complicated by metabolic abnormalities. Our patient presented with failure to thrive, likely as a manifestation of his severe hypercalcemia. Hypercalcemia is an uncommon but serious complication of SCFN with an unclear etiology. Many pathways for ectopic calcium production in the setting of SCFN have been suggested, including 1) inside necrotizing, inflammatory granulomas, macrophages are activated and secrete high levels of 1,25 dihydroxyvitamin D_3, which results in increased calcium resorption; 2) increased serum and urinary prostaglandin E levels, causing an increase in bone resorption; and 3) direct release of calcium from necrotic fat cells.

Severe hypercalcemia may have a nonspecific presentation, especially in infants, potentially leading to a delayed diagnosis. Delayed diagnosis may increase the risk of serious complications, such as shortening of the ST segment

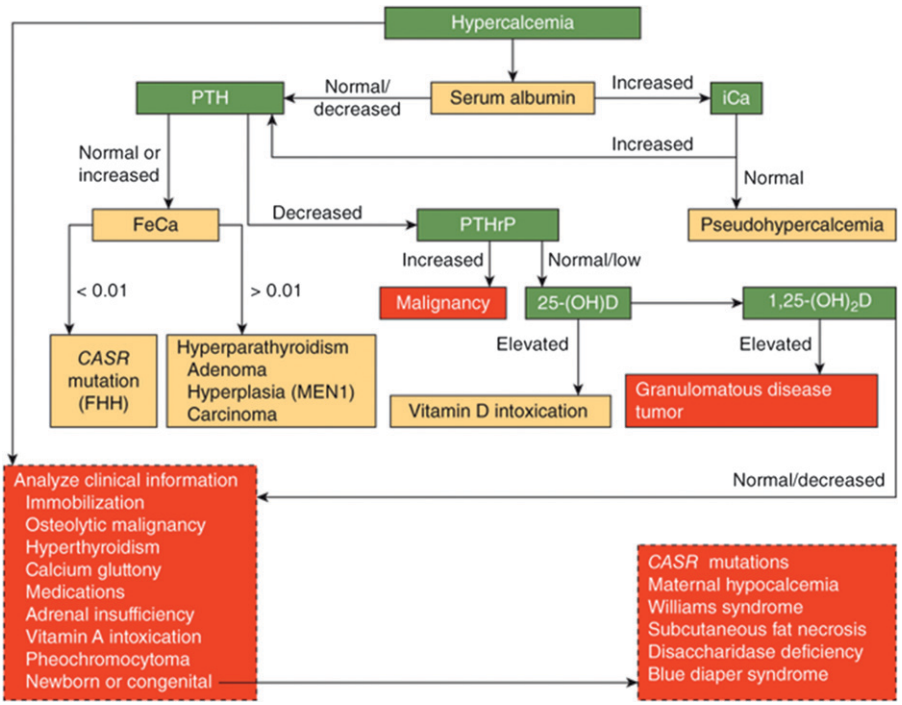

Figure. Algorithm for Interpreting Laboratory Evaluation for Hypercalcemia, (Reprinted with permission from Kelly A, Levine MA. Disorders of bone and mineral metabolism. In: Kappy MS, Allen DB, Geffner ME, eds. *Pediatric Practice: Endocrinology*. 2nd ed. New York, NY: McGraw-Hill; 2013. http://accesspediatrics.mhmedical.com/content.aspx?bookid=1082&Sectionid=61463542. Accessed June 9, 2015.)
FeCa=fractional excretion of calcium, FHH=familial hypocalciuric hypercalcemia, iCa=ionized calcium, MEN1=multiple endocrine neoplasia type 1, PTH=parathyroid hormone, PTHrP=parathyroid hormone-related protein, 1,25-$(OH)_2$D=1,25 dihydroxyvitamin D, 25-(OH)D=25-hydroxyvitamin D.

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leading to heart block, severe dehydration from resultant renal vasopressin resistance, seizures, lethargy, and renal complications (eg, nephrocalcinosis and nephrolithiasis). Hypercalcemia is often preceded by development of the classic rash but may persist for longer than 6 months.

Other complications associated with SCFN include hypoglycemia, anemia, thrombocytopenia, hypertriglyceridemia, and secondary infection.

Diagnosis

The diagnosis of SCFN can be made by observation of classic physical examination findings. Screening for hypercalcemia is strongly recommended because some cases of severe hypercalcemia may be asymptomatic. The differential diagnosis for the rash includes bacterial cellulitis, sclerema neonatorum, neurofibromatosis, erythema nodosum, and other panniculopathies.

Other causes of hypercalcemia, including hyperparathyroidism, hypervitaminosis D, hypophosphatasia, malignancy, multiple endocrine neoplasia, idiopathic infant hypercalcemia, and Williams syndrome, should be excluded.

Treatment

The skin lesions of SCFN self-resolve without substantial scarring or skin atrophy. Treatment is focused on management of hypercalcemia. Our patient received intravenous fluid hyperhydration, calciuric diuretics (furosemide 1 mg/kg twice daily), prednisolone 2 mg/kg daily to impede macrophage activation and promote calciuria, low calcium formula supplementation, and phosphorus supplementation. Bisphosphonates were reserved should his hypercalcemia become refractory and were not used. Because his serum calcium level normalized during the next several days, furosemide was discontinued. Prednisolone was weaned slowly during the next week. He is demonstrating adequate weight gain for his age, and gastroesophageal reflux symptoms have resolved. He maintains outpatient follow-up with an endocrinologist to monitor calcium and phosphorus levels, which have remained normal, and will continue follow-up for at least 6 months. He follows up with a nephrologist as an outpatient to monitor unresolved nephrocalcinosis without impairment of renal function.

Lessons for the Clinician

- When diaper rash does not respond and even gets worse with proper therapy, alternative diagnoses should be considered, especially when associated with feeding difficulty, irritability, and failure to gain weight.
- Subcutaneous fat necrosis (SCFN) is an uncommon condition associated with a complicated perinatal course.
- Hypercalcemia is an uncommon but serious complication of SCFN in newborns, and, therefore, neonates with SCFN should be monitored carefully for hypercalcemia.

Suggested Readings

Gomes C, Lobo L, Azevedo AS, Simão C. Nephrocalcinosis and subcutaneous fat necrosis [in Portuguese]. *Acta Med Port*. 2015;28(1):119–122

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Samedi VM, Yusuf K, Yee W, Obaid H, Al Awad EH. Neonatal hypercalcemia secondary to subcutaneous fat necrosis successfully treated with pamidronate: a case series and literature review. *AJP Rep*. 2014;4(2):e93–e96

Shumer DE, Thaker V, Taylor GA, Wassner AJ. Severe hypercalcaemia due to subcutaneous fat necrosis: presentation, management and complications. *Arch Dis Child Fetal Neonatal Ed*. 2014;99(5):F419–F421

Parent Resources from the AAP at HealthyChildren.org

- When Diaper Rash Strikes: https://www.healthychildren.org/English/ages-stages/baby/diapers-clothing/Pages/When-Diaper-Rash-Strikes.aspx.
- Infant Allergies and Food Sensitivities: https://www.healthychildren.org/English/ages-stages/baby/breastfeeding/Pages/Infant-Allergies-and-Food-Sensitivities.aspx.

For a comprehensive library of AAP parent handouts, please go to the *Pediatric Patient Education* site at: http://patiented.aap.org.

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Case 2: Diaper Rash and Feeding Difficulty in a 5-week-old Boy

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