An 8-Year-Old Boy Presenting with Eruptive, Pruritic Rash and Cough

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An 8-year-old overweight boy with a history of hydronephrosis, asthma, hearing loss, and speech and language delay presented to his primary care physician (PCP) with complaints of cough and a new pruritic rash that started in his groin and buttock and spread to his lower limbs. Physical examination revealed scattered, generalized, erythematous papules in various stages with vesicular eruptions. The family denied fever, his immunizations were up to date, and there were no known sick contacts. Home medications included albuterol as needed and diphenhydramine. He is allergic to ibuprofen. There are two pets in the home (a cat and a dog). The patient was diagnosed with varicella based on physical examination findings and sent home.

The patient returned to their PCP’s office 12 days later with concerns for persistent rash without crusting or drainage. No new environmental factors such as lotions, soaps, or detergents had been used, and the rash had not spread to other members of the household. Physical examination findings at that visit revealed generalized, discrete pink papules with a yellowish white center and without induration. The rash was not painful but itching was reported. Sparse lesions were noted on the soft palate and buccal mucosa, but otherwise were limited to the limbs, trunk, groin, and concentrated near the buttocks. The patient was well-appearing and afebrile.

Fasting laboratory analysis obtained by the PCP on the patient’s second visit was significant for glucose of 308 mg/dL, CO₂ of 17 mmol/L, hematocrit of 34.5%, total cholesterol of 487 mg/dL, triglycerides >575 mg/dL, and high-density lipoprotein (HDL) of 18 mg/dL (analysis was not able to calculate low-density lipoprotein [LDL]). The family was advised to go to Arkansas Children’s Hospital in light of elevated glucose and concerns for persistent rash.

On arrival at the emergency department, the patient’s family gave additional history of polyuria, polydipsia, and nocturia for 3 weeks, as well as intermittent headache for 1 week. His rash was noted to be consistent with eruptive xanthoma. Laboratory tests revealed a hemoglobin A1c of 11.9% and venous glucose of 285 mg/dL, but the patient was not in a state of diabetic ketoacidosis.

The boy was admitted to the hospital for initiation of insulin, diabetes education, and evaluation and management of hypercholesterolemia. He was started on a basal and bolus insulin regimen and his laboratory results were closely monitored.

HOSPITAL COURSE

Physical examination by the Endocrine service revealed an overweight (body mass index of 26.3 kg/m²), well-appearing boy with multiple pink-to-yellow papules concentrated on the groin and buttocks with faint overlying excoriations (Figure 1). Acanthosis was noted on the neck and axilla, but otherwise physical examination findings were negative. There was no significant abdominal tenderness or hepatomegaly.

For diagnosis, see page e315

Editor’s note: Each month, this department features a discussion of an unusual diagnosis. A description and images are presented, followed by the diagnosis and an explanation of how the diagnosis was determined. As always, your comments are welcome via email at pedann@Healio.com.
Due to hyponatremia (serum Na of 130 mmol/L [normal range for age being 138-145 mmol/L]) on routine laboratory analysis and persistent rash, a nonfasting triglyceride level was drawn the day after admission, showing a value of 11,183 mg/dL. Pancreatitis was ruled out with normal serum amylase and lipase. An electrocardiogram revealed no cardiac events. After unsatisfactory decline in triglyceride levels with improving glucose control on subcutaneous insulin, an intravenous insulin drip was initiated at 0.1 u/kg per hour with titrating dextrose-containing fluids to maintain glucose levels in the range of 150 to 200 mg/dL. The patient was allowed to eat a low-fat, carbohydrate-restricted diet, and rapid-acting insulin was given subcutaneously to cover oral carbohydrate intake. He was also continued on his basal subcutaneous insulin, which was ultimately increased to 0.65 units/kg per day while on the insulin drip. Glucose levels remained elevated (mid-to-upper 200-mg/dL range) despite the large doses of insulin, so glucose-containing fluids were decreased accordingly. Fenofibrate (48 mg by mouth once a day) was added to the regimen on day 2 of the insulin drip. A more thorough family history was obtained, revealing numerous relatives being treated for hypercholesterolemia.

The patient remained on the insulin drip for approximately 72 hours, resulting in a decreased triglyceride level (from 8,752 mg/dL at initiation to 2,165 mg/dL the morning of discontinuation). There was a further decrease in fasting level (1,458 mg/dL) the morning of discharge. Fenofibrate, aggressive glucose control, and a restricted diet were continued for therapy.

The patient was seen for fasting laboratory evaluation by his PCP 3 weeks after discharge and dramatic improvements in laboratory values were noted. Total cholesterol had decreased to 156 mg/dL, triglycerides to 128 mg/dL, and LDL to 26 mg/dL, and HDL had increased to 40 mg/dL. He was seen in the Endocrine and Diabetes clinic for follow-up 5 weeks after discharge from the hospital, and an improved hemoglobin A1c of 6.6% was obtained. GAD65 and islet cell antigen 512 antibodies were negative, suggesting type 2 diabetes. The xanthomas had completely cleared. He was continued on his insulin regimen of basal and bolus therapy, a carbohydrate-restricted diet, and fenofibrate for hypercholesterolemia. Metformin was added to his medication regimen. Genetic testing was obtained and sent to a consulting hospital for evaluation of lipoprotein lipase (LPL) deficiency. Typing and results are currently pending.

Diagnosis:
Familial Hypertriglyceridemia

We considered two separate conditions for this patient. The first was LPL deficiency, which is a rare, autosomal recessive disorder resulting in the significantly reduced clearance of triglyceride from the chylomicron. The other was familial hypertriglyceridemia, which is more common and autosomal dominant. Both conditions are associated with mild elevations in total cholesterol. Further, familial hypertriglyceridemia may be accompanied, and certainly exacerbated, by insulin resistance, obesity, and elevated glucose levels, making this a more likely diagnosis for our patient. A review of the literature reveals a lack of information pertaining to the evaluation and treatment of these disorders in the pediatric population. Immediate treatment of hypercholesterolemia and hypertriglyceridemia is sometimes necessary, as these conditions place the patient at risk of cardiovascular disease.
increased risk for premature coronary disease, acute pancreatitis, and cardiovascular events. This is even more vital in the patient with diabetes.

**DISCUSSION**

The prevalence of dyslipidemia in the pediatric population varies greatly, but all cases require immediate attention. Because dyslipidemia is relatively common in patients with diabetes, the current guidelines suggest screening beginning at the age of 10 years in all patients with diabetes and at the age of 2 years if there is a family history of hypercholesterolemia, myocardial infarction before the age of 55 years, or if the family history is unknown. General screening in the pediatric population may be considered earlier if there are findings suggestive of an inherited dyslipidemia, such as xanthomas or changes to corneal borders (arcus cornea). There are diagnostic criteria that help classify dyslipidemia and suggest pathways of treatment in the pediatric patient, but these have been somewhat controversial as long-term efficacy has been questioned. However, a more thorough and aggressive approach should be adopted in those children with metabolic syndrome, type 2 diabetes, or a family history of dyslipidemia or early heart disease. Other causes of hypercholesterolemia should be ruled out. Genetic testing is not usually necessary but can help confirm if the diagnosis is not clear.

For pediatric patients with hypertriglyceridemia in the nonurgent setting, diet modification and exercise are first-line therapy. When patients fail to meet goals with lifestyle interventions as demonstrated by repeat fasting lipid profiles, or in critically elevated triglyceride concentrations as in this patient, statins or fibrates can be used cautiously, although referral to a lipid specialist is suggested. As discussed, immediate treatment of significant elevations is required to prevent complications such as acute pancreatitis. Options for treatment of substantial triglyceride elevations in the hospital setting include insulin drip therapy, heparin drip, and apheresis. As noted above, our patient had acceptable results with initiation of insulin drip therapy to lower triglycerides. Insulin works by enhancing LPL activity and also acts as a powerful triglyceride-lowering agent by facilitating production of enzymes necessary to transport triglycerides out of the plasma. In the patient with diabetes with severely elevated triglyceride levels, the benefits of insulin are 2-fold: a reduction in glucose levels and a reduction in triglycerides.

**CONCLUSION**

Signs suggestive of high cholesterol should be investigated promptly to avoid immediate complications. We believe this case is unique because the patient was one of the youngest documented cases in our review of the literature. He responded well to insulin infusion therapy, but required 0.65 units/kg per day of basal insulin for optimal control in addition to rapid-acting coverage at discontinuation of insulin drip. Little is known about the treatment of children with hypertriglyceridemia in the face of severe insulin resistance; however, we have found this approach to be quite effective and safe. The results of the genetic screen are currently pending and the patient continues to do well.

**REFERENCES**