Think Metabolic Error in Cases of Near-Miss SIDS

BY NANCY WALSH
New York Bureau

NEW YORK — If a child presents in the emergency department with near-miss sudden infant death syndrome or with a Reye's syndrome–like illness, one should consider the possibility of an inborn error of metabolism, Dr. Joan Shook said at a meeting sponsored by the American College of Emergency Physicians.

In particular, think of medium-chain acyl-coenzyme A dehydrogenase (MCAD) deficiency, which is the most common of the inherited errors of fatty acid metabolism. If the condition goes undiagnosed, it carries a mortality of 25%, she said. MCAD is a mitochondrial enzyme essential for the β-oxidation of medium-chain fatty acids, a process that is required for energy production during fasting.

The pattern of inheritance seen with MCAD deficiency is autosomal recessive, so it's even worth thinking about in cases of full SIDS, because of the clear implications for future children in that family, she said.

The acute illness typically is characterized by vomiting and lethargy in a child 3-15 months of age, said Dr. Shook, professor of pediatrics and head of the section of emergency medicine, Baylor College of Medicine, Houston.

Laboratory tests, including a metabolic work-up, should be ordered promptly. Findings may include hypoketotic hypoglycemia, hyperammonemia, and an increased anion gap. Liver function tests are likely to be elevated.

Triggers for the acute Reye's-like crisis can include a febrile illness or a metabolic stressor such as fasting, surgery, and alcohol consumption. The acute illness can evolve into seizures, coma, cardiac arrest, and death.

Therapeutic measures during the acute episode include prompt rehydration and correction of hypoglycemia, and should address any identifiable stressors. During the acute episode, it's important to obtain urine and plasma, which can be frozen for further investigation, Dr. Shook said.

If the patient's clinical condition deteriorates and death appears imminent, then one should also consider obtaining skin specimens from the undersurface of the arm and the anterior surface of the thigh for later fibroblast culturing and genetic analysis, she said, noting that consent from the family is needed for this.

It is now recognized that many inborn errors of metabolism were likely misdiagnosed as Reye's syndrome before they were identified during the 1980s, and the incidence of Reye's syndrome has markedly diminished since their recognition. "A review of charts in children with Reye's would likely show that 10%-13% were, in fact, MCAD deficiency."

Neonatal screening for MCAD deficiency is not mandatory in all states, but this may change with further recognition that the disease's morbidity and mortality can be lowered by long-term measures, such as avoidance of catabolism and aggressive resuscitation during acute crises.

Information about screening for MCAD and other inborn metabolic errors can be found at http://genes-r-us.uthscsa.edu. ■

Gout and Metabolic Syndrome Link Reinforced by New Data

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The prevalence of metabolic syndrome may be nearly three times higher among individuals with gout, compared with unaffected individuals, judging from results of a recent data analysis.

Other researchers have suggested a link between gout and metabolic syndrome, but the degree of the overlap between the two conditions has been unclear, said Dr. Hyon K. Choi of the Arthritis Research Centre of Canada and his associates.

A total of 8,807 individuals aged 20 years or older participated in the third National Health and Nutrition Examination Survey (NHANES-III) from 1988 to 1994. Of those, 233 had gout, according to self-report (mean age of 58 years). All of the subjects were assessed for metabolic syndrome; the condition was deemed to be present if an individual had at least three of the following five metabolic abnormalities: abdominal obesity, hypertriglyceridemia, low HDL cholesterol, high blood pressure, and high fasting glucose.

Prevalence of metabolic syndrome was about 63% in the 233 individuals with gout and 25% in the 8,574 individuals without gout. The prevalence rates of each of the five the metabolic abnormalities associated with metabolic syndrome were considerably higher in adults with gout than they were in those without gout. For one, the prevalence of high blood pressure in individuals with gout (69%) was more than double the prevalence of those without gout. The association between metabolic abnormalities and gout was evident across subgroups of major associated gout risk factors including body mass index, hypertension, and diabetes, the investigators reported (Arthritis Rheum. 2007;57:109-15).

The interplay between hyperuricemia and high insulin levels caused by insulin resistance may explain the connection between metabolic syndrome and gout. The high insulin levels associated with insulin resistance are known to cause hyperuricemia, which enhances crystal deposition, thereby leading to symptomatic gout. Prevalence of hyperuricemia was 49% in individuals with gout and 18% in those without, according to the authors.

Prevalence of metabolic syndrome increased from 27% in participants with gout aged 20-39 years to 72% in participants aged 40-59. Prevalence of metabolic syndrome in individuals without gout increased from only 12% in adults aged 20-39 years to 31% in those aged 40-59 years, indicating that adults with gout are at greater risk of developing metabolic syndrome. The data also suggest that this risk is greater in older adults with gout than in younger adults with gout. Prevalence for metabolic syndrome in adults over age 60 years with gout (71%) was more substantial than in those without gout (49%).

Individuals with gout also may be at higher risk for developing atherosclerotic cardiovascular disease and type 2 diabetes, noted the researchers. The two diseases are known complications associated with metabolic syndrome. The study was funded by TAP Pharmaceutical Products Inc. and Savient Pharmaceuticals Inc. Dr. Choi reported receiving consulting fees from both companies. ■

Male Hypogonadism May Be More Prevalent Than Previously Thought

SEATTLE — Low-testosterone problems are not as rare as one might think because they're associated with two common conditions: erectile dysfunction and metabolic syndrome, Dr. Richard F. Spark said at the annual meeting of the American Association of Clinical Endocrinologists.

"Some new developments indicate that there are a lot more patients with hypogonadism than we have been aware of," said Dr. Spark, an endocrinologist at Beth Israel Deaconess Medical Center, Boston.

One of the first reports that erectile dysfunction could be associated with low testosterone was his own, published in 1980. He measured serum testosterone in 105 consecutive patients who were seen for what was then called impotence and found that 20 of them had low serum testosterone, and when they were treated for that, their erectile dysfunction went away (JAMA 1980;243:750-5).

In 2000, a meta-analysis of studies of testosterone replacement suggested that 57% of patients with erectile dysfunction treated with testosterone had resolution of their problem, including 64% of those with primary hypogonadism (J. Urol. 2000;164:371-5).

Testosterone has gotten a bad rap because of all of the press about athletes who abuse anabolic steroids, and because the controversies regarding estrogen/progesterone therapy for women have made people wary of hormone replacement, Dr. Spark said. "Until recently, the urologists had primarily insisted that there was no man [complaining of ED] in their practice who had low testosterone, and they all went on to have penile implants."

Low testosterone has also been associated with type 2 diabetes and metabolic syndrome, Dr. Spark said. In a study of 103 men with type 2 diabetes, 33% had low testosterone levels, and low testosterone was found in all the age groups (J. Clin. Endocrinol. Metab. 2004;89:5462-8).

Individuals with metabolic syndrome have a 2.6 times higher risk of having low testosterone than does the general male population, and low testosterone has been shown to predict onset of type 2 diabetes. "One should check testosterone in metabolic syndrome patients and look for metabolic syndrome in low-testosterone patients," he said.

—Timothy F. Kirn

Gemfibrozil's Benefit Seen in Kids With Severe Metabolic Syndrome

NEW ORLEANS — Gemfibrozil produces multiple benefits in children with severe metabolic syndrome, including a sharp reduction in triglyceride levels, increased HDL cholesterol levels, and a decrease in elevated liver enzymes, Courtney M. Smalley reported at the annual meeting of the American College of Cardiology.

The gemfibrozil-induced decrease in the elevated levels of alanine transaminase, aspartate transaminase, or both often present in children with severe metabolic syndrome suggests the fibrate therapy may reverse nonalcoholic steatohepatitis. This possibility has not been confirmed by liver biopsy, said Ms. Smalley, a medical student at the University of Arizona, Tucson.

She reported on 40 children with severe metabolic syndrome, mean age 13 years, who were placed on 600 mg gemfibrozil twice daily. After a mean 8.3 months on the fibrate, their triglyceride levels were down by 54% from a baseline of 388 mg/dL, and their mean HDL climbed by 17% from 36 to 42 mg/dL. Thirty of the subjects had evidence of fatty deposition in the liver at baseline from liver biopsy, elevated liver enzymes, or both. Gemfibrozil cut alanine transaminase by 38% from a baseline of 57 IU/L and aspartate transaminase by 28% from a baseline of 39 IU/L. Waist circumference, body mass index, and percent body fat did not change significantly.

This was an off-label use of gemfibrozil, which has not been studied in children with metabolic syndrome. It was selected for the study because it is inexpensive, easy-to-use, and has been around a long time. The fibrates' lipid-modifying effects make this drug class a better choice than statins for patients with the high triglyceride/low HDL lipid profile characteristic of the metabolic syndrome, Ms. Smalley said in an interview. Two patients developed myalgia within the first week of therapy and were taken off the drug. None reported gastric upset, a major side effect in adults on gemfibrozil.

—Bruce Jancin