Drugs Make Other Autism Interventions Easier

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Grapevine, Tex. — Physicians need to be alert to a cause of autism that might not be immediately apparent in milder cases, a Colorado pediatrician warned.

Smith-Lemli-Opitz syndrome (SLOS), a disorder caused by a defect in the cholesterol metabolic pathway, should be in the differential diagnosis for children presenting with autism, said Ellen Elias, M.D., director of the special care clinic of the Children’s Hospital, Denver.

Some SLOS children with autism never see a geneticist and may be followed by a developmental pediatrician or neurologist, she said. “Often, they are not diagnosed if they are a milder case without the usual facial features.”

Yet a simple blood test can alert parents to the 25% recurrence rate as well as treatment that can alleviate some behavioral problems in this syndrome, she said.

SLOS is an autosomal recessive disorder caused by a metabolic error in the cholesterol pathway. Children with SLOS have distinctive facial features: smaller heads, upturned noses, and small chins, growth retardation; mental retardation; and multiple birth defects. In milder forms of the syndrome, children might not have the distinctive facial features and may present with autism, Dr. Elias and her associates wrote in a poster presentation at the American College of Medical Genetics.

In a study of 15 patients with confirmed SLOS followed in the clinic, the researchers found that these males had the classic autism phenotype but didn’t have the classic physical features of SLOS. Two of the boys had sisters with SLOS but without autism. Dr. Elias predicts that the syndrome is far more common than the estimated 20,000 children with the classic form. “People at the mild end of the syndrome don’t get tested or identified,” she said.

“The incidence of autism has increased dramatically over the past 10 years,” she said. Although genetic etiologies are suspected, only 10% of autism patients are identified as having a genetic diagnosis.

The simple blood test for SLOS testing for elevated serum 7-dehydrocholesterol was developed in 1994 and can be used prenatally and in children suspected of having the syndrome. It also allows diagnosis of the children who fall into the milder end of the spectrum, particularly those who lack the typical facial features or birth defects associated with the classic SLOS.

In children presenting with autism without the typical features with SLOS, she advised physicians to test for SLOS in children with milder features. Physicians should look for growth retardation, a head that is on the small side, and webbing between the second and third toe. If children aren’t diagnosed correctly, they won’t receive adequate treatment, and there is a chance of siblings being born with the syndrome, Dr. Elias said.

Consider Genetic Disorder in Some Milder Autism Cases

Children with SLOS can benefit from cholesterol treatment, which lessens some behavioral side effects of the syndrome, such as irritability and attention deficit, she said. In addition, children with SLOS should not be treated with Haldol (haloperidol) or BuSpar (buspirone), which can exacerbate the biochemical parameters of the syndrome.

If SLOS is suspected, it is important that the blood sample be sent to a special laboratory, because many hospital-based laboratories cannot distinguish between cholesterol and its precursor, 7-dehydrocholesterol, she said.

“There is a tendency to look at these children and think they are normal in appearance and simply have autism,” Dr. Elias said. “It is important not to miss a diagnosis of a child with SLOS in a child presenting with autism, so that appropriate genetic counseling can be provided to the family and [cholesterol treatment] may ameliorate problematic behavior in the child.”

Dr. Leventhal said he treats them with the same stimulants used for attention deficit in children who are not autistic. “There are no studies of stimulants in children with autism, but there is no reason to think these agents would not apply here,” he said.

No one stimulant has proved better than another, he added. The biggest problem, he said, is getting autistic children to swallow pills. He suggested that “several regimens can be overcome by breaking up Ritalin or Adderall capsules and sprinkling the medication on food.”

Dr. Leventhal recommended serotonin reuptake inhibitors (SSRIs) for control of stereotypic behaviors, such as repetitive behaviors, self-stimulatory behaviors (“stimming”), habits, and tics. He cited studies showing improvements with fluoxetine (Arch. Gen. Psychiatry 1996;53:1001-8) and fluoxetine (Neuropsychopharmacology 2005;30:582-9).

An added benefit is SSRIs can reduce aggression, he added, describing aggression and irritability as another serious problem for people with autism. “It is one that limits its access to community,” he said.

Dr. Leventhal reported that he no longer uses traditional neuroleptics because of side effects. Atypicals are coming into use, he said, but there is not much evidence in this population, except for risperidone (Risperdal).

Johnson & Johnson, parent company of risperdone maker Janssen Pharmaceutica Inc., announced in May that the Food and Drug Administration had informed the company that risperidone was “not approvable” for autism. Dr. Leventhal expressed balafment at the decision, however, citing data from studies that found risperidone to be effective (J. Am. Acad. Child Adolesc. Psychi-