CNS Defects Linked to Parvovirus B19 Infection in Pregnancy

Subtle neurobehavioral effects in normal children may be tied to mild maternal parvovirus B19 infections.

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ST. PETERSBURG, FL. — Typical primary effects of parvovirus B19 infection during pregnancy include hydrops fetalis, fetal death, and spontaneous abortion, but a recent case and a review of the literature suggest that central nervous system abnormalities are a rare but possible effect of such infection, Dr. Kenneth Lyon Jones reported at the annual meeting of the Teratology Society.

Dr. Jones, a pediatrician, described a 11-year-old boy whose mother had documented parvovirus B19 infection early in her first trimester. The child had severe brain development defects secondary to the prenatal exposure. Mental retardation was severe; he had not learned to speak and had been diagnosed with hypertonic cerebral palsy.

Diagnosis of maternal infection was made during the first trimester. An ultrasound at 20.5 weeks' gestation indicated fetal ventricular enlargement, and at birth the boy weighed 2,899 g. At day 5 he received a blood transfusion because he had severe anemia, Dr. Jones said. Dr. Jones of the University of California, San Diego.

During the newborn period, ultrasound showed severe cerebral atrophy. At age 11, his height was 122 cm (below the 3rd percentile) and his weight was 27.3 kg (10th percentile).

The child was markedly hirsute and had a frontal hair upsweep, a large hemangioma over the helix of his right ear, a large space between his upper central incisors, and had been diagnosed with hypertonic cerebral palsy.

The most likely mechanisms of action include infection of cells in the CNS and hydrops secondary to severe anemia.

The first publication involved a series of 92 consecutive singleton pregnancies with serologic evidence of parvovirus B19 infection. There were 3 therapeutic abortions, 64 fetal deaths, 10 premature births (8 of the babies subsequently died), and 15 term births (1 baby subsequently died).

Of the 73 fetal or neonatal deaths, 21 had adequate histologic evaluation of the brain, and 9 of these showed CNS abnormalities. Of the 16 surviving babies, 5 had CNS abnormalities.

One of the 14 with CNS abnormalities had trisomy 13 syndrome; no etiology was determined in the remaining cases, but the findings suggested anemia might be an important mechanism for CNS abnormalities, Dr. Jones noted.

Based on the findings of the published reports, it appears there are three patterns of abnormalities associated with maternal parvovirus B19 infection: positional limb deformities, radiographic evidence of intracranial calcifications, and dysplastic changes, including agryia, macrogyria, polymicrogyria, and dysgenesis of the corpus callosum, he said.

“CNS involvement is a rare occurrence following maternal parvovirus infection, but it clearly occurs, and when it does, it’s clearly significant,” Dr. Jones said, noting the mechanism of action that most likely includes both infection of cells in the central nervous system and hydrops secondary to severe anemia.

It is possible that subtle neurobehavioral effects in otherwise normal children result from a mild case of maternal parvovirus B19 infection, he added.

Maternal Citalopram Treatment Prompts Adverse Event Reports

Diclectin Exposure Held Harmless To Neurocognitive Development

ST. PETERSBURG, FL. — A total of 228 adverse events associated with the use of citalopram (Celexa) during pregnanncy has been reported to the Food and Drug Administration’s Adverse Event Reporting System. The drug was approved in 1999, Dr. Edward J. Newcomer Jr., Ph.D., reported at the annual meeting of the Teratology Society.

Of these reports, 120 involved adverse developmental effects, and 38 of those events occurred during the peri- or postnatal period.

A total of 31 of the 38 cases occurred in the early neonatal period during the first week of life, and 18 of these involved neonatal withdrawal symptoms, including jitteriness, restlessness, tremor, and confusion associated with citalopram exposure. One or more of these symptoms occurred throughout pregnancy.

The doses used by the pregnant women ranged from 20 to 40 mg/day. Dr. Fisher, a pharmacologist with the FDA Center for Drug Evaluation and Research, Rockville, Md.

Reports of symptoms consistent with neonatal withdrawal syndrome and associated with maternal use of selective serotonin reuptake inhibitors (SSRIs) and selective norepinephrine reuptake inhibitors (SNRIs) prompted the FDA last year to issue labeling changes warning of the risk associated with their use during pregnancy.

Possible cases of neonatal withdrawal syndrome have been reported with all SSRIs, but in at least one study, the majority of cases were associated with paroxetine.

In that study of 93 cases, 64 were associated with paroxetine, 14 with fluoxetine, 9 with sertraline, and 7 with citalo- pram, which is marketed as Celexa by Forest Laboratories. (One patient received both paroxetine and fluoxetine.) Another large study showed that the association between paroxetine and neonatal symptoms was no greater than that of other SSRIs.

The citalopram reports noted by Dr. Fisher and the other reports involving various SSRIs and SNRIs and their association with neonatal withdrawal symptoms suggest a class effect. But the data remain insufficient for determining whether there is a significant difference among the individual drugs in this class, he told this newspaper.

As a rule, “the use of this agent has to be balanced with respect to the benefit to the mother if she is depressed. There is a general consensus that SSRIs and SNRIs are preferable to tricyclics in terms of safety and efficacy,” said Jeffrey Jonas, M.D., senior vice president of the Forest Research Institute, a division of Forest Labs.

Experts continue to urge clinicians to weigh the risks and benefits of SSRI and SNRI use in pregnancy and to consider the increased risk of maternal morbidity associated with untreated maternal depression.