

Parvovirus B19 in Pregnancy, CNS Defects Linked

Although rare, central nervous system abnormalities manifest as a significant effect of this infection.

BY SHARON WORCESTER
Tallahassee Bureau

ST. PETE BEACH, FLA. — 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' case involved an 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 2,898 g. At day 5 he received a blood transfusion because he had severe anemia, 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).

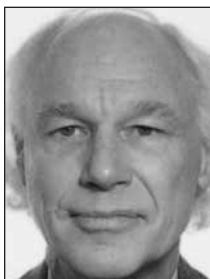
The child was markedly hirsute and had a frontal hair upsweep, a large hemangioma over the helix of his right ear, a large space between his upper central incisors, and clinodactyly of the index and fifth fingers of his left hand, Dr. Jones noted.

His inner canthal distance was 2.7 cm (25th percentile), and his palpebral fissure was 2.3 cm (below the 2nd percentile).

Valproic acid and carbamazepine treatment failed to control seizures, which he began having at birth.

A search of the literature revealed three publications documenting CNS abnormalities after maternal parvovirus B19 infection, Dr. Jones said. The first, which was published as an abstract, involved three cases. In one case, the fetus died, and in the other two cases the fetuses survived but had severe mental retardation.

Neuropathology at the time of death in the nonsurviving fetus, which was exposed to infection at 24 weeks' gestation, showed brain atrophy with widespread



dysplasia and focal destruction of spinal cord and piriform cells, among other abnormal findings.

One of the survivors was exposed to infection at 18 weeks' gestation. The child had cerebral palsy, developmental delay, and infantile spasms. Neuroimaging revealed enlarged ventricles with small periventricular calcifications, cortical dysplasia with polymicrogyria, and

periventricular hypodensity.

Subtle neurobehavioral effects in children may result from mild maternal infection.

DR. JONES

The final case in that report involved a fetus exposed at 23 weeks' gestation. A CT scan of the brain revealed periventricular calcifications.

The second publication was a case report involving a fetus that was exposed at 15 weeks' gestation and died 7 hours after birth. Neuropathology showed multinucleated giant cells, macrophages, microglia, and many small calcifications around the vessels, predominantly in the cerebral white matter. Polymerase chain reaction amplification showed that parvovirus DNA was present in the nuclei of the multinucleated giant cells and endothelial cells, Dr. Jones said.

The final publication involved a series of 92 consecutive singleton pregnancies with serologic evidence of parvovirus B19 in-

fection. 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 three patterns of abnormalities are associated with maternal parvovirus B19 infection: positional limb deformities, radiographic evidence of intercranial calcifications, and dysplastic changes, including agyria, 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 that the mechanism of action most likely includes both infection of cells in the central nervous system and hypoxia 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. ■

Investigational Prenatal Test Uses Endocervical Mucus

BY KATE JOHNSON
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COPENHAGEN — An investigational prenatal diagnostic test that uses fetal cells taken from maternal endocervical mucus could offer all the advantages of chorionic villus sampling, according to a study sponsored by Biocept Inc., the San Diego company that's developing the test.

"This is a completely noninvasive diagnostic test that you can do in the first trimester. It's not just a screening test, which is what the other noninvasive tests are," said study investigator Farideh Bischoff, Ph.D., of Baylor College of Medicine in Houston.

The idea of analyzing trophoblast cells taken from maternal blood or cervical mucus has been pursued for some time. However, inefficient endocervical sampling procedures and the scarcity of trophoblasts in maternal blood have hampered attempts to develop a reliable prenatal test.

The Biocept test involves collecting maternal endocervical mucus with a brush similar to that used to collect samples for Pap smears. A cell capture device is used

to isolate fetal trophoblasts from the mucus. Next, an antibody-based purification system filters out the maternal cells.

In a study she presented at the annual meeting of the European Society of Human Reproduction and Embryology, Dr. Bischoff described immunohistochemical staining and fluorescence in situ hybridization testing on purified cells from 100 women.

'This is a completely noninvasive diagnostic test that you can do in the first trimester. It is not just a screening test.'

The initial endocervical mucus sample contains very small numbers of trophoblasts and following the purification technique can strengthen the concentration to a purity of 85%-95%.

Diagnostic testing of the remaining trophoblast cells is then possible to detect chromosomal aneuploidies, she said.

"If you run a panel of probes you can detect trisomies. Alternatively, you can do DNA testing on the cells to screen for mutations. It basically allows you to do the same tests that investigators are doing with preimplantation embryos," she said.

Dr. Bischoff said Biocept is running a clinical evaluation study at centers nationwide to compare the results of the test with those of standard chorionic villus sampling in a group of pregnant women. ■

Small Study: ART May Be a Risk Factor for CHARGE, Goldenhar's

BY SHARON WORCESTER
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ST. PETE BEACH, FLA. — Assisted reproductive techniques may be a risk factor for CHARGE association and Goldenhar's syndrome, a small study suggests.

Of 31 patients with CHARGE association and 20 patients with Goldenhar's syndrome, 7 (23%) were conceived via maternal use of an assisted fertilization technique, Kerstin Stromland, M.D., reported at the annual meeting of the Teratology Society.

Of those with CHARGE association, one boy and one girl were the product of intracytoplasmic sperm injection, and another boy was conceived after his mother's use of ovulation stimulating hormone.

Of those with Goldenhar's syndrome, two twin boys (who had a healthy sibling) and one girl, who had a healthy twin sister, were born following intracytoplasmic sperm injection, and another girl was born after standard in vitro fertilization, said Dr. Stromland of Sahlgrenska University Hospital, Gothenburg, Sweden.

The possible link was identified after mothers completed a questionnaire asking about medical history and use of drugs, al-

cohol, or tobacco, and following the collection of data from medical records and interviews with parents of the children.

While there are a few publications suggesting a link between CHARGE association and Goldenhar's syndrome and assisted reproduction techniques (ART) this is the first to suggest a specific link between CHARGE association and intracytoplasmic sperm injection, Dr. Stromland said, noting that one possible reason for the lack of reports on such cases is the multiple malformations that characterize these syndromes. That is, patients' deformities are often registered as separate malformations, rather than malformations occurring as part of a syndrome.

Further study is needed to elucidate any relationship between assisted fertilization and these conditions, she concluded.

CHARGE association is a constellation of congenital malformations. The acronym stands for some of the most common features:

- ▶ Coloboma of the eye and cranial nerve abnormalities.
- ▶ Heart malformation.
- ▶ Choanal atresia.
- ▶ Retardation of growth after birth and of development.
- ▶ Genital hypoplasia in males and urinary tract.
- ▶ Ear malformations and/or deafness. ■