Fetal Monitoring Urged for Anti-Ro/La Antibodies

Early detection of autoantibodies in the fetus is vital when a woman has anti-Ro/La.

BY NANCY WALSH
New York Bureau

NEW YORK — Any pregnant woman who has anti-Ro/La antibodies should have weekly fetal echocardiograms beginning at 16 weeks' gestation to look for possible signs of congenital heart block, Dr. Jill P. Buyon said at a rheumatology meeting sponsored by New York University.

During pregnancy these autoantibodies, typically found in high titers in patients with systemic lupus erythematosus and Sjögren's syndrome but also in some asymptomatic individuals, begin to cross the placenta as early as 11 weeks. The autoantibodies accumulate in the fetal circulation and are associated with the development of various manifestations of neonatal lupus, particularly prolongation of the mechanical PR interval and congenital atrioventricular block.

The importance of early detection of these autoantibodies in the fetus is underscored by the fact that once third-degree, or complete, heart block has developed, it is irreversible with current therapies, according to Dr. Buyon, professor of medicine, department of rheumatology, New York University, New York City.

Moreover, anti-Ro/La congenital heart block carries a 20% mortality, and at present the majority of children who survive need a pacemaker.

Intense research interest therefore is focused on identifying markers of early cardiac injury, at a point before fibrosis and scarring are permanent, and on the potential for therapeutic interventions to reverse early changes.

The use of cardiac monitoring to detect prolongations of the PR interval greater than 150 milliseconds was recently evaluated in the observational PR Interval and Dexamethasone Evaluation (PRIDE) study of pregnant women who were positive for anti-Ro and/or anti-La antibodies. The study also attempted to provide some data on outcomes following the administration of steroids.

Fetal echocardiography was performed weekly between weeks 16 and 26, and then biweekly between weeks 26 and 34, according to Dr. Buyon, one of the study investigators. She and her colleagues were looking for prolongation of the PR interval, evidence of tricuspid regurgitation, and unexplained atrial echodensities.

Among the 88 patients who completed an evaluable course, there were three cases of third-degree heart block.

One of these patients had a normal PR interval, but some tricuspid regurgitation was noted at 17 weeks and atrial echodensity, at 22 weeks. A week later the fetus was in third-degree heart block and, despite treatment with maternal dexamethasone, 4 mg/day, severe hydrops developed and the pregnancy was terminated.

The second fetus had a normal PR interval between weeks 16 and 18 along with mild tricuspid regurgitation at week 17. The mother missed an appointment and, by the next time she was seen, third-degree block had developed in the fetus. This persisted despite administration of dexamethasone, and the child continued to be followed after birth (Arthritis Rheum. 2006;54:S689).

The third fetus also had a normal PR interval at 18 weeks, but 10 days later the fetus was in third-degree block and hydropic. Treatment with dexamethasone was unsuccessful, and the pregnancy was terminated at 20.5 weeks.

First-degree block was detected in an additional three fetuses. In one, the PR was normal at weeks 16-18, was prolonged at week 19, and normalized within 7 days of dexamethasone treatment.

The second had a prolonged PR interval at week 22 that resolved within 3 days of dexamethasone treatment. These two patients both had normal electrocardiograms at birth.

The third fetus had normal PR intervals throughout gestation but an electrocardiogram at birth showed first-degree block that has persisted to age 3 years.

Dexamethasone was also used in nine cases of second-degree block. Of these, four fetuses progressed to third-degree block, four remained in second, and only one was born in normal sinus rhythm. "This was a little disappointing," Dr. Buyon said.

Of the 79 neonates for whom birth electrocardiograms were available, 78 were normal, and all 46 for whom 1-year follow-up electrocardiograms were available were normal, she said.

In conclusion, the study suggests the following, according to Dr. Buyon:

► First-degree block in utero is reversible with dexamethasone, but if present at birth, close observation by a cardiologist is needed because of the possibility of later progression.

► There has not been evidence of conduction abnormalities developing later in neonates whose electrocardiogram was normal at birth.

► Advanced cardiomyopathy can occur within 7 days of a normal PR interval, so even weekly evaluation may not be sufficient.

► Tricuspid regurgitation may be an important early marker of injury.

Dexamethasone treatment poses significant hazards to both mother and fetus, with maternal risks including diabetes and hypertension, and fetal risks including intrauterine growth retardation, adrenal suppression, and decreased brain growth. Moreover, as was seen in PRIDE, efficacy is hardly guaranteed. Accordingly, other therapeutic approaches are being investigated, including inhibition of transforming growth factor-β to limit fibrosis and prophylaxis with intravenous immune globulin (see box). ■

Next: Will IVIG Prevent Heart Block?

Intravenous immune globulin (IVIG) has a history of safely being used in pregnancy, primarily for autoimmune thrombocytopenia and immune deficiency syndromes. A few cases of successful use in congenital heart block have also been reported.

To determine if this prophylactic approach could reliably decrease the placental transport of anti-SS-A/Ro and anti-SS-B/La antibodies, the Preventive IVIG Therapy for Congenital Heart Block (PITCH) trial is now enrolling patients.

Sponsored by New York University School of Medicine and the Alliance for Lupus Research, the trial aims to enroll 19 women who are antibody positive and have already had a child with congenital heart block or a rash that might have been neonatal lupus. Such mothers are at much higher risk of having another child with congenital heart block than are mothers positive for anti-Ro/La who have not already had an affected child.

Participants will be given 400 mg/kg of IVIG every 3 weeks for a total of five treatments between weeks 12 and 24 of pregnancy.

If fewer than three fetuses develop second- or third-degree heart block, another 35 women will be enrolled in the PITCH trial.

"Then, if there are fewer than six cases of heart block out of 54, we will be on the way to having a prophylactic therapy," said Dr. Buyon, who is principal investigator for the trial.

Information about PITCH is available at http://clinicaltrials.gov/show/NCT00460928.

Don't Soft-Pedal Disturbing Results From Ultrasound Exam

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

RIVIERA MAYA, MEXICO — Expect the unexpected during a fetal ultrasound exam, and if you find it, be kind but unambiguous in describing your observations and concerns.

"The ambiguity we sometimes use to try and soften what we are saying doesn't change the message, but it can change the interpretation," Dr. Nancy Chescheir said at a conference on obstetrics, gynecology, perinatal medicine, neonatology, and the law.

"If there is no fetal heart activity, tell the patient her baby's heart is not beating and that the fetus has died. If you see findings suggestive of a fetal anomaly, describe exactly what you see, express your concern, and refer the patient to an expert as quickly as possible," said Dr. Chescheir, the Betty and Lonnie S. Burnett Professor of obstetrics and gynecology at Vanderbilt University, Nashville, Tenn.

Many diagnoses of fetal demise or anomaly will be discovered during a detailed anatomic scan ordered on the basis of some increased risk, including a poor past pregnancy outcome, family history of genetic disorders, or abnormal early biomarker studies. In these cases, the patient probably already has an idea that there may be a serious problem.

"The patient is already suspicious. They watch the ultrasound; they may have had scans before, and they know what fetal heart activity looks like. If you are certain of the diagnosis of fetal demise, be very kind, do it in private, but be unambiguous about what you are seeing."

In cases of uncertainty, the 5-10-20 rules can be a help, Dr. Chescheir said. "If you have a 5-mm crown-rump length, you have to see a heartbeat or you have a dead baby. There's no need to have her come back in 48 hours for a repeat scan or to do hormone levels."

If the fetus measures only 4.5 mm from crown to rump, however, you should ask the woman to come back for a repeat scan when you anticipate a length of 5 mm. "You will probably have to wait at least 3 days to see this growth. If at that time, you have a 5-mm length and still no heartbeat, make the diagnosis and get on with your therapeutic options."

For a gestational sac with a mean diameter of 10 mm, you must see a yolk sac; if you don't, the pregnancy is not viable. Similarly, for a 20-mm mean gestational sac, you must see a fetal pole. The absence of one means the pregnancy is not viable, Dr. Chescheir said at the meeting, which was sponsored by Boston University.

Surveys about patient satisfaction with fetal ultrasound diagnosis agree on one thing, Dr. Chescheir said: Women don't appreciate the delay between the moment a problem is identified and the moment the doctor communicates the problem.

"They really don't like it if the sonographer is not allowed to say anything during the exam," Dr. Chescheir said. "If the sonographer is fairly certain about a fetal demise, she should be able to say something. You may not want her making the diagnosis, but she should be allowed to tell the patient something."

Having very clear office procedures can avert problems in this area, she said. ■