Brain Maturity Lags in Infants With Heart Defects

BY DOUG BRUNK
San Diego Bureau

SAN DIEGO — Brain development at birth is significantly delayed in full-term neonates with complex congenital heart defects, both on magnetic resonance imaging and by mean head circumference.

These observations "should stimulate discussion on the optimal timing of labor induction for those infants with prenatally diagnosed heart defects," Dr. Daniel J. Licht said at the annual meeting of the American Association for Thoracic Surgery.

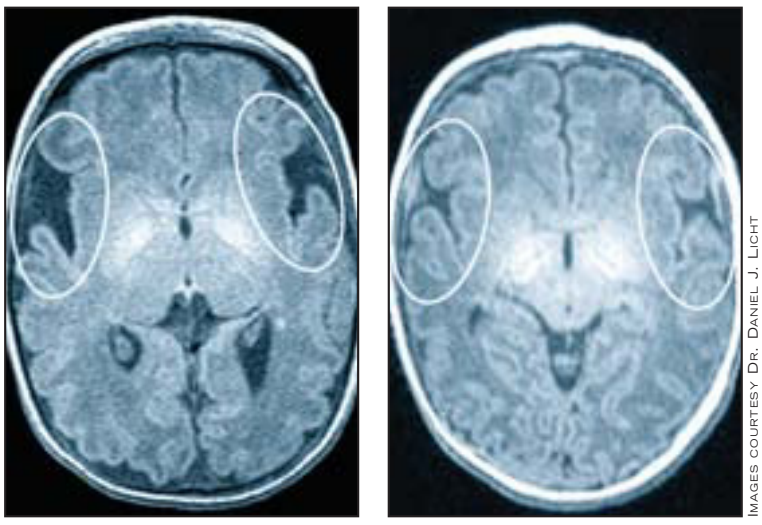
"Historically, the timing of delivery for neonates with prenatally diagnosed congenital heart disease was determined by lung maturity and surgical logistics. The current study suggests neonates with complex CHD should be delivered as close to term as possible," said Dr. Licht, a child neurologist at Children's Hospital of Philadelphia.

Previous studies have shown that at birth, term infants with complex congenital heart defects have smaller head circumferences and, on MRI, have been shown to have structural simplicity of the brain as seen by open operculum. These infants "also have an unexpectedly high proportion of preoperative and postoperative white matter injury in the form of periventricular leukomalacia," he said.

This finding has been corroborated by a report of biochemical immaturity of the white matter in infants with congenital heart defects as shown by MR spectroscopy (N. Engl. J. Med. 2007;357:1928-38).

Dr. Licht and his associates hypothesized that term infants with complex forms of congenital heart defects have structurally delayed brain development as measured by smaller head circumferences and a lower total maturation score (TMS), a validated MRI metric for assessing full brain maturity. The TMS is composed of four MRI characteristics: myelination, cortical folding, germinal matrix, and migrating bands of glial cells.

A 3-Tesla MRI was used to evaluate 29 full-term infants with hypoplastic left heart syndrome (HLHS) and 13 with transposition of the great arteries (TGA) just prior to heart surgery. Infants with evidence of perinatal distress, shock, or intrauterine growth retardation were excluded from the study "as these were felt to be independent risks for brain injury," Dr. Licht said.



IMAGES COURTESY DR. DANIEL J. LICHT

Open operculum, indicating structural simplicity of the brain, was seen in 86% of neonates with complex congenital heart defects on magnetic resonance imaging.

Clinical studies were reviewed by a single neuroradiologist who was blinded to the clinical data, and TMS was rated by two MRI readers who also were blinded to the data. Findings were compared with published normative data of similar gestational age. The mean gestational age of the 42 infants was 39 weeks and 64% were boys. Average birth weight was 3.4 kg.

The average head circumference for infants in the study was 34.5 cm, which is a full standard deviation below the expected normal of 35.5 cm. In addition, open operculum was seen on MRI in 36 of the infants (86%), and would be expected in less than 5%-10% of normal full-term infants

The average TMS for infants in the study was just over 10, which is significantly lower than reported normative TMS of 11.1 in noncardiac infants with a gestational age of 36-37 weeks.

"This average TMS … places our term infants with congenital heart defects at 35 weeks of gestational age, when white matter remains vulnerable and myelination is just beginning," Dr. Licht said. "We conclude that this group of otherwise healthy term babies with congenital heart defects has immature brains as evidenced by the high prevalence of small head circumferences and open opercula and corroborated with the finding of reduced TMS scores, suggesting a delay in brain maturity of a full month."

He noted that the relative immaturity of the central nervous system in these term neonates "may provide the substrate for the vulnerability to white matter injury in the pre-, intra-, and postoperative periods."

The study was funded by the National Institute of Neurological Disorders and Stroke and by the Dana Foundation. Dr. Licht had no conflicts to disclose. ■

Prognosis for PAD Linked to Stenotic Lesion Location

MUNICH — For peripheral arterial disease, like real estate, it's all about location.

In a review of 400 patients, those with proximally located peripheral arterial disease (PAD) within aortoiliac vessels, were more than twice as likely to die or have a cardiovascular disease event during follow-up as patients with peripheral artery disease lesions located exclusively in distal, infrailiac arteries, Dr. Victor Aboyans reported in a poster at the annual meeting of the European Society of Cardiology.

The study reviewed all 400 patients who underwent an initial, lower-limb angiography examination at the hospital during 2000-2005. Their average age was 68 years, and 78% were men. Arterial stenoses of 50% or more were located by two experienced vascular physicians.

Aortoiliac lesions were found in 211 patients. Many of these patients had lesions in distal arteries, too, although 56 of these patients only had aortoiliac stenoses. The other 189 patients in the study had stenotic lesions confined to distal parts of the lower vasculature, including femoropopliteal disease and infragenicular disease.

During follow-up through April 2007, the rate of total death in the patients with aortoiliac stenoses was about 2.5-fold higher than those PAD patients who only had distal lesions in an analysis that adjusted for differences in patient age, gender, smoking status, diabetes, heart failure, prescribed drug use, and several other comorbidities and variables, said Dr. Aboyans, a senior physician at Dupuytren University Hospital in Limoges, France.

—Mitchel L. Zoler

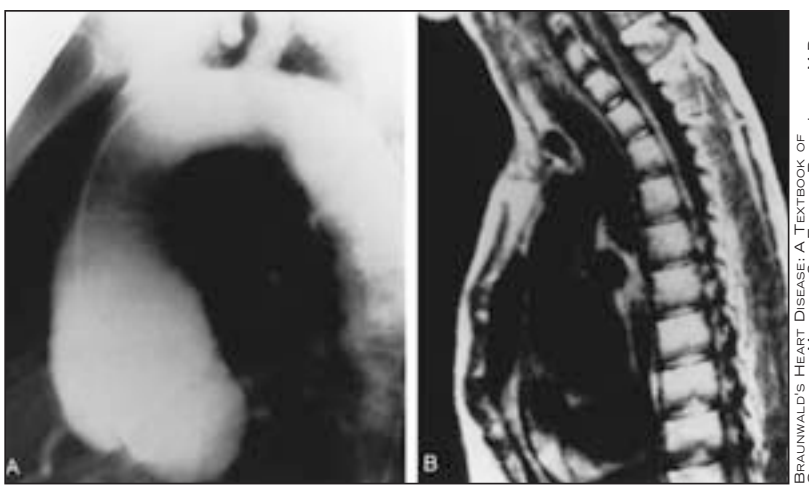
Aortic Root Surgery in Marfan Patients Amplifies Their Predisposition to Migraine

BY BRUCE JANCIN
Denver Bureau

MUNICH — Patients with Marfan syndrome have a sharply increased prevalence of migraine, especially migraine with aura, according to Dutch investigators.

Moreover, Marfan syndrome patients who undergo aortic root surgery experience a double headache of sorts; that is, an independent further increase in the risk of migraine, Dr. Jeroen C. Vis reported at the annual congress of the European Society of Cardiology.

The explanation for the association between aortic root surgery and a high rate of migraine in Marfan syndrome patients is unclear. One possibility is that the aortic graft throws off microemboli, which trigger headache attacks, according to Dr. Vis of Academic Medical Centre, Amsterdam.



BRAUNWALD'S HEART DISEASE: A TEXTBOOK OF CARDIOVASCULAR MEDICINE, 8TH EDITION, PETER LIBBY, M.D., ET. ALL, FIGURE 8-6, ©2008, 2005, 2001, 1997, 1992, 1988, 1984, 1980 BY SAUNDERS, AN IMPRINT OF ELSEVIER INC.

A: Lateral angiogram of the ascending aorta shows dilation of the sinuses of Valsalva and proximal ascending aorta and normal ascending aorta. B: Lateral MRI of the same patient is shown.

He reported on 97 adults with Marfan syndrome who had a mean age of 39 years and 80 age- and gender-matched controls. All underwent a clinical interview in which migraine diagnosis was based on International Headache Society criteria. Migraine was diagnosed in 44% of the Marfan patients, compared with 28% of controls. Thirty-seven percent of Marfan patients had migraine with aura, as did 10% of controls.

The prevalence of migraine among controls was higher than usual. This is most likely due to the influence of familial migraine; 16 of the 80 controls were first-degree relatives of participating Marfan syndrome patients, Dr. Vis said.

In this study, Marfan syndrome was an independent risk factor for migraine overall, and conferred an adjusted 2.4-fold increased risk, along with a 6.2-fold increased risk for migraine with aura. Thirty-five percent of the Marfan patients underwent aortic root surgery. A history of the surgery was independently associated with a 3.9-fold increased risk of migraine and a 4.5-fold greater risk of migraine with aura.

The investigators also looked at other cardiovascular features of Marfan syndrome. Neither mitral valve surgery, aortic dilatation, aortic dissection, mitral valve prolapse, nor mitral regurgitation showed to be independently associated with an increase in migraine. Aortic root surgery was unique in this regard.

Dr. Vis said that he and his colleagues plan next to look at headache patterns in patients without Marfan syndrome who have undergone aortic root surgery.

The goal of the study will be to determine whether a history of the surgery is also a risk factor for migraine and migraine with aura. ■