Dear Colleagues,

We hope the beginning of this New Year finds you well! We are pleased to bring you our first quarterly Fetal Connections issue of 2016.

Our Fetal Medicine Institute is committed to providing a continuum of care from the high-risk fetal period to a stable postnatal status. Our featured program for this issue, the Fetal Neonatal Neurology and Neurocritical Care Program, is a key part of this: together, we provide your pregnant patients with the best possible anticipatory care. Under the leadership of Dr. Taeun Chang, this multidisciplinary team has provided the latest treatments to the over 1,000 neonates they have consulted on since the inception of the program. They are pioneers in research and implementation of experimental therapies, leading the way through exciting new developments in the field and working towards significant improvements in neonatal and pediatric neurological outcomes.

The Case of the Quarter on page 2 highlights the complex and collaborative nature of the cases on which this program works.

The Fetal Medicine Institute is excited to kick off this New Year with the announcement of our Inaugural International Symposium on the Fetal Brain to be held on September 15 and 16, 2016. With 10 highly regarded international experts and a multidisciplinary panel of speakers, our agenda is filled with opportunities for innovative talks, meaningful discussions, and collaborative learning. We hope you can join us at the W Hotel in Washington, DC, for this pioneering event. For more information on this Symposium, visit childrensnational.org/isfb2016.

Best Wishes,

Adrè J. du Plessis, MBChB, MPH
Director, Fetal Medicine Institute
Director, Fetal Brain Program
Division Chief, Fetal and Transitional Medicine

Our Fetal-Neonatal Neurology and Neurocritical Care Program

In our Fetal-Neonatal Neurology and Neurocritical Care Program, we believe that every fetus and newborn with a neurologic condition should have the opportunity to be treated by a pediatric neurologist. Launched in 2004, our program is comprised of a core group of four pediatric neurologists sub-specializing in the fetal and newborn brain: Taeun Chang, MD, Adrè du Plessis, MBChB, Joseph Scafidi, DO, MS, and Tammy N. Tsuchida, MD, PhD.

The Fetal-Neonatal Neurology and Neurocritical Care Program consists of a specialized team of pediatric neurologists uniquely integrated with the Children’s National Division of Neonatology and the neonatal ICU (NICU) to provide expertise in the diagnosis and care of acute neurologic conditions in the newborn infant. For patients referred in the fetal period, our highly coordinated level of care allows for continued follow-through with the same specialized team both before and after delivery, ensuring a smooth continuity of care. Newborns in our NICU receive the most advanced neuroimaging and neurodiagnostic studies clinically available, and these studies are subsequently interpreted by leading experts in the neonatal brain.

(Continued on page 2.)
Changes in the Field
The field of neurology is transitioning from a past that was full of limitations to a future of bold potential and treatments, and neonatal neurology is the most actively changing sub-discipline within pediatric neurology. In the past decade, we have seen the standardization of therapeutic hypothermia for birth asphyxia/hypoxic-ischemic encephalopathy, consortiums for neonatal seizure treatments, development of neonatal seizure detection software for EEGs, and federal funding of over a dozen preterm or term neuroprotective clinical trials.

Our Program
The neonatal brain and neonatal brain injury represent the most active clinical and translational research focus in our NICU. Our goal is to advance neuroprotective and repair therapies for the fetus and newborn infant.

Fetal neurology consultations are seen within the Fetal Medicine Institute clinic location, both for the physical comfort of the expecting mother as well as the ease of coordination between fetal radiology, our genetic counselors, and staff. After graduating from our NICU, our patients are followed in the outpatient neurology clinic locations in Maryland, Virginia, and the District of Columbia. Cerebral palsy, seizures, and neurocognitive disabilities are managed in individual neurology or joint physical medicine (Perinatal Brain Injury) clinics.

Our clinical mission can only be achieved by working synergistically with Fetal Medicine, Neonatology, Neuroradiology and numerous pediatric specialists to coordinate the acute and long term neurologic workup and care of newborns and early infants. Fetal cases with primary or secondary neurologic involvement expand our interdisciplinary relationships to include obstetricians and maternal–fetal medicine experts. This newsletter’s Case Review highlights the complexity and coordination involved in providing accessible and personalized advanced medical care.

Program Care Recommendations
Careful prediction of neurodevelopmental prognosis requires an accurate and specific neurologic diagnosis. Pediatric neurologists can now reach a specific clinical and genetic diagnosis in the majority of our patients. Magnetic resonance imaging (MRI) of the brain has improved our ability to narrow biochemical or genetic testing in the evaluation of neurologically affected fetuses, infants and children. In the case of brain injury, MRI is useful in predicting functional deficits based on location and severity of injury.

In the fetal patient, a fetal MRI is indicated due to the limited resolution of fetal ultrasound in delineating the brain, brainstem and/or cerebellar parenchyma. Depending on the gestational age, the structures(s) of interest may be less than a few millimeters in size. Repeat or follow-up fetal MRIs may be necessary if (1) we wish to improve our ability to capture small structures later in gestation; (2) we need to assess structures not present or fully developed at the gestational age of the initial referral; or (3) we need to evaluate the progression (or repair) of a neurologic condition (i.e. hydrocephalus, fetal stroke) to make decisions regarding immediate postnatal treatments.

As neonatal neurologists, we understand the importance and responsibility of delivering an often somber diagnosis to parents – whether prenatally or postnatally - in a compassionate manner. Starting from the womb and throughout postnatal care, we offer assistance and hope in helping parents navigate medical decisions to achieve the maximal outcome and quality of life for their child.
A fetal patient at 36 weeks gestational age (GA) was referred to the Fetal Medicine Institute for severe ventriculomegaly and enlarged cisterna magna. Combined fetal US and MRI studies confirmed findings of severe hydrocephalus, with possible Blake pouch cyst but excluded Dandy-Walker malformation. Delivery by elective Caesarean section was planned at 38 weeks.

Delivery proceeded uneventfully, but infant was noted to have numerous raised brown hairy nevi covering her body (see Fig 3). The neonatologist at the birth hospital consulted a Children’s National neonatal neurologist and a diagnosis of Congenital Giant Melanocytic Nevi (CGMN) with Neurocutaneous Melanosis (NCM) was made.

Congenital hydrocephalus can be caused by genetic abnormalities or acquired injury during fetal development— in this case, a complication of NCM. It involves excessive accumulation of cerebrospinal fluid in the ventricles and extra-cerebral spaces of the brain.

Congenital melanotic nevi are reported in at least 1% of newborns, and up to 30% of nevi that develop in the general population are determined to be prenatal in origin, having only migrated to the surface at a later time (prenatal nevi)1. Giant CMN (nevus ≥ 20cm in a projected adult size) occurs in 1 in 20,000 – 500,000 live births with a 3:2 female predominance2. NCM occurs in 2.4-50% of these cases. Symptomatic NCM is associated with fatality within 3 years.

The infant was transferred to Children’s National NICU as planned for the hydrocephalus. Placental pathology with special staining showed nests of melanocytes throughout. A postnatal brain MRI confirmed meningeal involvement, especially at the base of the brain, and hydrocephalus.

Video EEG showed epileptiform activity but no seizures. A skin punch biopsy by dermatology revealed clusters and nests of dendritic melanocytes in the superficial dermis at the dermal epidermal junction. No atypical or mitotic figures were seen. CSF cytology sent at the time of ventricular-peritoneal shunt placement by neurosurgery was absent of malignant cells. The infant was discharged home in eight days with follow up appointments scheduled with five subspecialists and serial MRI and EEG studies.

Despite the CGMN/NCM diagnosis and two subsequent shunt revisions, this infant grew and developed appropriately for age. Unfortunately, the spread of melanocytes progressed throughout the dermal, pleural, and peritoneal surfaces, resulting in her decline at two and a half years and demise at 3 years of age.

Findings from the follow-up post-natal MRI study performed at 3 days of life

Generalized ventriculomegaly/hydrocephalus, enlarged cisterna magna, and increased tegmentovermian angle were similar to the prenatal MRI. Signal hyperintensity involving the cerebellar surface, amygdalae, and suprasellar cistern consistent with leptomeningeal and parenchymal melanosis (see Figs. 4-5).

Cerebrospinal fluid flow obstruction at the meningeal level caused the hydrocephalus and posterior fossa CSF space enlargement.

(Fig 4) T1-weighted sagittal post-contrast MRI of the brain redemonstrates tetraventriculomegaly, an increased tegmentovermian angle, and enlargement of the cisterna magna. Hyperintense signal along the cerebellar cortex (white arrows) and within the suprasellar cistern (black arrow) represents leptomeningeal melanosis.

(Fig 5) T1-weighted coronal post-contrast MRI of the brain again shows the increased amygdalae signal compatible with the presence of abnormal parenchymal melanin (arrows).

Key Clinical Findings

- Fetal MR showed global ventriculomegaly, an enlarged cisterna magna, and an increased tegmentovermian angle. These findings suggested hydrocephalus (see Fig 1).
- The torcular was normally positioned, and the vermis was normally formed. These findings excluded a Dandy-Walker malformation (see Fig 1).
- Signal abnormalities in the amygdalae and along the cerebellar cortex were characteristic for neurocutaneous melanosis (see Figs. 2).


(Fig. 1) T2-weighted sagittal MRI of the fetal brain shows tetraventriculomegaly, an increased tegmentovermian angle, and enlargement of the cisterna magna (black arrow). The torcular is normally positioned (white arrow) and the vermis is normally formed, albeit slightly distorted by mass effect in the cisterna magna.

(Fig. 2) T1-weighted coronal MRI of the fetal brain demonstrates abnormal hyperintense signal along the upper margin of the left cerebellar hemisphere (arrow). Marked lateral ventriculomegaly and enlargement of the cisterna magna are also notable.

(Fig. 3) Infant was noted to have numerous raised brown hairy nevi covering her body.
FETAL ADVANCEMENTS

Both Washingtonian and Northern Virginia Magazines have named 18 of our Fetal Medicine Institute physicians to their 2015 Top Doctors lists. For more Fetal Advancements, view our digital version at ChildrensNational.org/Fetal-Connections.

Corrections: In our Summer 2015 issue, we mislabeled the Fetal Echocardiogram in Figure 3, Page 3. For the updated version, please see our online issue at childrensnational.org/fetal-connections.

U.S. NEWS & WORLD REPORT

Children’s National – 2015 Honor Roll
Nationally ranked in:
- Cardiology & Heart Surgery #19
- Diabetes and Endocrinology #18
- Gastroenterology and GI Surgery #9
- Neonatology #4
- The only program in Washington, DC/VA/MD with a Top 10 ranking
- Nephrology #13
- Neurology & Neurosurgery #4
- Oncology #13
- Orthopedics #18

Fetal Connections

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Fetal Connections is written for physicians and should be used for medical education purposes only. To view past issues of Fetal Connections, visit www.ChildrensNational.org/Fetal-Connections.

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Fetal Connections

Washingtonian Top Doctors 2015*

Anthony Sandler, MD
Surgery

Jeffrey Becker, MD
Cardiology

Charles Berul, MD
Cardiology

Michael Boyajian, MD
Plastic and Reconstructive Surgery

Roberta DeBiasi, MD
Infectious Diseases

Mary Donofrio, MD
Cardiology

Emily Hattwick, MD
Orthopaedic Surgery and Sports Medicine

Richard Jonas, MD
Cardiac Surgery

Robert Keating, MD
Neurosurgery

Northern Virginia Top Doctors 2015*

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Cardiology

Michael Boyajian, MD
Plastic and Reconstructive Surgery

Dorothy Bulas, MD
Fetal Imaging

Roberta DeBiasi, MD
Infectious Diseases

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Billie Short, MD
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Brian Stone, MD, MBA
Neonatology

Bud Wiedermann, MD
Infectious Diseases

Fetal Advancements

3rd Annual Pediatric Innovation Symposium:
Anita Krishnan (PI) and Mary Donofrio (Co-I), finalists

Publications:


* Physicians listed are those who are part of the Fetal Medicine Institute. This is not inclusive of all Children’s National physicians named to the lists.