Recommendations for Achondroplasia Evolving With Recent Observations
Moise Danielpour, MD

Achondroplasia is the most common of all hereditary skeletal dysplasias, or dwarfing conditions. It is an autosomal dominant syndrome with most new cases arising from a spontaneous mutation. The condition is associated with symmetric shortening of the limbs secondary to abnormal development of endochondral bone.

Many patients with achondroplasia can suffer from neurological manifestations including hypotonia, hydrocephalus, sleep apnea, spinal compression syndromes and, significantly, foramen magnum stenosis. Foramen magnum stenosis, or narrowing of the opening at the base of the skull, can lead to compression of the cervicomedullary junction, resulting in significant morbidity and even sudden death.

David Rimoin, MD, one of the world’s leading medical geneticists, editor of the definitive Principles and Practice of Medical Genetics, and founder of the International Skeletal Dysplasia Registry 40 years ago, documented that some children may be symptomatic for foramen magnum stenosis early but actually improve with time. This allowed us to reserve surgical intervention for a much smaller subgroup of patients than previously appreciated. Unfortunately, we have had little in the way of objective tools to use in determining which patients need early surgery and which do not.

A number of children referred to me for neurological evaluation have described symptoms related to foramen magnum compression, but based on the accepted methods of evaluating them, such as MRI studies, the degree of stenosis would not appear to require surgery. In observing the children and talking with their parents, however, it became clear that some of these children had symptoms only when they were sleeping or when they were placed in their car seats. In both of these situations, it was evident that the stenosis had worsened.

Continued on Page 3 (see “Achondroplasia”)

Figure 1: MRI CINE flow studies of the cervical spine; arrows indicate the foramen magnum. The child’s neck in a flexed position (A) shows a narrowed cervical canal and reduction in cerebrospinal fluid flow compared to a similar study in extension (B).
Aggressive, timely intervention often can effectively treat acute ischemic stroke, even reversing devastating stroke symptoms in certain cases. A new mechanical thrombolysis device, the Penumbra System™, extends the window of opportunity for treatment up to eight hours after the onset of acute stroke. This treatment is allowing more patients to reach a specialized stroke center in time to have a chance at successful treatment and improved outcome.

The Penumbra System revascularization device can be used to aspirate soft clots out of blocked arteries in the brain after an acute stroke. It received Food and Drug Administration (FDA) approval in December 2007, and Cedars-Sinai was the first medical center in California to offer this treatment.

In a related technology development, a new stent designed specifically to open partially blocked brain arteries is now also available at major medical centers specializing in neuro-endovascular procedures. Because brain arteries are less muscular and therefore more delicate than those of the heart, the Wingspan™ stent has been designed to be more flexible and safer to treat partially blocked arteries in the brain. Currently approved by the FDA as a humanitarian use device (IRB #10705), the Wingspan stent will be tested in a major Phase III clinical trial funded by the National Institutes of Health (NIH). Cedars-Sinai will be one of approximately 50 institutions nationwide participating in the SAMMPRIS (Stenting vs. Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis) study of the Wingspan intracranial stent with Gateway™ balloon.

We recently provided treatment for a 78-year-old patient who was able to take advantage of both of these innovative devices. She was brought by ambulance to Cedars-Sinai’s Emergency Department early one morning, unable to speak and suffering right-side paralysis. According to her husband, she was in otherwise good health and had exhibited no neurological symptoms the previous night.

The stroke neurology team immediately evaluated the patient, and a stat head CT scan was obtained, which showed no bleeding into the brain. The follow-up cerebral angiogram (Fig. 1) and CT perfusion scan (Fig. 2) showed a blockage of the left middle cerebral artery. Over half of the brain in that area – which controls speech and strength – had dangerously low blood flow.

Because the patient’s symptoms had begun sometime during the night, we could not conclude that onset had occurred within the three-hour window needed for administration of clot-busting or blood-thinning drugs, but we knew the stroke had occurred within the eight-hour time frame indicated for use of the Penumbra System device.

Less than an hour after the CT studies were conducted, we performed the Penumbra...
Stroke: continued from Page 2

procedure, suctioning out the clot, but a firm cholesterol plaque remained in the artery, causing a partial blockage. We then used the Gateway angioplasty balloon and Wingspan stent to fully open the artery, completing both procedures in a very short period of time.

A follow-up perfusion study confirmed that normal blood flow was restored, and within hours the patient had regained the ability to speak and had full use of her right side.

Successful treatment of acute stroke depends not only on the availability of innovative technology but on a stroke intervention team that is committed to aggressively pursuing every option. This patient was rapidly approaching the point at which her stroke symptoms could not have been reversed and she probably would have been dependent upon professional nursing care for the rest of her life. Instead, she quickly recovered without any permanent deficits, a real-life testament to the efficacy of these new devices.

Achondroplasia: continued from Page 1

tions, the children’s necks were in flexion.

This observation, along with the well-recognized finding that many of the patients who are symptomatic prefer to keep their neck in an extension position, made me question whether the degree of foramen stenosis or even hydrocephalus is dependent on dynamic phenomenon.

Children with achondroplasia have large heads for the size of their bodies and the tip of the cervical spine narrows significantly when the neck is in flexion, as opposed to extension. This group of patients was developing transient hydrocephalus and transient compression of the spinal cord when the neck was in flexion, but the problems were not evident on MRIs, which were typically performed with the neck extended.

As a result of these observations, we began performing CINE MRIs, specialized flexion-extension and cerebral spinal fluid flow studies, to aid in evaluating these patients—a practice that has now been adopted at other leading centers. An article describing our experience was published in the December 2007 issue of the Journal of Neurosurgery: Pediatrics.

One boy, who was a patient of Dr. Rimoin’s since he was born, was very symptomatic. He would awake from sleep, vomit and experience severe headaches. He was in and out of the hospital frequently with respiratory issues, numerous infections and apparent life-threatening events.

Although he had not been considered a surgical candidate previously, flexion-extension flow studies showed a dynamic compression of the spinal cord. We performed decompression surgery and the change was dramatic. The night after surgery, he no longer had apneic events or significant oxygen desaturation. He is now about two years out from surgery and is like a different kid, without headaches or multiple admissions to the hospital.

We are currently conducting laboratory studies to determine underlying causes of this phenomenon. Our hypothesis is that the gene defect affecting bone development in achondroplasia may also cause hypertrophy of ligaments. When these children flex their necks, the ligament in front of the spinal canal folds over and secondarily presses on the spinal canal and its contents at the level of the foramen magnum.

Cedars-Sinai is one of only a few centers in the world offering specialized care and research for achondroplasia and other dysplasias, bringing together experts in many fields to focus on the unique needs of these patients. As an international consulting and referral service, we have a deep and broad base of patient data from which to study these disorders and advance the standard of care.

Persistence is Key When Origin of Seizures is Elusive

Adam N. Mamelak, MD

Localizing the origin of epileptic seizures is usually a fairly straightforward process. But some challenging cases require a methodical series of evaluations to correctly identify the problem area and ensure that the most appropriate intervention is chosen.

We were referred a 36-year-old male who had a history of medically refractory epilepsy since age 14. Although his seizures were rare initially, they had increased in frequency and were occurring at least once a week. They usually began with an aura consisting of a tingling pain in the patient’s left chest. These sensations were followed by staring, unresponsiveness and rubbing of the hands, lasting one to two minutes. Multiple medications failed to provide control.

An MRI of the brain was normal, and an EEG was not definitive, suggesting only that the seizures might arise from the right or left temporal lobe. A PET scan also was non-localizing. We followed these studies with stereotactic placement of multiple depth electrodes in both side of the brain, with targets in the amygdala, hippocampus, the orbitofrontal region, the supplementary motor cortex.

Continued on Page 4 (see “Seizures”)
Seizures: continued from Page 3

area, and the anterior cingulated gyrus. The patient underwent two weeks of 24-hour video-EEG monitoring with the electrodes in place, and multiple stereotypic seizures were recorded. These studies identified a right temporal origin but with a very rapid spread, suggesting a neocortical rather than mesial temporal lobe origin.

Six weeks later, the patient underwent a right frontotemporal craniotomy for placement of subdural grids and further seizure monitoring (Fig. 1). These results demonstrated a right anterior temporal onset with spread and involvement of the medial temporal lobe.

With the origin of the seizures confirmed, we removed the grid and performed a right anterior temporal lobectomy (Fig 2). The patient’s recovery was uneventful and he has been seizure-free for nearly two years. He has returned to driving and participating in all normal activities.

Dr. Mamelak is Director of Functional Neurosurgery and Co-Director of the Pituitary Center at Cedars-Sinai Medical Center.

Figure 2: Postoperative MRI showing the temporal lobe removed.

Patients Finding Long-Term Relief From Sympathetically Maintained Pain of the Face

Steven Graff-Radford, DDS

Trauma-related facial pain that is exacerbated by involvement of the sympathetic nervous system has been particularly resistant to treatment, but we are using a new approach that appears to provide long-term relief.

Whereas classic trigeminal neuralgia causes sharp, “electric” intermittent pain, traumatic neuralgia is characterized by continuous, unremitting, burning, throbbing pain. The condition is typically precipitated by trauma to the face, such as dental work, a root canal, sinus surgery, a face-lift, or a viral infection such as shingles or even herpes simplex in the oral cavity.

A subset of these patients has sympathetically maintained pain, which, in theory, should be relieved by blocking the sphenopalatine ganglion. But attempts to block the ganglion, even with radiofrequency ablation, have usually failed to provide long-term results. Many patients may respond temporarily, but we have rarely been able to achieve a sustained response.

We therefore considered blocking the sphenopalatine ganglion to determine if this would provide better results. This ganglion lies deep to the maxilla and has some parasympathetic fibers as well as sympathetic. Patients diagnosed with traumatic trigeminal neuralgia underwent a sphenopalatine ganglion block performed by the Pain Center anesthesiologists under fluoroscopic guidance, with the patients sedated. According to our observations, while more patients had a favorable response to this procedure than stellate ganglion block, the response was short-lived. We attempted using radiofrequency ablation of the sphenopalatine ganglion, but again, no long-term responses were attained.

At the suggestion of the neurosurgeons on our team, about eight months ago we began ablating the sphenopalatine ganglion with the Gamma Knife®, using MRI for localization. Because gamma rays produce slow nerve degeneration from within, results are not immediate, but we are seeing a significant reduction in symptomatology in a large number of patients. Most patients get a response around three to four months after the single Gamma Knife treatment. Although it is early to make long-term predictions, we are very encouraged at the effects. In the 24 years that I have been treating chronic neuropathic pain, this is the first time we have been able to non-pharmacologically, consistently stop pain for these patients.

Recent advances are also providing greater relief for patients suffering from classic trigeminal neuralgia. With high-resolution brain imaging, we are able to identify the blood vessel in the cranium that presses on the trigeminal nerve to cause the classic electric-like pain. Then, operating intracranially and performing a microvascular decompression, we have had an extremely high success rate. Additionally, the Gamma Knife can be used in trigeminal neuralgia to noninvasively disrupt the gasserian ganglion. Finally, balloon gangliolysis, a quick outpatient procedure done under fluoroscopic guidance, is effective in a large number of cases.

Treating nerve pain of the face demands a multidisciplinary approach, not only to ensure that the best treatment option is available, but to provide complementary therapies. Viewing our patients holistically, we can offer the services of dentists, physicians, surgeons, psychologists, behavioral medicine specialists and others who combine their skills to treat chronic pain and help patients cope.