Pediatric Neurosurgeons Refine Tools And Procedures, Target Clinical Goals

Minimally invasive procedures and molecular-scale therapies for pediatric neurosurgery at Morgan Stanley Children's Hospital of NewYork-Presbyterian/Columbia University Medical Center and NewYork-Presbyterian Hospital/Weill Cornell Medical Center currently range from high-frequency radiosurgery to microinfusion techniques.

The young brain and nervous system benefit when tissue involvement is limited. In most tumor resection procedures, however, surgeons prefer generous margins to ensure removal of all malignant cells. "But in the brain and in the spinal cord, you really don't have any margins," noted Anders Cohen, MD. "We have to go through the brain, but we try to be minimalists."

Dr. Cohen has thus adapted the use of high-frequency radiosurgery for both dissection and tumor excision in pediatric neurosurgery, performing high-risk procedures with reduced damage to adjacent tissue when treating spinal cord tumors, gliomas, and other intracranial lesions. Where electrocautery may cause 500 to 1000 microns of lateral heat damage, Dr. Cohen reduces the spread to as little as 20 microns with the help of tools and techniques he has developed in recent years.

In a considerable simplification, Neil Feldstein, MD, has retooled Dr. Cohen's procedure to treat Chiari's malformations such as herniations on the back of the skull or downward displacement of the cerebellum. Standard decompressive surgery usually involves removing the base of the skull and part of the first cervical vertebra. The dural membranes are then opened to foster manipulation of cerebellar tissue; following this, a graft is sewn into the dural opening to make it larger but watertight. Complications from this procedure affect 1% to 2% of patients.

"We're trying to see if we can do the same operation without actually opening up the dural membranes," says Dr. Feldstein. Performing this operation for the past 3 years, Dr. Feldstein finds that patients heal faster and avoid the major risks associated with the exposure of spinal fluid.

Richard Anderson, MD, has developed a minimally invasive dorsal rhizotomy for children with cerebral palsy spasticity, enabling children to recover more quickly with less pain. This is an improvement on functional dorsal rhizotomy, still performed in many institutions, which usually involves removing 5 levels of bone and a 12- to 15-cm incision.

"Now I'm doing the same operation by removing only one level of bone with about a 1-inch incision," said Dr. Anderson. NewYork-Presbyterian Hospital is among a handful of hospitals in the country to perform this procedure.

Pediatric neurosurgeons are hoping to develop pinpoint therapies that operate on a cellular level. Saadi Ghatan, MD, is focusing on the possibility that the CXCR-4 gene is involved in the pathogenesis and disease progression of medulloblastomas. Looking at tumor samples and observing how they behave in culture, researchers have found that the gene product has roles in both pattern formation in neural development and as chemokine receptors in the immune system.

A second focus of interest for Dr. Ghatan is the role of apoptosis in neural tube closure. Apoptosis has long been recognized as a crucial part of neural development, and new insights into these fundamental processes may generate novel ways to prevent and treat neural tube defects, which include the various disorders of embryologic induction, and pediatric brain tumors.

Research by Mark Souweidane, MD, aims at developing local delivery schemes for tumors in children that arise in the deep structures of the brain. Over the past 7 years, his laboratory has experimented with techniques that allow interstitial delivery of therapeutic molecules, avoiding the adverse effects of systemic administration and allowing better concentration of medication in the area of interest. "We expect this work to quickly develop into Phase I studies for children with inoperable, deep-seated, and brainstem tumors," he said.

In addition, Dr. Souweidane is working in collaboration with the laboratory of Ronald Crystal, MD, on a Phase I study of gene therapy for Batten disease, the rapidly progressive neurodegenerative storage disease in children. Delivery of the absent gene product via microinfusion techniques, together with postoperative analysis of its distribution, offers unprecedented challenges to pediatric neurosurgery, making this gene transfer clinical trial one of the earliest to be opened to children with such disorders.

New postoperative devices are also responsible for advancements in the pediatric neurosurgery field. For example, Dr. Anderson has presented dramatic results with spinal instrumentation for children's injuries to the upper spine. In the usual procedure, wires and bone taken from the rib or hip are used to reinforce the spine. For several months after the operation, children must wear a halo vest with pins in the skull, and they often require further surgery. However, using C1 to C2 transarticular screws, Dr. Anderson developed a procedure to stabilize the spine without the cumbersome halo, with the bone resulting in complete fusion.

"The concept is that by putting the instrumentation directly across the joint, it fixes the spine and holds it in place so bone can fuse," he said. Patients who have undergone the older procedure but need further surgery frequently ask Dr. Anderson whether they need to go back into that halo brace. When he answers "no," he said, "it's like the sun has started

shining again."

Richard Anderson, MD, is Attending Pediatric Neurosurgeon at Morgan Stanley Children's Hospital of NewYork-Presbyterian/Columbia University Medical Center, and is Assistant Professor of Neurosurgery at Columbia University College of Physicians and Surgeons.
E-mail: rca24@columbia.edu.

Anders Cohen, DO, is Assistant Attending Neurosurgeon at NewYork-Presbyterian Hospital/Weill Cornell Medical Center, and is Assistant Professor of Neurological Surgery at Weill Medical College of Cornell University. E-mail: ajc9006@nyp.org.

Neil Feldstein, MD, is Director, Pediatric Neurological Surgery at Morgan Stanley Children's Hospital of NewYork-Presbyterian/Columbia University Medical Center, and is Assistant Professor of Neurosurgery at Columbia University College of Physicians and Surgeons.
E-mail: naf6@columbia.edu.

Saadi Ghatan, MD, is Assistant Attending Neurosurgeon at Morgan Stanley Children's Hospital of NewYork-Presbyterian/Columbia University Medical Center, and is Assistant Professor of Neurosurgery at Columbia University College of Physicians and Surgeons.
E-mail: sg2160@columbia.edu.

Mark M. Souweidane, MD, is Vice Chairman, Department of Neurological Surgery and Director of Pediatric Neurosurgery at NewYork-Presbyterian Hospital/Weill Cornell Medical Center, and is Associate Professor of Neurological Surgery and Pediatrics at Weill Medical College of Cornell University.
E-mail: mmsouwei@med.cornell.edu.

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