Trigeminal neuralgia: predicting outcomes, a focus at the University of Pittsburgh for over 30 years

by Amin Kassam, MD and Michael Horowitz, MD

Trigeminal neuralgia (TN) was first described in the late 17th century by Fehr in a eulogy. John Locke later described TN afflicting the Countess of Northumberland, wife of the English ambassador to France. Nicholas Andre coined the term “tic douloureux” and in 1756 discussed surgical treatments in five patients who suffered with a “cruel and obscure illness, which causes ... in the face some violent motions, some hideous grimaces, which are an insurmountable obstacle to the reception of food, which put off sleep ....” In 1966, Peter Jannetta proposed the etiology of TN to rest in the compression of the trigeminal nerve by small vessels near the brainstem. Since that time, microvascular decompression (MVD) has become a mainstay in the management of this painful condition.

In its classic or typical form, TN involves a unilateral, lancinating, electrical pain in one or more of the trigeminal nerve distributions. Patients usually describe typical trigger points on the face and triggering stimuli or activities. Pain generally has a memorable onset, may be positional in nature, and has variable periods of remission. Most patients will describe some modicum of pain relief from medications that include carbamazepine, phenytoin, baclofen or neurontin.

Atypical TN denotes a syndrome in which patients describe unilateral pain which, while in a trigeminal distribution, is more burning or aching in nature. This discomfort rarely responds to any of the above mentioned medications. Some patients have previously suffered with typical TN, but over the years evolved into an atypical condition. These patients may have traveled through a stage termed transitional TN which has characteristics of both typical and atypical TN.

This review looks at results in 2003 MVD procedures for typical TN and 672 MVD procedures for atypical TN performed at UPMC Presbyterian. Our goal was to help determine patient characteristics predictive for outcome following MVD and also assess surgical complication rates in these two populations.

Outcomes were divided into three categories. “Excellent” denoted patients that were pain free off medications. “Good” denoted patients with infrequent pain controlled with low dose medications. “Poor” described patients with no post surgical pain relief on or off medications.

Immediate post-op pain relief for typical TN results

Immediate excellent post-operative pain relief was achieved in 80.3% of patients undergoing MVD for typical TN. 16.5% received good (partial) relief while 3.2% had no response (96.8% significant pain reduction with surgery). When patients available for >5 year follow-up were studied separately for their immediate post-operative results 84.1% had experienced excellent results, 14.1% had a good result, and 1.8% had no surgical response (98.2% significant pain reduction with surgery).

Immediate post-op pain relief for atypical TN results

Immediate excellent post-operative pain relief was achieved in 46.9% of patients undergoing MVD for atypical TN. 39.7% received good relief while 13.4%
An international leader

For the past quarter century, the University of Pittsburgh Medical Center has been at the forefront in the treatment of cranial nerve abnormalities. In 1999 the Department of Neurological Surgery established the Center for Cranial Nerve Disorders to intensify this treatment effort and examine new areas of research. This center has since established itself as an international leader in the field. Each year the center evaluates over 500 patients suffering from hemifacial spasm, facial pain (trigeminal neuralgia), tinnitus, vertigo, disequilibrium, deep ear pain (geniculate neuralgia), throat pain (glossopharyngeal neuralgia), and posterior scalp pain (occipital neuralgia).

At the heart of the Center for Cranial Nerve Disorders is a team that can provide multimodality comprehensive treatment ranging from microvascular decompression (MVD) to percutaneous surgeries to Gamma Knife radiosurgery.

This multispecialty center is staffed by two microvascular neurosurgeons (Amin Kassam, MD, center director and Michael Horowitz, MD, associate director) specializing in microvascular decompression of the cranial nerves, two neurosurgeons specializing in percutaneous and radiosurgical approaches to cranial nerve diseases (L. Dade Lunsford, MD and Douglas Kondziolka, MD), one neurosurgeon with expertise in the management of chronic pain syndromes (John Moossy, MD), two otolaryngologists focusing on disorders of the ear and throat (Ricardo Carrau, MD and Barry Hirsch, MD), a neurologist specializing in cranial nerve dysfunction and head pain (Michael Soso, MD) an oral surgeon (Mark Ochs, MD) with significant experience treating oral pain syndromes, a neuro-ophthalmologist (Misha Pless, MD), and a cadre of neurophysiologists who help diagnose disease processes and monitor surgical procedures to ensure maximum safety and efficacy.

In addition to its unsurpassed clinical experience, the center is also a leader in research activities. Optimum management for atypical trigeminal neuralgia, the impact of Botox on hemifacial spasm, and identification of patients with vertigo most likely to respond to vascular decompression are some examples of continued study.

This edition of the University of Pittsburgh Neurosurgery News focuses primarily on recent research carried out by the Center for Cranial Nerve Disorders relating to trigeminal neuralgia, glossopharyngeal neuralgia, and hemifacial spasm. It also discusses work being performed at the university in minimally invasive endoscopic approaches to the management of cranial nerve disorders. Additional information can be obtained by contacting the Department of Neurological Surgery at (412) 647-3685. You can also learn more on our website at www.neurosurgery.pitt.edu.
Microvascular decompression sound, effective treatment for...

...trigeminal neuralgia

(from page 1)

had no response (86.6% significant pain reduction with surgery). When patients available for ≥5 year follow-up were studied separately for their immediate post-operative results 58.2% had experienced excellent results, 33.2% had a good result, and 8.6% had no surgical response (91.4% significant pain reduction with surgery).

Long term post-op pain relief for typical TN results

Long term excellent pain relief in those patients available for follow-up was achieved in 73.7% while good pain relief was preserved in 6.8%. 19.5% had no long term pain relief. Therefore, reduction in significant pain relief in this population declined from 98.2% immediately post-operatively to 80.5% at five years or more from MVD.

Long term post operative pain relief for atypical TN results

Long term excellent pain relief in those patients available for follow-up was achieved in 34.7% while good pain relief was preserved in 16.4%. 48.9% had no long term pain relief. Therefore, reduction in significant pain relief in this population declined from 91.4% immediately post-operatively to 51.1% at five years or more from MVD.

The majority of patients had been treated with carbamazepine prior to presenting for MVD. We found that 92% of patients that had taken carbamazepine for typical TN had failed prior to MVD while 96% of patients with atypical TN failed carbamazepine prior to MVD.

In our review of factors predictive of immediate post-operative relief following surgery for typical TN we found that trigger points and memorable onset of pain were positive predictors of excellent outcomes while preoperative sensory loss, prior MVD, and previous destructive lesion were negative predictors. Only trigger points were positive predictors for good long term outcomes while bilateral pain was a negative predictor of long term excellent outcomes.

The most striking finding in this study is the poor results for atypical TN. Despite postoperative pain relief in 86% of patients, only 51% have long term relief and only 35% have excellent long term outcomes. Similar to typical TN, memorable onset and trigger points were positive predictors for excellent postoperative relief following MVD for atypical TN. Preoperative sensory loss was a negative predictor for long term pain relief.

These results are consistent with our belief that there is a group of patients along the continuum of typical to atypical TN that may benefit from MVD. We refer to these patients as transitional patients. These patients are characterized as having the constant burning pain of atypical TN but also some components of typical TN such as trigger points for their pain and sudden memorable onsets of their pain. Sensory loss would be more consistent with patients that have progressed further along the continuum.

...glossopharyngeal neuralgia

(from back cover)

success rate of 92%, while 8% experienced no significant change in symptoms after surgery.

We attempted to identify any predictors of long-term success. Long-term relief assessed by direct communication with patients was noted to be complete in 58% of patients and partial in 18%, for a total long-term success rate of 76%.

Predictors of Success

Univariate and multi-variate analyses were performed on presenting symptoms and symptom combinations. If the patient had tongue pain, whether or not any additional symptom was present, he or she had a 50% likelihood of cure. The cure rate was 65% with presence of throat pain. If a patient presented with headache as a prominent component to his or her symptoms, he or she had only a 20% likelihood of cure even when more typical symptoms such as throat or ear pain were also present. 100% of patients presenting with isolated throat pain obtained complete relief after MVD.

Complications

Our rates of CSF leak as well as post-operative cranial nerve palsies are now seen in less than 2% and less than 3% of patients, respectively.

Our analysis of 217 patients undergoing treatment by microvascular decompression for glossopharyngeal neuralgia shows MVD to be an effective treatment modality with a low complication rate. Complete or significant partial relief of pain was experienced immediately by 90% of the 217 patients treated and long-term by 75% of patients in whom follow-up was obtainable. Complete relief off all medication was seen immediately in 67% of patients and long-term in 58% of patients. This procedure appears to be most efficacious for patients presenting with isolated throat pain only.
Hemifacial spasm (HFS) is a rare condition with an annual incidence of less than one per 100,000 people in the United States. Nevertheless, for this small group of patients it can represent a severe functional handicap.

Over the past three decades microvascular decompression (MVD) has proven to be a safe and effective means of treating hemifacial spasm (HFS) with good to excellent long term results in 85% of patients. Over the past decade, Botulinin toxin (Botox®, Allergan Inc.) has gained increasing popularity in the treatment of HFS. Currently, the majority of patients referred to our center have had previous exposure to Botox. Recently, we had noticed an increase in the amount of residual or recurrent HFS concomitant with an increase in the number of patients receiving prior Botox treatment. Typically, this recurrence rate is reported to be between 7-15%. We sought to examine the differences in both overall outcome and subsequent recurrence rate in HFS patients treated with MVD who had previously been exposed to Botox as compared to those who had not.

Eighty-eight patients underwent (MVD) for (HFS) from January 1998 to June 1999 at the University of Pittsburgh. Each patient was asked about improvement in their HFS, timing of improvement (gradual or sudden), recurrence of HFS, timing of recurrence, and resolution of HFS using a functional outcome scale with subjective quantification (0-100%). This continuous scale was broken down into complete improvement (100% reduction in spasm), dramatic improvement (66-99%), significant improvement (33-65%), some improvement (<33%), and preoperative state (0%). For the purposes of this review anything less than either complete resolution (100%) or dramatic improvement (66-99%) was considered as a failure as such a result would not allow the patients to participate in the activities of daily living they deemed important.

Patients were divided into two groups, those who had never been exposed to Botox and those who had previously received Botox.

**Results**

The average duration of symptoms prior to MVD was 7.1 years. Patients commonly sought medical treatment prior to surgical care. Almost 62% of these patients received at least one Botox treatment before presenting for surgery. The Botox users and non-users had similar demographic and clinical characteristics, except that prior Botox users had longer duration of HFS.

**Immediate Outcome**

On postoperative day 1, 96% had no or occasional HFS (96.9% Botox group, 94.4% no Botox group, p>0.1). On postoperative day 2 or 3, 88% had no or occasional spasm (84.4% Botox group, 94.4% no Botox group, p>0.1).
Long-Term Improvement

The average follow-up period from the date of surgery was 13.0 months. Fifty-five percent stated they had complete improvement with another 35% describing dramatic improvement (66-99% reduction in spasm), i.e., able to drive/read unencumbered and comfortable in social situations without the use of concealing glasses. Eighty percent of these patients reported only minor episodic HFS when compared to their preoperative state, quantitatively rating the amount of recurrence as 15% or less when compared to before surgery. Almost 13% reported a 33% or more recurrence of their HFS. The remaining patients reported their recurrence between 15-33%. When recurrence did occur, it did so between 1 day and 10 months postoperatively (average 3.1 months), with most occurring more than 1 month after surgery. Thus though the overall recurrence rate was 34.5%, the incidence of clinically significant recurrence impacting on functional activity was 12.7%.

When the patients with recurrence were questioned about prior Botox exposure the results were as follows. The recurrence rates were 47.1% among the previous Botox users and 14.3% among the non-users (p=0.019). All of the patients with clinically significant recurrence (greater than 33%) had been exposed to Botox. The exposure within this group appeared to be relatively high with a range from 8-40 sessions.

Facial Nerve Function

Facial nerve function by House-Brackman scores was assessed following the MVD procedure. Almost 43% had unchanged postoperative facial nerve function. Almost 39% improved at least one House-Brackman score. Almost 19% had worsened at least one grade from their preoperative House-Brackman score.

Complications

Twenty-seven percent suffered from a Bell's palsy (delayed onset, transient weakness) postoperatively. These were not considered as iatrogenic facial nerve paresis as all patients had near normal facial nerve function immediately following surgery but developed weakness subsequently.

This occurred between 1 day and 6 weeks following surgery (mean 13.6 days) and lasted an average of 12 weeks before functional recovery occurred. All patients recovered. Eighty percent of patients with a Bell's palsy had received Botox prior to MVD, thus making them 3.2 times as likely to develop a Bell's palsy as those who did not receive Botox.

Additional complications following MVD included 7.3% who suffered a CSF leak, 5.5% who had a perioperative wound infection. There were no mortalities within this series. More than 18% reported subjective hearing loss following surgery. Five of these reported partial and 2 complete hearing loss on the operative side. For those reporting partial hearing loss, one had objective audiographic evidence of a deterioration supporting the subjective hearing loss reported postoperatively, one had some change in the audiogram, and the others had no change. Using only this objective data, the rate of perioperative unilateral hearing loss was 5.5% (3.6% complete hearing loss, 1.8% hearing reduction, and all of these patients were prior Botox users).

Discussion

Primary treatment of HFS with Botox has gained increasing popularity with several reports suggesting excellent clinical results. We believe that in addition to the concern of increasing the incidence of recurrence and decreasing the efficacy of MVD in patients with HFS, episodic yet regular Botox exposure may increase the incidence of drug related neurologic deficits such as ptosis (75% incidence in those undergoing at least 10 treatments), diplopia and facial weakness.

Using the information obtained from this review we have considerably changed our approach to the treatment of the over one hundred patients with HFS that we have operated upon since July 1999. In order to reduce the incidence of objective unilateral hearing loss from the 3% reported in this series we have moved to a two-stage approach in the event that intraoperative BAEP waveV during decreases in amplitude by 50% on three separate occasions – “three strikes and you’re out rule.” Using this approach we have had only one documented case of complete unilateral hearing loss during a first time MVD for HFS. The 11% incidence of patients with significant spasm on day 3 was also concerning with regards to long-term outcomes.

We have completely eliminated this complication with no instances of complete facial paralysis in the subsequent series.

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*Hemifacial spasm treatment is aided by “image fusion” where a microscope image (upper right) and endoscope image (circular image) are displayed to a surgeon simultaneously. The microscope is used to position the endoscope safely. The endoscope allows for angled telescopic views with minimal or no retraction. For a sample video of image fusion, please visit our website at [www.neurosurgery.pitt.edu/cranialnerve/disorders/hemispasm.html](http://www.neurosurgery.pitt.edu/cranialnerve/disorders/hemispasm.html).*
Study to examine the benefits of brain bypass surgery

by Howard Yonas, MD

While the words “bypass surgery for the brain” sound exotic and new, we have had the ability to connect arteries from the scalp directly to vessels on the surface of the brain for over 30 years. The procedure won favor in the early 1980’s because a new generation of surgeons trained in micro vascular techniques proved capable of safely making the connection between 1-2 mm arteries. It was clear that some patients, who frequently experienced transient deficits merely by standing up, dramatically benefited from this procedure.

Despite the fact that a bypass procedure is best suited for correcting an insufficient blood supply to the brain, we did not have technology capable of examining cerebral blood flow until the early 1990’s.

Without a rational basis for choosing the ideal patient for bypass surgery a large number of patients underwent this procedure with the hope of preventing future strokes.

In 1980 the National Institutes of Health (NIH) funded the first randomized surgical trial which examined the efficacy of bypass surgery as it was being utilized. Even though the study was well designed, the conclusion that bypass surgery did not make a significant difference over “best medical therapy,” left many physicians doubting the universal application of these conclusions.

Within the last decade two strategies for identifying patients with compromised blood supply have been developed. Both have been shown capable of identifying a group of patients with a significantly increased two-year stroke risk (30% vs 5% for the compromised vs the non-compromised group). One strategy utilizes positron emission tomography (PET) to identify a brain region that is consuming a high percentage of available oxygen (oxygen extraction fraction, OEF). The second strategy involves examining the blood flow response to a challenge induced by a medication normally capable of increasing brain blood flow by over 30%. The extent of flow reserve has been shown to have a relationship to the OEF.

Based upon the above studies, the NIH has accepted a proposal from Dr. Robert Powers, Director of the PET center at Barnes Hospital in St. Louis, to direct a national trial designed to re-examine the benefit of bypass surgery in patients identified as having symptomatic occlusion of one carotid artery. Patients found to have elevation of oxygen extraction following a transient ischemic event or a minor stroke event will be given the opportunity to be randomized to either a superficial temporal to middle cerebral artery bypass or to “best medical therapy.”

While bypass surgery has been shown to be able to increase oxygen availability in some studies and to decrease the incidence of subsequent ischemic events in other studies, the efficacy of this procedure to significantly lessen future stroke events still needs to be proven by the Carotid Occlusion Surgery Study (COSS).

At the University of Pittsburgh, we have pioneered the identification of patients at increased ischemic risk and I will direct the COSS study here. Patients from around the country are likely to travel to the PET facility at UPMC Presbyterian to obtain the required studies because of this center’s expertise with OEF measurements. Dr. Carolyn Meltzer is the director of this facility.

Drs. Lawrence Wechsler, Tudor Jovin and James Gebel are specialists in stroke neurology within the UPMC Stroke Institute who will be part of the team involved in identifying patients for the study and for maintaining their care and follow up during the study.

The study is scheduled to begin in April of 2002 and continue for five years. COSS plans to examine almost 1,000 patients with symptomatic carotid occlusion in order to identify 300 with elevated OEF.

The clinical goal of the study is to show that bypass surgery will reduce the subsequent stroke rate by greater than 50% in this well chosen sub group.
**Albright Honored as Children's Neurosurgery Chair**

The University of Pittsburgh Office of the Provost sponsored a lecture March 14 to inaugurate the endowed Children's Neurosurgery Chair in honor of Dr. A. Leland Albright, professor of neurosurgery and chief of neurosurgery at Children's Hospital of Pittsburgh. Dr. Albright presented the lecture, titled “Neurosurgery and Cerebral Palsy in the 20th Century: Knives, Needles and Neurotransmitters.”

Dr. Albright is a nationally known expert in treating children with movement disorders and spasticity, specifically the involuntary tightness of certain muscles caused by cerebral palsy and severe brain injuries.

**Recent Grant Awards**

- “Neural Stem Cell Based Cytokine Delivery to CNS Tumor Sites and its Combination with Peripheral Vaccines,” Dr. Hideho Okada, MD, PhD from National Brain Tumor Foundation ($335,000). Study to determine whether modification of tumor-microenvironment can improve the efficacy of immunotherapy by local delivery of neural stem cell transfected with granulocyte macrophage-colony stimulating factor.
- “Assessment of Lenticulostriate Occlusion Primate Model of Focal Cerebral Ischemia,” Dr. Edwin Nemoto, PhD from Layton Bioscience, Inc. ($174,123). This study is to determine whether selective occlusion of the lateral lenticulostriate arteries produces a consistent and clinically well-tolerated focal ischemic brain lesion in the rhesus monkey (Macaca mulatta).
- “Data Communication with Implantable Micro Devices,” Dr. Mingui Sun, PhD from National Institute of Neurological Disorders and Stroke ($1,200,988). This biomedical engineering development project aims to establish an information link between implantable devices within the brain and the external computer system for various neural prosthetic and therapeutic applications.
- “Evaluation of MacroPore TS in a Canine Model,” Dr. William C. Welch from Macropore, Inc. ($51,062). This study will evaluate MacroPore TS as an anti-adhesive agent.
- “Signal Transduction Inhibitory Strategies for Glioma Therapeutics,” Dr. Ian Pollack from Wichman Foundation ($40,000).

**Media**

- Dr. Douglas Kondziolka was featured on the WQED-TV (Pittsburgh) news magazine On Q March 13. Dr. Kondziolka discussed his neuron transplant study.

**Announcements**

- Dr. L. Dade Lunsford served as visiting lecturer and professor at Stanford University’s Department of Neurosurgery, February 21-22.
- Dr. Douglas Kondziolka served as visiting professor at the University of Colorado, February 22, and at the State University of New York at Syracuse, March 13-14.
- Dr. Peter Gerszten was awarded the Volker Sonntag Award from the Joint Section on Disorders of the Spine and Peripheral Nerves of the AANS/CNS for $30,000 for his study “Evaluation of the CyberKnife® Stereotactic Radiosurgery System for the Treatment of Spinal Lesions.” Dr. William Welch and members of the Department of Radiation Oncology will serve as co-investigators.
- In May 2002, Dr. Jeffery Balzer, PhD will be installed as the president of the American Society for Neurophysiological Monitoring.
- Dr. P. David Adelson was elected as secretary/treasurer 2002-04 for the Joint Section of Neurotrauma and Critical Care of the American Association of Neurological Surgeons/Congress of Neurological Surgeons.

**Welcome**

Hae-Kwan Park, MD, observing visiting fellow from Korea working with Drs. Amin Kassam and Michael Horowitz; Naren Nathoo, MD, observing visiting fellow from South Africa working with Drs. L. Dade Lunsford and Douglas Kondziolka.

**New Employees**

Kelly Eddy, staff nurse to Dr. Ghassan Bejjani; Cynthia Watkins, clinic receptionist.

**Upcoming Events**

- April 26: Dr. James T. Rutka, professor and chairman for the division of neurosurgery at The Hospital for Sick Children, University of Toronto, will speak as part of the Department of Neurological Surgery's Visiting Lecture Series. The lecture will be held at the Duquesne Club at 8:00 p.m. A reception and dinner will precede the lecture. Deadline for registering is April 24. For more information, please contact Wendy Edwards at (412) 647-0990.
- April 29 - May 3: Principles and Practice of Gamma Knife Radiosurgery. Training course targeted to neurosurgeons, radiation oncologists and physicists interested in Gamma Knife certification. Other course dates for this year are in June, July and September. Contact Charlene Baker at (412) 647-7744 for more information.
- June 1: Functional Gamma Knife Radiosurgery. One-day course targeted at neurosurgeons, radiation oncologists and medical physicists working with a gamma knife radiosurgery unit. Contact Charlene Baker at (412) 647-7744 for more information.
The term glossopharyngeal neuralgia (GPN) has only relatively recently been introduced into medicine, having been first proposed by Harris in 1921 and reported on by Doyle in 1923. Its diagnosis has changed little from a 1927 description by Dandy as “paroxysmal pain frequently brought on by eating and swallowing with involvement of the root of the tongue and pharynx with radiation to the throat and/or deep ear structures.” However, the relative rarity of this condition has made its recognition difficult, often resulting in a significant delay to diagnosis. Once GPN is established, various treatment modalities can be employed, both medical and surgical. At our institution, we employ non-ablative procedures and thus treat GPN by microvascular decompression (MVD) of cranial nerve nine. To determine short and long-term outcomes as well as to identify predictors of success, we undertook a retrospective review of all patients in our database that underwent MVD for GPN.

**Immediate Results**

Microvascular decompression for GPN afforded patients complete immediate relief in 67% of all patients operated upon between 1973 and 2000. An additional 25% obtained partial relief for a total immediate improvement of 92%.

(see glossopharyngeal on page 3)