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NEUROSURGERY

COMMENTARY

Neurosurgery is still one of the fastest evolving areas of medicine. A little more than half a century ago, through the careful observations, shrewd judgment, and meticulous technique of pioneers such as Harvey Cushing and Walter Dandy (to name just a couple), this field gained acceptance. In the 1970s use of the operating microscope and popularization of microsurgical techniques by Gazi Yasargil and others produced excellent results and elevated neurosurgery to a higher level of performance and capability. In the 1980s and 1990s, the introduction of minimally invasive techniques and radiosurgery brought neurosurgery into a new era yet. The field continues to evolve and now with the concept of nano-neurosurgery on the horizon we are contemplating a quantum leap in this specialty.

Reviewing the literature of the last three months one gets a very clear impression of the ever-evolving nature of neurosurgery. Of the abstracts reproduced here, the first one by Gupta et al provides valuable data on the treatment strategy of craniocervical tuberculosis which has been a surgical problem by common opinion. Although their sample size is modest, they show that rigid external fixation may suffice as an effective treatment and obviate the need of surgery. The next abstract on the other hand confirms the observation developed over the last two decades that a disease that was largely medical may have better results with surgical management and may be more feasible: Cohen-Gadol et al from Mayo clinic report the long-term outcome of patients with epilepsy surgery on temporal lobes in cases where seizures were not due to any lesions. In 81% the outcome was excellent - they were either seizure-free or had aura or seizures only transiently on drug withdrawal. About three quarters of these patients were able to maintain excellent status in a 10-year follow-up.

The next three abstracts (Regis et al, Mingione et al, and Soderman et al) point out the feasibility of radiosurgery in neurosurgical problems. These include a randomized controlled trial on the safety and efficacy of radiosurgery for trigeminal neuralgia, observations on the efficacy of gamma knife on the recurrent or residual pituitary macroadenoma, and use of radiosurgery in dural arterio-venous fistulas. Traditionally, all three problems have been surgical but now radiosurgery is emerging as a distinctly feasible alternative. The last three abstracts by Leary et al (Michael Apuzzo, editor of Neurosurgery, is a co-author) point out the future direction in which the field of neurosurgery may show tremendous growth. Nanotechnology may ultimately change this specialty more than any other advances have done so far.

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TUBERCULOSIS OF THE CRANIOVERTEBRAL JUNCTION: IS SURGERY NECESSARY?

OBJECTIVE: Tuberculosis of the craniocervical junction is an uncommon entity and its optimal management remains controversial. In this study, we present the evolution of

management protocol of this disease in our institute in the past 3 decades. **METHODS:** A total of 51 patients with craniocervical junction tuberculosis presenting as

atlantoaxial dislocation from 1978 through 2004 were reviewed. The disease was rated from Stage I to Stage III, depending on the radiological findings. All patients received antitubercular treatment for 18 months. In the initial period of this study (1978-1986), all patients (n = 10) underwent surgery, usually a posterior fusion. In the second period (1987-1998), patients with less severe disease (Stages I and II, n = 14) were managed with external rigid immobilization, whereas patients with severe disease (Stage III, n = 11) underwent either a transoral decompression with or without posterior fusion or posterior fusion alone. More recently (1999-2004), all patients (n = 16) in all stages

(Stages I-III) have been managed without surgery by a rigid external immobilization. **RESULTS:** Except for two patients who died (one because of miliary tuberculosis, the other because of acute hydrocephalus), clinical recovery occurred in all. Follow-up imaging demonstrated radiological healing as well, with regrowth of the destroyed bone. **CONCLUSION:** The mainstay of management of tuberculosis of the craniovertebral junction is prolonged antitubercular treatment with a rigid external immobilization. Surgery is not necessary, even in patients with advanced stages of disease. Complete clinical and radiological healing occurs in all patients with conservative treatment.

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LONG-TERM OUTCOME OF EPILEPSY SURGERY AMONG 399 PATIENTS WITH NONLESIONAL SEIZURE FOCI INCLUDING MESIAL TEMPORAL LOBE SCLEROSIS

OBJECT: The authors reviewed the long-term outcome of focal resection in a large group of patients who had intractable partial nonlesional epilepsy, including mesial temporal lobe sclerosis (MTS), and who were treated consecutively at a single institution. The goal of this study was to evaluate the long-term efficacy of epilepsy surgery and the preoperative factors associated with seizure outcome. **METHODS:** This retrospective analysis included 399 consecutive patients who underwent epilepsy surgery at Mayo Clinic in Rochester, Minnesota, between 1988 and 1996. The mean age of the patients at surgery was 32 +/- 12 years (range 3-69 years), and the mean age at seizure onset was 12 +/- 11 years (range 0-55 years). There were 214 female (54%) and 185 male (46%) patients. The mean duration of epilepsy was 20 +/- 12 years (range 1-56 years). The preceding values are given as the mean +/- standard deviation. Of the 399 patients, 237 (59%) had a history of complex partial seizures, 119 (30%) had generalized seizures, 26 (6%) had simple partial seizures, and 17 (4%) had experienced a combination of these. Preoperative evaluation included a routine and video-electroencephalography recordings, magnetic resonance imaging of the head according to the seizure protocol, neuropsychological testing, and a sodium amobarbital study. Patients with an undefined epileptogenic focus and discordant preoperative studies underwent an intracranial study. The mean duration of follow up was 6.2 +/- 4.5 years (range 0.6-15.7 years). Seizure outcome was categorized based on the modified Engel

classification. Time-to-event analysis was performed using Kaplan-Meier curves and Cox regression models to evaluate the risk factors associated with outcomes. Among these patients, 372 (93%) underwent temporal and 27 (7%) had extratemporal resection of their epileptogenic focus. Histopathological examination of the resected specimens revealed MTS in 113 patients (28%), gliosis in 237 (59%), and normal findings in 49 (12%). Based on the Kaplan-Meier analysis, the probability of an Engel Class I outcome (seizure free, auras, or seizures related only to medication withdrawal) for the overall patient group was 81% (95% confidence interval [CI] 77-85%) at 6 months, 78% (CI 74-82%) at 1 year, 76% (CI 72-80%) at 2 years, 74% (CI 69-78%) at 5 years, and 72% (CI 67-77%) at 10 years postoperatively. The rate of Class I outcomes remained 72% for 73 patients with more than 10 years of follow up. If a patient was in Class I at 1 year postoperatively, the probability of seizure remission at 10 years postoperatively was 92% (95% CI 89-96%); almost all seizures occurred during the 1st year after surgery. Factors predictive of poor outcome from surgery were normal pathological findings in resected tissue (p = 0.038), male sex (p = 0.035), previous surgery (p < 0.001), and an extratemporal origin of seizures (p < 0.001). **CONCLUSIONS:** The response to epilepsy surgery during the 1st follow-up year is a reliable indicator of the long-term Engel Class I postoperative outcome. This finding may have important implications for patient counseling and postoperative discontinuation of anticonvulsant medications.

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PROSPECTIVE CONTROLLED TRIAL OF GAMMA KNIFE SURGERY FOR ESSENTIAL TRIGEMINAL NEURALGIA

OBJECT: Stereotactic radiosurgery is an alternative to conventional surgery for the treatment of trigeminal neuralgia. The authors conducted a prospective evaluation of the safety and efficacy of this method in a large series of patients. **METHODS:** A total of 100 patients presenting with trigeminal neuralgia were treated and followed up for a minimum of 12 months. The mean age was 68.2 years; 54 patients were male, and 46 were female. Seven had a history of multiple sclerosis, and 42 had already received conventional surgical treatment for trigeminal neuralgia. The intervention consisted of gamma knife surgery to the retrogasserian cisternal portion of the fifth cranial nerve. The median dose used at the maximum was 85 Gy (range 70-90 Gy). The number and intensity of pain attacks were recorded by the patient from 3 months before radiosurgery to a minimum of 12 months after treatment. Before and a

minimum of 12 months after treatment, the patient completed a quality-of-life questionnaire. Neurological examination and quantitative sensory testing to evaluate sensory perception were performed by an independent neurologist over this same time period. At the last visit 83 of 100 patients were reported to be pain free. Fifty-eight of these 83 patients had stopped taking medication during the study. All quality-of-life parameters were improved ($p < 0.001$). Six patients reported facial paresthesia, and four patients reported hypesthesia. These symptoms were classified as mild. None of the complications reported for other techniques were observed. **CONCLUSIONS:** Radiosurgery is a safe and effective alternative treatment for trigeminal neuralgia and is associated with a particularly low rate of hypesthesia.

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GAMMA SURGERY IN THE TREATMENT OF NONSECRETORY PITUITARY MACROADENOMA

OBJECT: The authors report on a retrospective analysis of the imaging and clinical outcomes following gamma surgery in 100 patients with nonsecretory pituitary macroadenoma. **METHODS:** Between June 1989 and March 2004, 100 consecutive patients with nonsecretory pituitary macroadenoma were treated at the Lars Leksell Center for Gamma Surgery, University of Virginia Health System (Charlottesville, VA). Ninety-two patients had residual or recurrent macroadenoma following one or more surgical procedures. In eight patients, gamma surgery was the primary treatment. Ten patients received conventional fractionated radiotherapy before the gamma surgery. Sixty-nine patients required hormone replacement therapy for one or more deficits before gamma knife treatment. Peripheral doses between 5 and 25 Gy (mean 18.5 Gy) were administered. Imaging and endocrinological follow-up evaluations were performed in 90 patients; these studies ranged from 6 to 142 months (mean 44.9 months) and 6 to 127 months (mean 47.9 months), respectively. Tumor

volume decreased in 59 patients (65.6%), remained unchanged in 24 (26.7%), and increased in seven (7.8%). The minimal effective peripheral dose was 12 Gy; peripheral doses greater than 20 Gy did not seem to provide additional benefit. Of 61 patients with a partially or fully functioning pituitary gland and follow-up data, 12 (19.7%) suffered new hormone deficits following gamma surgery. In patients with endocrinological follow-up data that had been collected over more than 2 years, the rate of new deficits was 25%. No neurological morbidity or death was related to treatment. **CONCLUSIONS:** Current experience suggests that gamma surgery is an appropriate means of managing recurrent or residual nonsecretory pituitary macroadenoma following microsurgery and a primary treatment in selected patients. To evaluate definite rates of recurrence and new endocrine deficiencies, long-term follow-up studies are needed.

GAMMA KNIFE SURGERY FOR DURAL ARTERIOVENOUS SHUNTS: 25 YEARS OF EXPERIENCE

OBJECT: The aim of this study was to assess the clinical efficacy of gamma knife surgery (GKS) in the treatment of dural arteriovenous shunts (DAVSs). **METHODS:** From a database of more than 1600 patients with intracranial arteriovenous shunts that had been treated with GKS, the authors retrospectively and prospectively identified 53 patients with 58 DAVSs from the period between 1978 and 2003. Four patients were lost to follow-up evaluation and were excluded from the series. Thus, this study is based on the remaining 49 patients with 52 DAVSs. Thirty-six of the shunts drained into the cortical venous system, either directly or indirectly, and 22 of these were associated with intracranial hemorrhage on patient presentation. The mean prescription radiation dose was 22 Gy (range 10-28 Gy). All patients underwent a clinical follow-up examination. In 41 cases of DAVS a follow-up angiography study was performed. At the 2-year follow-up visit, 28 cases (68%) had angiographically proven obliteration of the shunt and in another 10 cases (24%) there was significant flow regression. Three shunts remained unchanged. There was one immediate minor complication related to the

administration of radiation. Furthermore, one patient had a radiation-induced complication 10 years after treatment, although she recovered completely. There was one posterior fossa bleed 2 months after radiosurgery; a hematoma, as well as a lesion, was evacuated, and the patient recovered uneventfully. A second patient had an asymptomatic occipital hemorrhage approximately 6 months postradiosurgery. The clinical outcome after GKS was significantly better than that in patients with naturally progressing shunts ($p < 0.01$, chi-square test); figures on the latter have been reported previously. **CONCLUSIONS:** Gamma knife surgery is an effective treatment for DAVSs, with a low risk of complications. Major disadvantages of this therapy include the time elapsed before obliteration and the possibility that not all shunts will be obliterated. Cortical venous drainage from a DAVS, a risk factor for intracranial hemorrhage, is therefore a relative contraindication. Consequently, GKS can be used in the treatment of both benign DAVSs with subjectively intolerable bruit and aggressive DAVSs not responsive to endovascular treatment or surgery.

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TOWARD THE EMERGENCE OF NANONEUROSURGERY: PART I--PROGRESS IN NANOSCIENCE, NANOTECHNOLOGY, AND THE COMPREHENSION OF EVENTS IN THE MESOSCALE REALM

Since its original conception in 1959, the notion of nanotechnology and its potential ramifications have not only created fascination, but also intense scientific effort and scrutiny. Currently, research activities are being principally conducted in mesoscale, the realm between nanoscale and macroscale, with the rudiments of nanoscience being defined in realities and principles that will determine activities and discoveries in the future. This paper reviews and discusses the evolution of nanoscience, its contemporary status, and the discoveries that currently constitute the main components of the body of knowledge

from a neurosurgical perspective. Specific attention is given to the developments in imaging, fabrication, nanostructures, nanoelectromechanical systems, molecular manufacturing, nanocomputation, and emerging physical and chemical concepts in mesoscale, as they will establish foundations for the realization of nanomedicine and nanoneurosurgery.

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**TOWARD THE EMERGENCE OF NANONEUROSURGERY: PART III--NANOMEDICINE:
TARGETED NANOTHERAPY, NANOSURGERY, AND PROGRESS TOWARD THE REALIZATION OF
NANONEUROSURGERY**

The notion of nanotechnology has evolved since its inception as a fantastic conceptual idea to its current position as a mainstream research initiative with broad applications among all divisions of science. In the first part of this series, we reviewed the structures and principles that comprise the main body of knowledge of nanoscience and nanotechnology. In the second part, we discussed applications of nanotechnology to the emerging field of nanomedicine, with specific attention on medical diagnostics and imaging. This article further explores the applications of nanotechnology to nanomedicine. Specific attention is given to developments in therapeutic modalities, including

advanced drug delivery systems and targeted nanotherapy, which will form the basis for the treatment arm of mature nanomedicine. A variety of modalities are discussed, including polymeric nanoparticles, micelles, liposomes, dendrimers, fullerenes, hydrogels, nanoshells, and smart surfaces. Applications of nanotechnology to nanosurgery and nanoneurosurgery are presented. Femtosecond laser systems, nanoneedles, and nanotweezers are presented as technologies that are operational at the nanoscale level and have the potential to revolutionize the practice of neurosurgery in a profound and momentous way.