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NEUROSCIENCES UPDATE

NEUROLOGIC SURGERY AND CLINICAL NEUROLOGY NEWS



Mayo Clinic Intracranial Aneurysm Practice Specializes in Medical, Surgical, Endovascular Treatments



Fredric B. Meyer, MD

Intracranial aneurysms are common disorders, occurring in approximately 2% of the general population. They can be either asymptomatic or symptomatic, presenting acutely with a subarachnoid or cerebral hemorrhage. When an aneurysm ruptures, it is fatal approximately 40% of the time.

Because of this high potential mortality, expert, immediate, and comprehensive aneurysm management is a medical imperative. Explains Fredric B. Meyer, MD, neurologic surgeon at Mayo Clinic in Rochester: "If a patient survives the initial hemorrhage, then the optimal outcome is obtained by a multispecialty approach that commences in the emergency department and extends through the time of treatment of the lesion, subsequent management in the intensive care unit, and then recovery in a rehabilitation unit if necessary."

Dr Meyer adds that optimal outcomes of all aneurysm cases—not just ruptures—are best achieved through an advanced multidisciplinary team approach. Among the larger referral practices for the treatment of aneurysm in North America, Mayo Clinic neurosciences physicians manage all manifestations of this complex clinical presentation. Team members have special expertise and extensive experience treating all forms, especially skull base, posterior circulation, and giant aneurysms, and can quickly apply the most effective and least invasive treatment. The severity of the health threat depends on many

variables, including size, location, patient age, and prior neurologic history. "Hence, there are differences between small, asymptomatic aneurysms in the anterior circulation compared with similar-sized aneurysms in the posterior circulation or large, complex giant aneurysms," Dr Meyer says. "Accordingly, not all aneurysms necessarily require treatment. Furthermore, the risks of intervention must be balanced against the predicted natural history of the aneurysm if left untreated."

To Treat or Observe?

When a patient is referred to the Mayo Clinic Cerebrovascular Clinic for treatment of an intracranial aneurysm, the first step is to investigate whether to treat or observe the aneurysm. When an aneurysm is large or symptomatic or when the patient has a history of subarachnoid hemorrhage, treatment usually is advocated because these characteristics place the patient at greater risk of hemorrhage, especially in the posterior circulation (Figure 1). However, in older patients who harbor a small asymptomatic aneurysm, proceeding with treatment poses a more difficult question. Recent prospective clinical

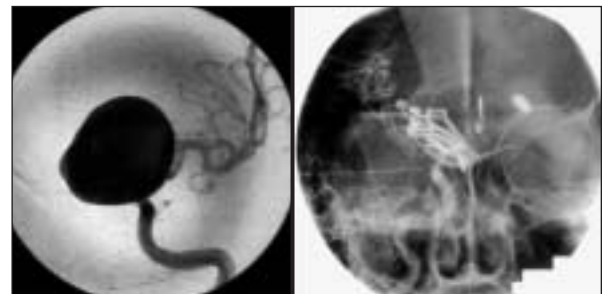


Figure 1. Giant cavernous intracranial aneurysm. *Left, Before treatment. Right, After treatment by direct clipping.*

Inside This Issue

- Pituitary Tumors:
Endoscopic Transnasal
Surgery, a Mayo Clinic
Neuroendocrinology
Specialty 3
- Stereotactic Radiosurgery:
An Effective Alternative
to Open Surgery for
Intracranial Disorders. . . 5
- Neurosurgical Management
of Refractory Partial
Epilepsy 6
- Physician Directory. 8

trials suggest that aneurysms smaller than 7 mm in the anterior circulation have a lower risk of hemorrhage. Therefore, the decision to treat also must take into account patient age, the presence of comorbid conditions, and neurologic function. Sometimes, the safer approach is observation only.

Surgery

In direct surgical repair with the patient under general anesthesia, the aneurysm is approached through a craniotomy. The advantages of the surgical approach are that the surgeon can visualize the aneurysm, and treatment is most often definitive and curative. The disadvantages are that surgery is invasive, carries the risks of any invasive procedure, and requires 3 to 5 days of recovery time in the hospital.

Endovascular Obliteration

Coil embolization is performed by an interventional team. A catheter is passed through the femoral artery into the cerebral circulation, and a thrombogenic wire coil is inserted into the aneurysm where it is detached from the guide and left in place. Sometimes balloons or stents are used with the coils.

The advantage of endovascular treatment is that it is less invasive than direct surgery and therefore generally more easily tolerated by patients. Early data suggest that the results are good. A disadvantage of endovascular treatment is that the aneurysm may not be obliterated completely. This technique achieves complete aneurysm obliteration in about 60% to 70% of cases. The long-term durability of coil embolization is uncertain. At Mayo Clinic, all patients who undergo endovascular aneurysm occlusion procedures are followed at regular intervals to ensure that there is no recurrence.

Combined Treatment

Some complex aneurysms are difficult to treat and require advanced surgical and endovascular skills. In addition to size, these lesions often have broad necks that incorporate the origin of perforators or major blood vessels. Sometimes these aneurysms are dochlioectatic, a term used to describe giant fusiform aneurysms of a major blood vessel, most commonly the internal carotid, middle cerebral, basilar, or posterior cerebral arteries. Direct occlusion of a fusiform aneurysm by default would cause loss of the parent blood vessel.

In these circumstances, straightforward clipping or endovascular occlusion is often not an option because of the risk of stroke. Intervention often requires advanced techniques such as intracranial vascular reconstruction using microsurgical techniques, bypass surgery, or resection of the aneurysm under deep hypothermia (Figure 2). A final alternative is a combined interventional surgical approach in which an intracranial bypass graft is constructed first, followed by endovascular proximal vessel occlusion or embolization (Figure 3).

The Continuum of Care

Patients who undergo treatment for aneurysms that have hemorrhaged or for complex aneurysms often require special care in the neurology intensive care unit. Patients are aggressively treated to avoid potential sequelae of aneurysmal subarachnoid hemorrhage, including hydrocephalus, vasospasm, and cardiopulmonary complications," Dr Meyer explains. After recovery, all patients are seen in the Cerebrovascular Clinic to make sure they have no delayed complications. For incompletely obliterated aneurysms, a follow-up plan is developed to watch for possible aneurysm regrowth.

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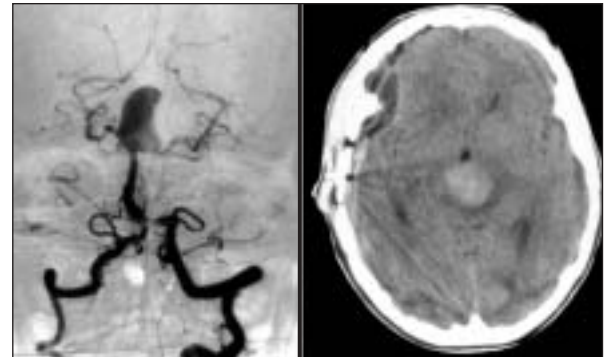


Figure 2. Giant basilar aneurysm treated by direct clipping under deep hypothermia.

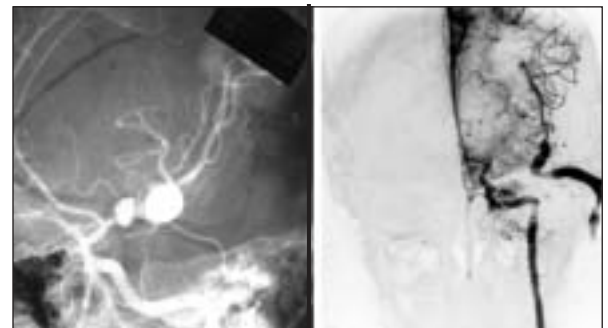


Figure 3. A fusiform middle cerebral artery aneurysm. Left, Before treatment. Right, After treatment by saphenous vein bypass and trapping.

Pituitary Tumors: Endoscopic Transnasal Surgery, a Mayo Clinic Neuroendocrinology Specialty



John L. D. Atkinson, MD

Tumors of the pituitary gland are uncommon and rarely cancerous. However, these characteristics do not lessen the need for physician vigilance. "Pituitary tumors typically require swift and immediate evaluation and treatment because of the pivotal role the gland plays in normal biologic functioning and its critical anatomic placement next to the brain," says Mayo Clinic neurologic surgeon John L. D. Atkinson, MD, who specializes in pituitary gland surgery. Left untreated, pituitary tumors can disrupt growth and vision and, in rare instances, cause death.

Mayo Clinic neuroendocrinology surgeons have contributed to refining state-of-the-art surgical treatments for pituitary disorders. Says Dr Atkinson: "The cross-disciplinary training of our large, integrated multi-specialty practice provides neuroendocrinologic expertise in diagnosis and medical, surgical, and radiologic management of pituitary masses in both adults and children."

Transnasal Endoscopic Surgery

Located as it is within the sella turcica, the pituitary gland is not readily accessible. Since the 1960s, the standard surgical practice for most pituitary tumors has been via the sublabial transseptal approach (Figure 1). In recent years, the minimally invasive alternative approach of endoscopic transnasal pituitary surgery has yielded excellent results and reduced patient discomfort. Postoperative recover now usually requires only an overnight hospital stay. Adds Dr Atkinson: "At our institution, we have elected to use the nasal endoscope only for access to the sella turcica. We use the operating microscope for tumor removal."

The nasal endoscopic approach offers the advantage of entry through a nasal opening and therefore does not require an incision. With the patient under general anesthesia, the nasal endoscope is used to identify the sphenoid ostium. Next, the nasal mucosa is incised and mobilized, and the posterior vomer is removed. Bone punches are used to further expose the sphenoid sinus. The operating microscope is then brought into the field, and the resection is performed as it is in the sublabial transseptal approach—

only through a smaller opening, approximately 10° off center (Figure 2).

Results

In 1999, Dr Atkinson and his colleagues compared outcomes in 26 patients who underwent endoscopic transnasal surgery with 44 who had sublabial transseptal surgery. Says Dr Atkinson: "Because of markedly less nasal trauma with the endoscopic approach, patients experienced significantly less pain and discomfort in the first 2 weeks postoperatively, and the amount of tumor removed was the same in both groups."

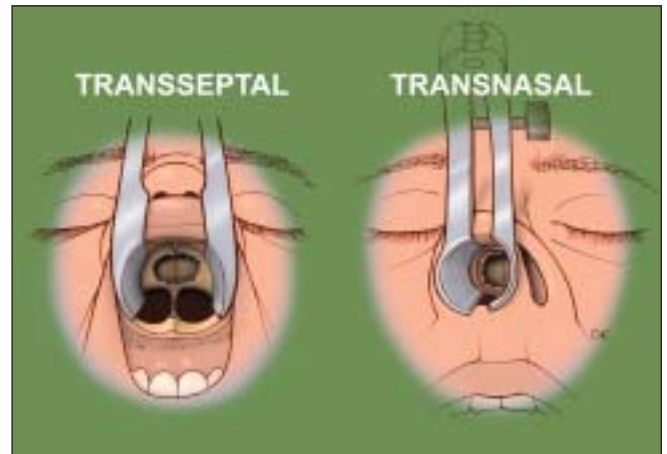


Figure 1. Frontal view of the surgical approaches used in the sublabial transseptal and endoscopic transnasal procedures. (From *Mayo Clin Proc.* 1999;74:661-670.)

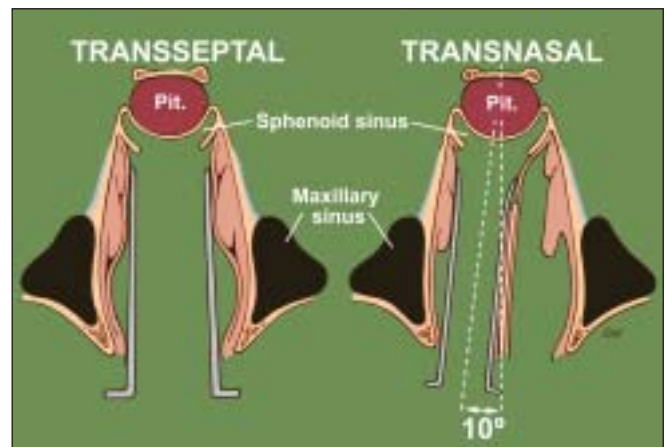


Figure 2. A transverse view of the 2 surgical approaches used. Note the smaller surgical field, angled approximately 10° off center in the endoscopic transnasal approach. Pit., pituitary. (From *Mayo Clin Proc.* 1999;74:661-670.)

Advantages and Disadvantages

The advantages of the endoscopic transnasal approach are that it minimizes patient discomfort, avoids nasal complications, and reduces recovery time. The endoscopic approach has potential disadvantages as well. Some tumors are so large they cannot be successfully removed endoscopically. Because the approach to the sella through a nostril is approximately 10° off center and visibility is reduced, this technique requires a skilled and experienced neurosurgeon to avoid complications.

Disorders Within the Sella Turcica

Approximately 5% to 10% of sella abnormalities considered for surgery are not true pituitary tumors. The sella is a challenging anatomic area because it crosses the boundary of the pharynx, the brain, and the skull base. As a result, an array of tumors can be confused with tumors in the area of the sella, but in fact, some are not true tumors of the gland itself.

Distinguishing between other sella tumors and pituitary tumors is important because management depends on precise diagnosis. Making the clinical diagnosis requires experts in multiple fields, especially neuroradiology.

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Excess Growth Hormone

About 1 in 100 patients presents with excess growth hormone that is not from the pituitary gland but originates elsewhere in the body. Because there can be ambiguity related to pituitary disorders, Mayo Clinic pituitary specialists are often called upon to offer second opinions in an effort to help patients and their clinicians sort out the correct diagnosis.

Technology and the Team

Mayo Clinic neuroendocrinology surgeons excel in the treatment of pituitary disease and tumors,

especially complicated cases in highly critical anatomic areas or in very young patients. “A young person with a pituitary tumor needs expert care at the first medical encounter because of the central role the pituitary gland plays in growth,” Dr Atkinson says. “Delay in treatment could put the patient at risk of suffering stunted growth, reduced life span, or impaired vision if the nerves of the eye are involved and treatment is managed poorly.”

Recent improvements in endoscopic technology and practices have enabled most advanced neurosurgical centers to safely offer this procedure. As a result, it is becoming the treatment of choice for most surgical pituitary cases. Studies show high-volume practices yield the best surgical results because the continual performance of the procedure hones skills.

Mayo Clinic patients receive care from a fully integrated team of neuroendocrinology experts. Says Dr Atkinson: “Our excellent results with the technically challenging endoscopic transnasal procedure are a direct result of this interdisciplinary team approach.”

The multispecialty team comprises experts in different but related medical fields who are brought together by the demands of the patient’s condition. Each team member applies unique skills to the same patient problem and disease context. The multispecialty team is important to optimal pituitary patient outcome because pituitary pathology is extraordinarily diverse. For example, some disorders may look similar radiographically—for example, adenohypophysitis, Rathke cleft cysts, meningiomas, or craniopharyngiomas—but their treatments are markedly different. “Expert training in multiple disciplines is required to make the best diagnostic and management decisions,” Dr Atkinson says.

Stereotactic Radiosurgery: An Effective Alternative to Open Surgery for Intracranial Disorders



Bruce E. Pollock, MD

Stereotactic radiosurgery is an advanced noninvasive surgical technique that uses various devices (such as the Leksell Gamma Knife) to deliver a precise, high dose of single-fraction radiation to an image-defined target. It is an outpatient procedure performed with the patient under local anesthesia and requires virtually no recovery time. Worldwide, an estimated 20,000 patients undergo stereotactic radiosurgery each year.

Mayo Clinic neurosurgeons with specialty training in this area have been performing stereotactic radiosurgery in Rochester since January 1990. They have obtained excellent results in the 2,800 radiosurgical procedures performed since then. The procedure is now an integral part of neurosurgery and radiation oncology practice at Mayo Clinic.

Says Bruce E. Pollock, MD, consultant in neurologic surgery and director of the radiosurgery program at Mayo Clinic: "When performed at advanced medical centers that have extensive experience with the procedures and technologies, stereotactic radiosurgery is a viable—and can be the preferred—alternative to conventional open surgery."

Most patients treated with stereotactic surgery have intracranial lesions, although it may be used elsewhere in the body. The procedure is used to treat both malignant and benign tumors and vascular malformations such as arteriovenous malformations (AVMs) (Figure). Says Dr Pollock: "An AVM causes progressive blockage of the involved blood vessels, and for many patients, stereotactic radiosurgery is the only reasonable management option."

Trigeminal neuralgia is another condition for which radiosurgery has been an effective treatment.

Quality Assurance
Misapplications of therapeutic ionizing radiation in either amount or target or to the wrong patient are required by law to be reported to the US Nuclear Regulatory Commission as a "radiation-related medical event."

This reporting requirement provides a convenient measure for evaluating the expertise and care with which a given medical center performs stereotactic radiosurgery.

At Mayo Clinic, only 1 of 2,800 patients treated during the past 13 years has incurred a clinically insignificant minor error in which the amount of radiation delivered varied by an extremely small amount. "Given that there have been approximately 17,000 patient positionings during this interval, this record is a testament to our ongoing quality assurance efforts," Dr Pollock says. "We believe our safety precautions are second to none."

In addition to the extensive experience that comes with a large stereotactic radiation practice, Mayo Clinic maintains a computer database and film library of every patient and procedure.

Indications and Advantages

Stereotactic radiosurgery is used to treat benign tumors (eg, schwannomas, meningiomas, and pituitary adenomas), malignant tumors (both primary and metastatic), vascular malformations (eg, AVMs and dural arteriovenous fistulas), and functional disorders (eg, trigeminal neuralgia). Each patient typically experiences 1 or more movements in and out of a special machine that focuses high-intensity radiation to the target area. Each movement directs the radiation to a different portion of the target. Radiation applied to the target tissue disrupts the integrity of the DNA so that tumors are unable to divide and grow. "Although stereotactic radiosurgery does stop tumors from getting bigger, it does not do so rapidly," Dr Pollock

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Left, Arteriovenous malformation (AVM) before radiosurgery. Right, Angiogram 3 years later showing complete obliteration (cure) of the AVM.

notes. “Patients should expect results over months to years.” Because this outcome may be different from their expectations, preprocedure counseling of patients is often helpful.

The advantages of this approach are effective results, limited risk of infection, and fast recovery. Compared with conventional open surgery, stereotactic radiosurgery can be 30% to 70% less expensive. Lower direct and indirect costs affect both the patient and society.

Contraindications and Disadvantages

A very large lesion or tumor—3.0 to 3.5 cm—is inappropriate for stereotactic radiosurgery and typically requires an open operative procedure to make space and relieve the pressure. Between 30% and 40% of cases referred for stereotactic radiosurgery are directed to surgical resection or outpatient radiotherapy.

With only 20 to 30 years of data on this procedure, it is not known definitively how durable the results are. Questions remain to be answered such as, “Will the tumors remain contained and cease to grow for the life expectancy of patients?” In view of this point, the age of the patient may help determine whether stereotactic radiosurgery or conventional resection is the correct treatment approach; ie, younger patients would have a greater need for durable results than would older patients.

Stereotactic surgery poses a slight risk of radiation-induced tumors—about 1 in 10,000 patients develops a second tumor. Even though the risk is small, it should be discussed fully with patients.

Research From the Stereotactic Radiosurgery Center

Recently, Dr Pollock collaborated with colleagues from the University of Pittsburgh to develop a radiosurgery-based AVM grading system to predict patient outcomes after stereotactic radiosurgery for AVMs. Unlike the Spetzler-Martin grading system, designed to predict outcomes after surgical removal of AVMs, the radiosurgery-based system was designed to suit the unique concerns of radiosurgery.

Using 3 variables (AVM size, patient age, and AVM location), the grading system allows physicians to predict in advance the likely success rate of radiosurgery for an AVM procedure in an individual patient. “For example, younger patients with small AVMs have more than a 90% chance of AVM cure without new neurologic deficits,” Dr Pollock says. “Conversely, older patients with larger AVMs may only have a 50% chance of a similar outcome.” Publication in the February issue of the *Journal of Neurosurgery* on radiosurgery of deeply located AVMs describes the utility and predictive power of this system.

Neurosurgical Management of Refractory Partial Epilepsy



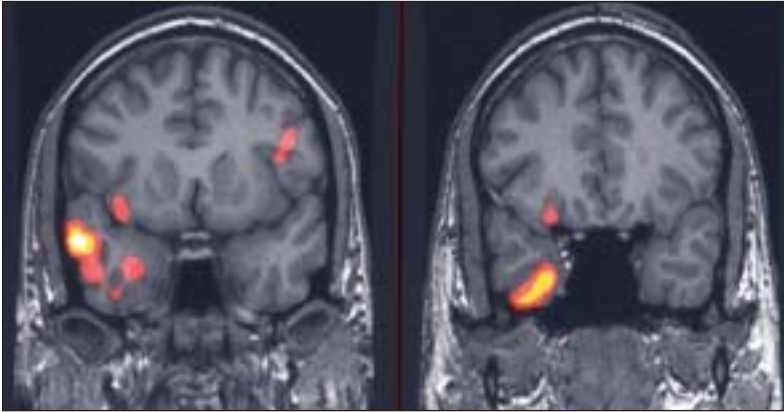
Gregory D. Cascino, MD, Fredric B. Meyer, MD, W. Richard Marsh, MD

In patients with partial epilepsy, seizures originate from a specific region of the brain as opposed to generalized seizure activity that involves both cerebral hemispheres at onset. Partial epilepsy is the most common seizure disorder, affecting more than 1 million patients in the United States.

Seizures are produced by the abnormal excitability and excessive discharge of neurons. Disturbances in these areas may be biochemical or consist of microscopic or macroscopic structural abnormalities or lesions.

The most frequently occurring type of seizure in adults is a complex partial seizure that originates in the mesial temporal lobe. Its optimal management requires a comprehensive team approach, says Gregory D. Cascino, MD, chair of the Mayo Clinic Division of Epilepsy in the Department of Neurology. “Because of the complex etiology of seizures, multiple advanced neuroimaging techniques are needed to discern the underlying pathology and the site of seizure onset. Obtaining this information is vital to successful treatment,” Dr Cascino says.

Dr Cascino notes that a patient’s early response to antiepileptic drug therapy is highly predictive of its ultimate success as a treatment approach. If patients have not experienced seizure remission with medical therapies within 5 years of diagnosis,



SISCOM study scans showing epileptogenic zone of patients with non-substrate-directed partial epilepsy. The methods used for SISCOM at Mayo Clinic are particularly helpful in determining alterations in localized cerebral blood flow, changes intimately associated with the epileptogenic zone.

they are unlikely to do so. “In fact, an estimated 30% to 40% of patients with partial epilepsy suffer from seizures that do not respond adequately to medication,” Dr Cascino says. This form of the disorder may be referred to as “intractable epilepsy” if the seizures are disabling and associated with an enormous physical, social, and emotional burden.

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Why Consider Surgery?

Surgery should be considered when the seizure disorder, its medical treatment, or both seriously affect daily living. For example, common limits that patients with intractable partial epilepsy encounter are the inability to legally drive a motor vehicle or to reliably and professionally pursue a career.

Seizures associated with loss of consciousness, postural tone, or recurrent episodes are especially disabling and often prompt referral for evaluation and possible surgery.

In evaluating patients for surgery, salient conditions must be considered such as the disabling effect of the seizures before surgical treatment, frequency of seizing activity, types of seizures, comorbid conditions, psychosocial effects of the disease, and underlying disease.

Patients with medial temporal lobe epilepsy and lesional epilepsy are generally considered excellent candidates for surgery because these syndromes may be surgically remediable; ie, these individuals are rendered seizure-free.

Frequency of seizures is not as meaningful a measure as might be assumed, Dr Cascino says. “Most patients with medically refractory partial seizures of temporal lobe origin experience several seizures—2 to 4—a month. All too often physicians are satisfied with this level of control if the generalized tonic-clonic seizures are medically controlled. However, even 1 seizure per month may radically and negatively affect a person’s quality of life.” In

addition, the continued presence of psychomotor seizure activity may expose the patient to chronic antiepileptic drug toxicity. These are the factors to take into account when considering surgery for a patient with intractable partial epilepsy.

Potential treatment options for intractable partial epilepsy include antiepileptic drug therapy, vagus nerve stimulation, and epilepsy surgery. Of these, surgical treatment for intractable partial epilepsy is more effective than other forms of therapy in reducing seizure activity.

Substrate-Directed Syndromes

The hallmark pathology of medial temporal lobe epilepsy is mesial temporal sclerosis. In select patients with intractable temporal lobe epilepsy, surgery is more effective than medical therapy.

Patients with lesional epilepsy often have a mass that can be surgically excised. It may be a primary brain tumor, vascular anomaly, or malformation of cortical development (MCD). Commonly encountered during surgery in patients with lesional epilepsy are low-grade glial neoplasm, cavernous hemangioma, and focal cortical dysplasia.

Approximately 80% of patients with unilateral mesial temporal sclerosis, low-grade glial neoplasm, or cavernous hemangioma are rendered seizure-free after surgical treatment. More than 90% of patients with these pathologic findings have an excellent surgical outcome, experiencing only occasional auras or rare, nondisabling seizures. Patients with focal cortical dysplasia or other MCDs face less favorable surgical outcomes.

Non-Substrate-Directed Syndromes

Epilepsy characterized by localization-related seizures and normal MRI studies is classified as non-substrate-directed partial epilepsy. The anatomic focus of the epileptogenic zone in these patients commonly involves the neocortex, particularly the extrahippocampus. The most frequent area of seizure onset in patients with neocortical nonlesional partial epilepsy is the frontal lobe. Surgical findings include gliosis, focal cell loss, MCD, or no histopathologic alteration.

The anatomic region of seizure onset may be a continuum in these patients. As a result of this lack of discrete focus for the epileptogenic zone, it is harder for neurosurgeons to achieve complete resection of the epileptogenic zone. A large resection increases the likelihood of rendering the patient seizure-free, but it also increases the potential for operative morbidity.

Imaging Advances

To more precisely define the epileptogenic zone of patients with non-substrate-directed partial

epilepsy, Mayo Clinic neuroscientists have participated in the development of a functional neuroimaging procedure, SISCOM (Figure).

SISCOM is an advanced imaging technique that uses computer-aided subtraction of interictal from ictal single photon emission computed tomography (SPECT) coregistered to 3-dimensional MRI. Explains Dr Cascino: "The methods used for SISCOM at Mayo Clinic are particularly helpful in determining alterations in localized cerebral blood flow—changes intimately associated with the epileptogenic zone." "The SISCOM-imaged region of blood flow alteration functions as a surrogate for localization of the epileptogenic zone independent of the pathologic finding.

Although SISCOM improves surgical outcomes because it helps more precisely define the area to be excised, it has disadvantages too—the need for hospitalization and long-term electroencephalographic monitoring, the use of radioisotopes for 2 imaging procedures, and the prerequisite for patients to have habitual seizure activity.

The results of a Mayo Clinic study in 2000 underscore the important contributions SISCOM technology can make to the treatment of non-substrate-directed epilepsy. Approximately 75% of the 36 patients evaluated had an abnormality localized by SISCOM.

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