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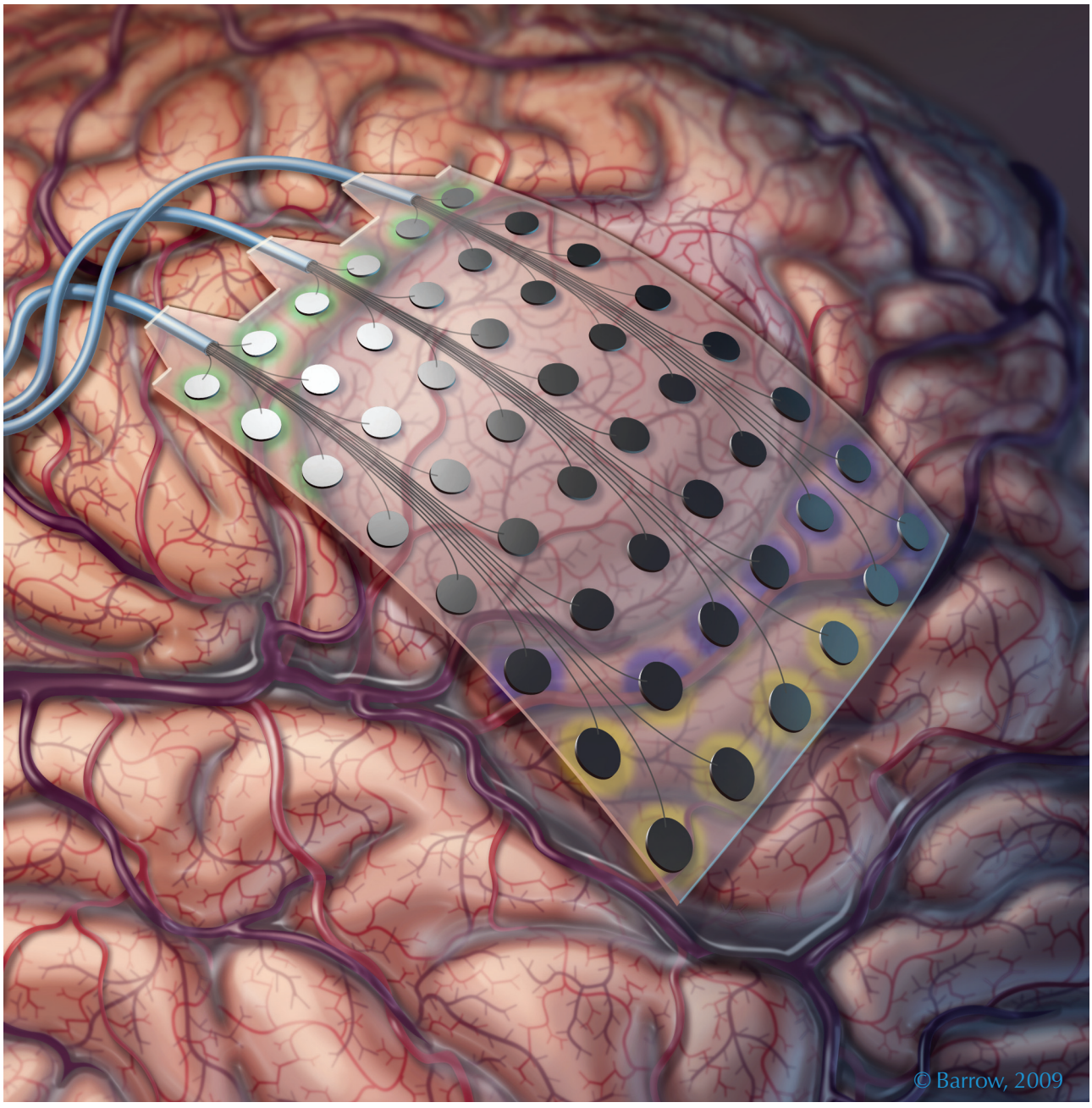

DEFINING ELOQUENT CORTEX WITH SUBDURAL ELECTRODE ARRAYS

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C O M M E N T S

Neurosurgeons and their patients can confront many challenging dilemmas during treatment. For example, the resection of primary low-grade cortical tumors, especially those with indistinct borders with normal tissue, can be associated with significant postoperative neurological deficits. The traditional approach for minimizing damage to functional cortex while maximizing outcomes has been intraoperative awake stimulation. However, not all patients are candidates for this procedure. In this issue, Little et al. evaluate the advantages and disadvantages of using an alternative procedure, subdural grid electrodes, for mapping functional gyri to define the safest corridor for tumor resection.

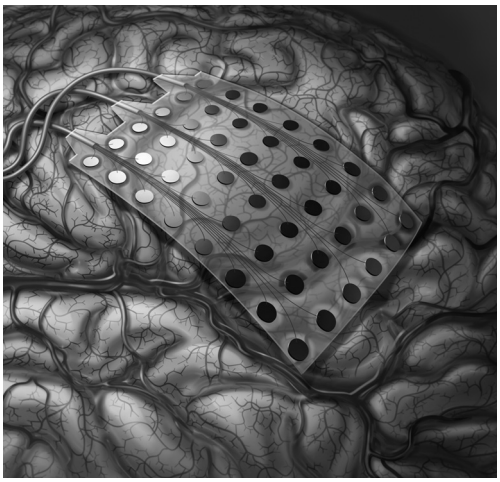
Also in this issue, Garrett and Eschbacher review dysembryoplastic neuroepithelial tumors (DNET), lesions recognized only in the last 20 years. These lesions are usually considered benign, but their natural history is not yet defined. The authors discuss the potential for malignant transformation of the rare recurrent DNET and suggest that the prudent course is regular clinical and radiographic follow up for patients harboring these tumors.

Another article focuses on skull base allergic fungal sinusitis, a neurosurgical entity that can be mistaken for a skull base tumor and should be considered in the differential diagnosis of a paranasal sinus mass in young atopic patients. In particular, in hot, arid climates such as the Southwest, *Bipolaris* should be suspected as the cause of such infection, as occurred in the six patients reported by Van Gompel and coworkers.

This issue also features other unusual cases treated at our institution. For instance, Aliabadi and colleagues report a 14-year-old boy with encephalopathy and signs of meningeal inflammation. Unexpectedly, the cause was tuberculosis. The boy had likely contracted the disease before his family emigrated from Kenya—a reminder that travel and immigration patterns must be considered in the diagnosis of patients with unusual presentations. Finally, Wilson et al. report a patient with a diskal cyst that caused radiculopathy, which was clinically indistinguishable from the radiculopathy associated with a disk herniation.

The articles in this issue are just a sample of the challenging clinical problems that clinicians and researchers at Barrow devote their careers to solving. To help us continue to share our experiences with the medical community throughout the world, please consider sending a tax-deductible donation in the enclosed self-addressed and stamped envelope. Thank you.

Robert F. Spetzler, MD
Editor-in-Chief



This issue's cover depicts functional mapping of the cortex with a subdural electrode array to define the borders of eloquent cortex to aid tumor resection. See the article by Little et al. on page 4. The illustration is by Mark Schornak.

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Functional Cortical Mapping Using Subdural Grid Electrodes in Patients with Low-Grade Gliomas Presenting with Seizure

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Functional stimulation mapping with subdural electrode arrays to define eloquent cortex is a standard technique in epilepsy surgery. Before tumors in eloquent regions of the brain are resected, epilepsy surgeons may use this technique as an alternative to awake craniotomy for mapping. We performed detailed functional mapping in 18 patients with low-grade gliomas before they underwent resection. All patients harboring tumors with abnormal enhancement underwent complete resection of the abnormality. The region of T2-weighted abnormality was resected completely in 5 (28%) patients and almost completely in 4 (22%). The most common complication was subdural fluid collection after grid placement. All patients achieved a good outcome at 1 year. Subdural cortical mapping allowed aggressive tumor cytoreduction and was associated with an acceptable rate of neurological morbidity. However, the overall morbidity rate was higher and duration of hospitalization was longer compared to those associated with other tumor mapping methods.

Key Words: brain mapping, cortical stimulation, primary brain tumor, subdural grid electrodes

Abbreviations Used: CT, computed tomography, MR, magnetic resonance; mRS, modified Rankin Scale; WHO, World Health Organization

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Primary low-grade brain tumors in eloquent cortex are challenging lesions to resect. The margin between infiltrating tumor and normal white matter is often indistinct, and their removal risks significant postoperative disability. Several mapping techniques have been developed to limit postoperative neurological morbidity while optimizing the extent of resection. These techniques include intraoperative direct cortical stimulation in awake patients, functional magnetic resonance imaging, magnetoencephalography, and functional mapping with subdural cortical electrode arrays.[2,4-8] Intraoperative awake stimulation has emerged as the gold standard for resection of these lesions because of the low incidence of postoperative deficits and the ability to map subcortical white matter tracts.[3,9] However, not all eligible patients are able to undergo awake craniotomy because of the surgeon's or patient's preference or because the institutional expertise needed for mapping is lacking.

We hypothesized that we could leverage our epilepsy experience to develop an alternative to awake mapping using subdural electrode arrays. Subdural arrays are a standard tool in epilepsy surgery for refining seizure localization and mapping functional cortex before lesionectomy. In this new application, the mapping information is used to identify functional gyri, thereby defining a corridor into the tumor and determining which gyri are safe to resect. To assess the utility of and complications associated with this strategy, we reviewed our experience in 18 patients presenting with first-time seizure

related to an intrinsic brain tumor located near eloquent cortex.

Methods

Between 1999 and July 2006, 18 consecutive patients (10 females, 8 males; mean age, 30 years; age range, 18-44 years) presenting with seizure with a primary low-grade (i.e., WHO grade I and II) brain tumor underwent subdural grid implantation and functional mapping followed by tumor resection. Indications for subdural grid mapping included the presence of a suspected low-grade tumor adjacent to or within eloquent cortex, good functional status with the ability to participate in the mapping process, and the recommendation from a weekly, multidisciplinary treatment planning conference. Only patients with a pathologically confirmed diagnosis of a low-grade intrinsic brain tumor are included in the present analysis. This study was approved by the Institutional Review Board of St. Joseph's Hospital and Medical Center.

The tumor was located in the left frontal lobe in six patients, in the right frontal lobe in two patients, in the left temporal lobe in four patients, in the left frontotemporal region in one patient, in the left parietal lobe in three patients, in the right parietal lobe in one patient, and in the left insula in one patient. All tumors were low grade (i.e., WHO grade I or II). Three patients had an oligodendroglioma, eight had an astrocytoma, three had an oligoastrocytoma, three had a ganglioglioma, and one had a juvenile pilocytic astrocytoma (Table 1). All patients presented with seizure.

Mapping and Tumor Resection

In the first stage, a modest-sized craniotomy was individually tailored centered over the lesion while the patient was under general anesthesia. Grids (Ad-Tech Medical Instrument Corp., Racine, WI) were slipped beneath the bone edges into the subdural space to cover the cortical region of interest. Mapping was undertaken in the epilepsy monitoring unit where patients underwent video-electrocorticography. Grid-stimulation studies were performed in sessions using a Grass Model S12 Isolated Biphasic Stimulator (Astro-Med, Inc., West Warwick, RI). The peak current setting was used to test for sensory phenomena; cessation of motor function of the tongue, hand, and foot; and muscle twitches. Electrode pairs also were tested for the patient's ability to perform selected neuropsychological tests during cortical stimulation. Language domains mapped included reading, naming, and comprehension.

The goal of functional mapping was to determine safe cortical borders of resection by identifying gyri with eloquent function. Resection of the cortical surface of tumor proceeded from gyrus to gyrus, respecting pial borders. Wherever tumor appeared to infiltrate gyri containing no eloquent function, the tumor was resected along with a margin of normal-appearing brain tissue extending to the pial border of adjacent sulci. Gyri containing eloquent function were spared, even if imaging abnormalities indicated involvement of tumor.

Once the cortical borders of the resection were determined in this manner, the tumor was debulked internally. The margin of resection along the tumor's interface with the deep and subcortical white matter was determined by the extent of abnormalities evident on MR imaging and by visual inspection. Complete resection of regions with abnormal enhancement was the first priority, and resection of areas of T2-weighted hyperintensity was the second priority. The aim of surgery was tumor resection, not seizure control.

Outcome Analysis

The functional status of patients was estimated by the modified Rankin Scale (mRS). Minor neurological morbidity was defined as an mRS of 2 or better, and major morbidity was defined as an mRS score of 3 or worse. Permanent deficits were defined as those present 1 year after surgery.[5]

Tumor and residual volumes were estimated by calculating the volume of a modified ellipsoid shape (length x width x thickness/2) on MR images obtained within 48 hours of surgery. Degree of resection was stratified based on reduction in the extent of T2-weighted abnormality according to published methods: 100% (complete), > 90% (near complete), and 50 to 90% (subtotal).[7] Reduction in the abnormal enhancement was also tabulated.

Results

Mapping Results and Surgical Strategy

Useful mapping results were obtained in all patients. Domains mapped included motor function in 18 patients, sensory function in 6 patients, and language function in 14 patients (Table 1). The mean number of mapping sessions was 2.6 (range, 2 to 4 sessions). One patient was unable to complete her language-mapping objectives because of baseline dysphasia, but she was able to complete motor mapping. On two occasions, mapping sessions had to be terminated because seizure activity was induced by stimulation. In both patients, mapping was completed during subsequent sessions. The mean length of hospitalization was 9 days (range, 5 to 15 days).

In 10 patients the mapping data suggested that there was a sulcal margin between tumor and eloquent cortex. Therefore, complete resection of the region of abnormal enhancement and debulking of the region with T2-weighted signal change were planned. In the other 8 patients, mapping suggested that at least a portion of the tumor was located within eloquent cortex. In these cases, resection was limited to spare the eloquent gyri.

Operative strategy influenced the degree of cytoreduction. Regions of T2 weighted abnormality were completely or almost completely resected in 8 (80%) patients who had a sulcal margin between their tumor and functional cortex. In contrast, near complete resection was achieved in 1 patient (13%) whose tumor resided within functional cortex. Complete resection was achieved in all 13 patients with nodular or patchy en-

Table 1. Clinical Summary of 18 Patients with Low-Grade Tumors

Patient	Age/ Sex	Location	Tumor	Functions mapped	Estimated resection enhancement (%)	Estimated resection T2 abnormality	mRS			Interval to recurrence/ progression (yrs)
							At 1 yr	At last f/u	Interval (yrs)	
1	28/M	L temporal	oligodendro	Mo, S, La	100	subtotal	0	0	5	n/a
2	33/M	L frontal	astro	Mo, S, La	n/a	near complete	2	6	2.5	2
3	44/F	L parietal	JPA	Mo, La	100	subtotal	2	2	2	n/a
4	19/F	R frontal	ganglio	Mo	100	complete	0	0	3	n/a
5	32/M	L insula	astro	Mo, La	n/a	subtotal	0	6	2.5	2
6	37/F	L frontal	oligoastro	Mo, La	100	subtotal	0	0	1	n/a
7	31/M	L frontal	astro	Mo, La	100	subtotal	0	0	2	n/a
8	28/F	R frontal	oligoastro	Mo	100	subtotal	1	0	2	n/a
9	32/M	L parietal	astro	Mo, S, La	n/a	complete	2	0	3	n/a
10	34/F	L frontotemp	oligoastro	Mo, S, La	100	near complete	1	6	3	2.5
11	20/F	L frontal	astro	Mo, La	100	near complete	0	6†	3	n/a
12	38/F	L frontal	astro	Mo, La	100	complete	1	0	6	n/a
13	37/M	L temporal	astro	Mo, La	100	subtotal	2	6	7	5
14	21/M	L parietal	ganglio	Mo, S	n/a	near complete	0	0	3	n/a
15	31/F	R parietal	astro	Mo, S	n/a	subtotal	2	2	1.5	n/a
16	41/F	L temporal	oligodendro	Mo, La	100	subtotal	1	6	7	5
17	18/F	L frontal	oligodendro	Mo, La	100	complete	1	1	2	n/a
18	21/M	L temporal	ganglio	Mo, La	100	complete	0	0	6	n/a

†death unrelated to tumor. mRS = modified Rankin Score, f/u = follow up, yrs = years, L = left, R = right, M = male, F = female, Mo = motor, La = language, S = sensory, JPA = juvenile pilocytic astrocytoma, oligodendro = oligodendroglioma, ganglio = ganglioglioma, oligoastro = oligoastrocytoma, astro = astrocytoma, n/a = not available.

hancement on preoperative MR imaging (Fig. 1).

Outcomes

At 1 year all patients had achieved a good outcome (Table 1). There were no cases of permanent major neurological morbidity. At 1 year, four (22%) patients had minor postoperative deficits attributable to surgery, two of which had resolved by long-term follow-up (*Patients 8* and *9*). Difficulty naming objects persisted in two patients with posterior temporal lesions (*Patients 13* and *16*). During the mean follow-up of 3.5 years, five (28%) patients experienced tumor progression or recurrence.

Perioperative complications after grid implantation included 2 patients (11%) with subdural fluid collections that accumulated in a delayed fashion (Days 2-5) and required evacuation to relieve mass effect. Mapping and tumor resection were completed successfully in both patients during the same hospitalization. One patient (6%) required a wound revision at 2 years for exposed bone.

Discussion

Patients with low-grade tumors within or near eloquent cortex are a therapeutic challenge. The technique of mapping using subdural grid electrodes was adapted from epilepsy surgery to address a group of patients who, because of patient, surgeon, or institutional resources, were not candidates for awake cortical stimulation during resection.

Our data and the work of others highlight the advantages and disadvantages of invasive cortical mapping with subdural grids. First, cortical grid stimulation mapping offers the opportunity for significant tumor cytoreduction with acceptable neurological morbidity. In their series of high-grade gliomas resected with the aid of subdural grid mapping, Kral et al. used larger craniotomies and obtained a 31% rate of gross total resection with no permanent disability.[7] Second, reliable information can be obtained without the constraints of mapping in the operative suite. Occasionally, awake craniotomies are terminated because of seizure activity, airway concerns, or claustrophobia.[8] If a seizure is induced during grid stimulation, mapping can be completed successfully during a follow-up session. Third, physicians can counsel their patients about specific, potential postoperative deficits based on the mapping data obtained preoperatively. Fourth, accomplishing functional mapping and tumor resection through the same modest-sized craniotomy centered over the lesion avoids a large bone flap. Fifth, our epilepsy experience and the work of Berger et al.[1] indicate that children may benefit from this technology because functional data can be obtained and verified outside the

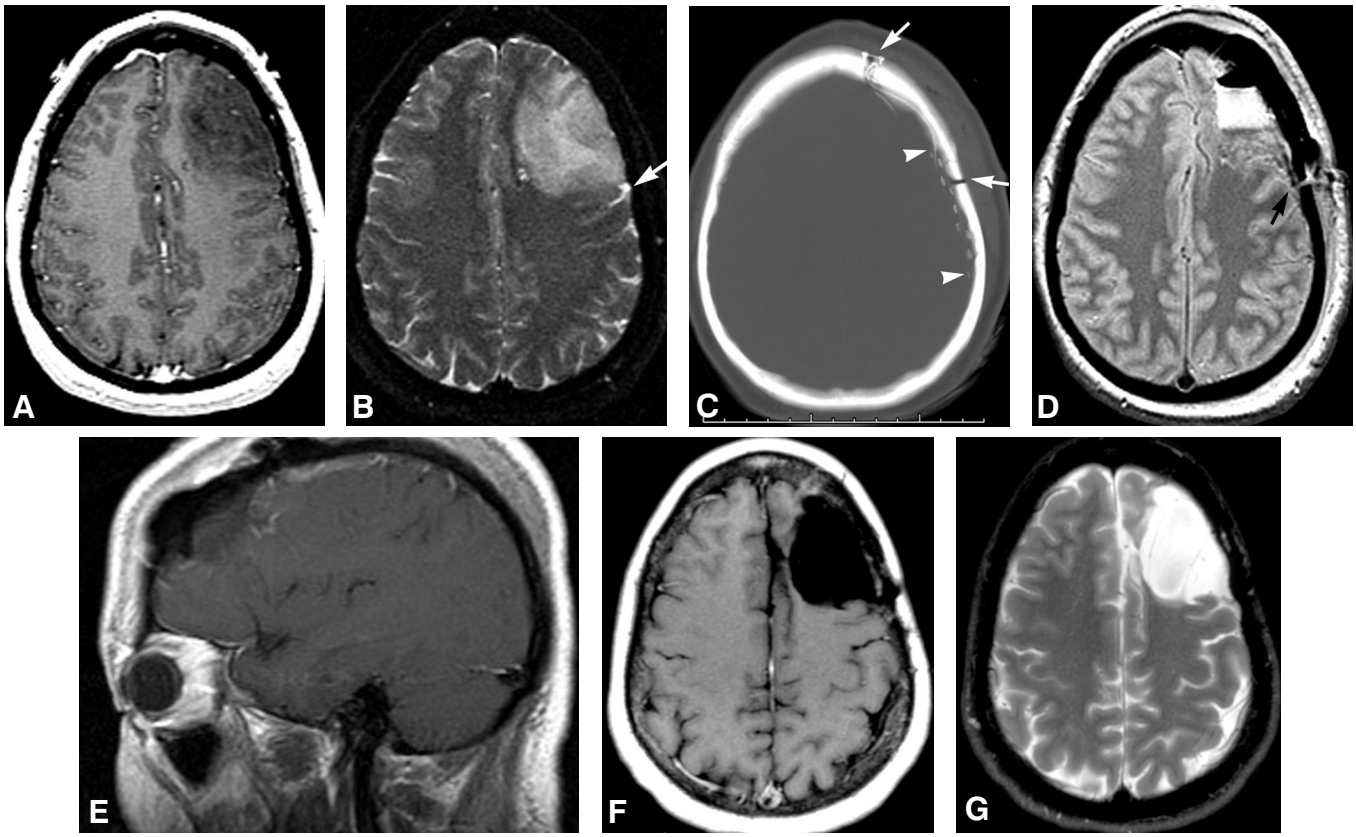

Figure 1. Patient 12. (*A*) Preoperative axial enhanced T1-weighted MR image shows a low-grade lesion in the left frontal lobe with patchy enhancement near Broca's area and the motor cortex in a 38-year-old woman. (*B*) Axial T2-weighted MR image shows a sulcus (*arrow*) at the posterior-inferior margin of the tumor. Mapping suggested that this sulcus was the margin between noneloquent and eloquent cortex. Resection proceeded to the sulcal margin. The functional cortex was spared, but the gyrus, which was partially infiltrated with tumor, was removed completely. (*C*) CT scan shows the position of a single 6 x 8 grid (*arrowheads*) placed over the posterior and inferior aspects of the lesion to map the boundaries of the motor and language cortices. Grids were slipped under the bone edges (*arrows*) to increase the mapping area without increasing the size of the bone flap. Immediate postoperative (*D*) axial T2-weighted and (*E*) enhanced T1-weighted sagittal MR images confirm sparing of the sulcal margin (*arrow*) as noted above the frontal operculum. Three-year follow-up enhanced axial (*F*) T1-weighted and (*G*) T2-weighted MR images show no tumor recurrence.

operative theater. Finally, this technique can easily be adopted by epilepsy surgeons because the technique is already part of their armamentarium.

Our experience also highlights the disadvantages of this strategy. First, only cortical mapping data can be obtained. The technique does not map the portion of a gyrus that is nestled in a sulcus or subcortical white matter pathways. Second, the resolution for mapping is limited by contact placement prefabricated at 1-cm intervals. Cortical stimulation with a probe may yield 5-mm sensitivity. Furthermore, grid mapping requires two craniotomies, two general anesthetics, and arguably a longer hospital stay to complete mapping. Finally, there is no real-time mapping feedback to guide the extent of resection. We speculate that these limitations may explain the rate of neurological morbidity in our series. In two recent series using awake cortical stimulation, the rates of gross total resection were 25% to 30%.[3,8] Furthermore, the rates of new postoperative deficits in language, motor, and sensory functions have ranged from 0% to 29%. We also noted several complications likely related to grid implantation, including subdural fluid collections and wound breakdown.

Conclusions

Our data demonstrate that cortical mapping using subdural grids to define eloquent cortex before tumor resection offers the opportunity for significant tumor cytoreduction with an acceptable rate of neurological morbidity. However, the overall morbidity rate may be higher and hospital stays may be longer. In low-grade neoplasms where it can be difficult to determine the margin between tumor and normal white matter, functional mapping provides another tool for the surgeon to develop a preoperative resection strategy to minimize injury to eloquent cortex. Although this strategy requires a patient's cooperation during mapping sessions and tolerance of staged craniotomies, it may be an option for patients who would be unwilling or unable to participate in an awake craniotomy.

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Dysembryoplastic Neuroepithelial Tumor: A Review

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Most DNETs are benign, low-grade lesions. However, a small number appear to have the potential for malignant transformation. We report a patient with a biopsy-proven DNET with features of an ogliodendroglioma and review the clinical features of DNETs and their potential for malignant transformation.

Key Words: dysembryoplastic neuroepithelial tumor, malignant transformation

Abbreviations Used: DNET, dysembryoplastic neuroepithelial tumor; MR, magnetic resonance; SGNE, specific glial neuronal element; WHO, World Health Organization

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In 1988 Dumas-Duport et al. first used the term dysembryoplastic neuroepithelial tumor to describe low-grade tumors found in young patients with intractable partial seizures.[4] In 1993 the distinct pathological entity known as DNET was given a place in the WHO classification of brain tumors as a grade I tumor of neuroepithelial origin.[3,10,11] Many studies have reported successful surgical management of this low-grade tumor in the treatment of refractory epilepsy. We report the case of a young man who experienced possible seizure activity and was found to have a biopsy-proven DNET.

Case Report

A 30-year-old man with no significant medical history experienced the sudden onset of right facial numbness, which resolved completely within hours. When questioned he stated that he had experienced occasional sensory abnormalities in his right arm and leg throughout the previous year. Computed tomographic scans showed a nonhemorrhagic hypodense lesion in the mesial temporal lobe, thalamus, and posterior limb of the internal capsule. The lesion was hyperintense on T2-weighted MR images, hypointense on T1-weighted images, and nonenhancing (Fig. 1). Based on the imaging studies, the diagnosis was unclear and we recommended that the patient undergo a needle biopsy to guide further treatment.

An intraoperative frozen specimen was interpreted as either an oligodendroglioma or a DNET. The final pathological evaluation described nodular, neoplastic, glioneuronal elements with oligoden-

droglial-like features and areas of microcystic change and hyalinization. On immediate postoperative MR imaging, a small hemorrhage was visible in the tumor bed. The patient suffered no adverse events and was discharged home neurologically intact after a brief period of observation. Interestingly, on follow-up imaging the lesion had partially regressed. We hypothesized that the compressive forces of the intraoperative hemorrhage had partially obliterated the tumor.

Discussion

In 1988 Dumas-Duport and colleagues first characterized DNETs when they described neuroepithelial tumors in 39 patients with medically intractable partial complex seizures.[4] Their cohort was a combination of epilepsy patients undergoing surgery at St. Anne Hospital in France and at the Mayo Clinic in Rochester, Minnesota. They noted a distinct cortical tumor with multinodular architecture, associated cortical dysplasia, and both neuronal and glial elements. After resection their patients were followed a mean of 9 years. Their outcomes were excellent. Of the 39 patients, 30 were seizure free, 4 experienced only rare seizures, and the number of seizures was reduced significantly in the remaining 3 patients. Two patients died. Despite being seizure free, one patient committed suicide 3 months after surgery. The second patient received whole brain radiation and polychemotherapy and was found to have extensive radionecrosis at autopsy.

Although the report by Dumas-Duport et al. is considered the first to describe these tumors and their specific histology,[4] they did credit Cavanagh of London who published an article in 1958 called, *On Certain Small Tumors Encountered in the Temporal Lobe*.[1] The multinodular lesions that Cavanagh described were found while he performed temporal lobectomies for temporal lobe epilepsy. Cavanagh described the lesions as hamartomas but opined that areas of "early neoplastic change" were susceptible to malignant transformation into gliomas. Dumas-Duport et al.[4] considered the tumor to be at least partially neoplastic and argued that these lesions formed during embryonic development.

Dumas-Duport's argument that DNETs had embryonal origins was four-fold. First, these tumors exhibited multiple cell lineages that could arise from multipotent cells present during early development. Second, these tumors manifest early in life. Third, there is often an adjacent bone deformity, which suggests that the tumors are long standing with an early onset. Finally, the presence of cortical dysplasia implies that these lesions occur during cortical formation and are not neoplasms that arise within normally developed cortex. The actual origins of these indolent tumors and whether they are truly neoplastic are still debated.

Classification

The original paper describing DNETs focused on the theory that these tumors had embryonal origins. However, it was clear that their clinical course differed from that of tumors classified as embryonal tumors of neuroepithelial origin. Tumors listed in the WHO classification scheme as embryonal are all considered WHO grade IV lesions (Table 1).[12] Thus the term *dysembryoplastic* was coined to indicate both the origin of these tumors and the observation that they share features with less aggressive, dysplastic lesions. However, the authors did not think that the term was an entirely accurate description of these tumors, which share some similar histologic features with neoplastic lesions. Nonetheless, the term dysembryoplastic still served to denote the predominantly benign clinical course of these tumors.

In 1993 DNETs were placed in the WHO brain tumor classification scheme as a neuronal/mixed glial-neuronal tumor of neuroepithelial origin.[3,10,11] They are

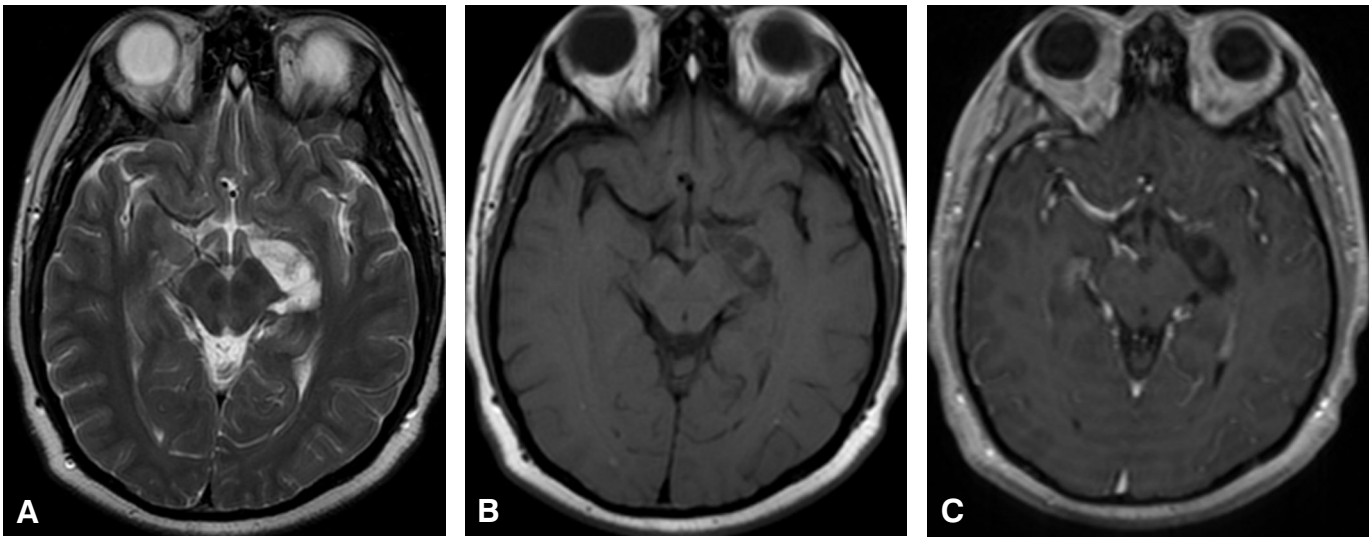

Figure 1. (*A*) Axial T2-weighted MR image shows a hyperintense lesion in the mesial temporal lobe. Axial T1-weighted MR images (*B*) with and (*C*) without contrast show a hypointense lesion that does not enhance.

Table 1. Tumors classified as embryonal within category of tumors with neuroepithelial origins.† [12]

Medulloblastoma
Desmoplastic/nodular medulloblastoma
Medulloblastoma with extensive nodularity
Anaplastic medulloblastoma
Large cell medulloblastoma
CNS primitive neuroectodermal tumor
CNS neuroblastoma
CNS ganglioneuroblastoma
Medulloepithelioma
Ependymoblastoma
Atypical teratoid/rhabdoid tumor

†According to the 2007 WHO classification of brain tumors.

Table 2. Tumors classified as neuronal and mixed neuronal-glial tumors within category of tumors with neuroepithelial origins[12]

Dysplastic gangliocytoma of cerebellum (Lhermitte-Duclos)
Desmoplastic infantile astrocytoma/ganglioglioma
Dysembryoplastic neuroepithelial tumor
Gangliocytoma
Ganglioglioma
Anaplastic ganglioglioma
Central neurocytoma
Extraventricular neurocytoma
Cerebellar liponeurocytoma
Papillary glioneuronal tumor
Rosette-forming glioneuronal tumor of fourth ventricle
Paraganglioma

classified as Grade I tumors along with the other low-grade neuronal tumors such as gangliogliomas and gangliocytomas (Table 2).[12] Although still debated, most contemporary neurosurgeons consider these tumors to be frankly neoplastic.

Histology

Three histologic forms of DNET have been described: complex, simple, and nonspecific.[2] The complex form (Fig. 2), which is the type originally described by Dumas-Duport et al.,[4] consists of SGNE (Fig. 3), glial multinodular architecture, and associated cortical dysplasia. The nodular component of a DNET contains both glial and neuronal components and can resemble both gliomas and gangliogliomas. The neuronal component often consists of neurons "floating" in a basophilic mucinous matrix (Fig. 4). The axons are surrounded by "tumoral" oligodendrocyte-like cells. These cells exhibit oligodendroglial features, including prominent perinuclear halos (Fig. 5). The simple form, which was also described by Dumas-Duport et al.,[4] consists only of the SGNE. The nonspecific form is more controversial: It has neither the SGNE nor the multinodular architecture. It resembles a low-grade astrocytoma but has clinical and radiological features more consistent with a DNET.[5]

Imaging Features

On neuroimaging DNETs are cortical lesions with little mass effect and a predilection for the temporal lobes. On computed tomography DNETs are typically well-demarcated, hypodense, cortical lesions that can be associated with deformation of the overlying skull. In a radiological study, fewer than 20% contained calcifications in contrast to gangliogliomas, which had a much higher rate.[16] MR images often show a solid and cystic mass with the cystic portions appearing slightly more intense than cerebrospinal fluid. A cystic signal pattern is not specific to DNET; the pattern is also found in other tumors frequently associated with epilepsy such as gangliogliomas and gliomas. The solid components often appear multinodular, hypointense on T1-weighted MR images, hyperintense on T2-weighted MR images, and occasionally weakly enhancing.[6,17]

Clinical Course

Consistent with their original description, DNETs are tumors associated with epilepsy in young adults. In 2006 Chan et al. reported the outcomes of patients who underwent surgical removal of a DNET for seizure control and reviewed the published series of DNETs.[2] The mean long-term outcome of 18 patients with DNETs surgically resected for the treatment of epilepsy was 10.8 years. They found that 66.7% of their patients achieved Engel Class I outcomes, indicating that they were free of disabling seizures. In the reviewed series of surgical outcomes for DNETs, 52.4 to 90% of the patients achieved Engel Class I. Interestingly, the results that they had previously reported for the same group of patients at a mean of 2.7 years of follow-up were predictive of their long-term outcomes. Their results, combined with those of other studies, led them to conclude that a patient who is seizure free 3 years after resection of a DNET can be considered cured.

Nonetheless, DNETs can recur as Nolan et al. reported in 2004.[13] Of 26 children who underwent surgical resection of their tumor for seizure control, 3 demonstrated a recurrence within 1 to 5 years. In this series, the rate of incomplete resection was high (63%), and all patients who experienced a recurrence showed some degree of residual tumor on postoperative imaging.

Potential for Malignant Transformation

In published series the clinical course of DNETs has been stable. Only rarely does diagnostic imaging reveal a postoperative recurrence. Recent case reports, however, have shown that these

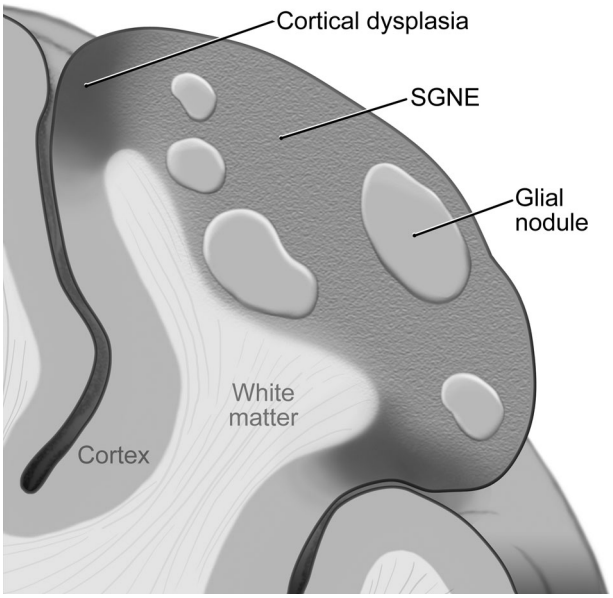

Figure 2. Schematic representation of the complex form of DNET.

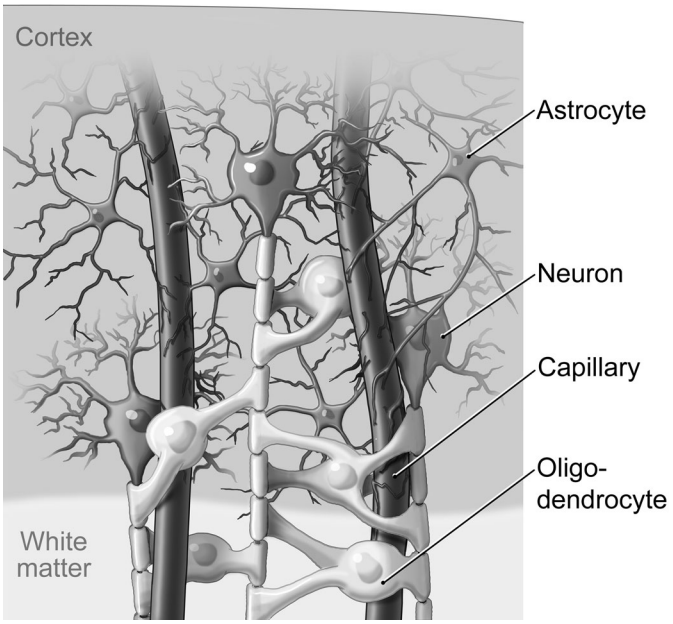

Figure 3. Schematic representation of the SGNE of a DNET showing the neuronal elements that form the columnar structures perpendicular to the cortical surface.

lesions may undergo malignant change. In 2000 Hammond et al. reported the first malignant transformation of a DNET that had been surgically resected.[7] The patient, a 29-year-old man who suffered from partial seizures, had a nonenhancing lesion in his left frontal cortex. He first underwent surgery in 1984, when his tumor was labeled as a "fibrillary astrocytoma." The surgeons reported subtotal resection. The patient received no radiation or chemotherapy, but 11 years later his seizures recurred. MR imaging showed a partially enhancing cystic lesion. After repeat resection the pathology was confirmed as a grade IV astrocytoma. Retrospective histological review of the initial tumor found it to be a DNET with SGNEs, glial nodules, and associated cortical dysplasia.

In 1974 Rushing et al. described a 14-year-old boy who underwent subtotal resection of a tempoparietal mass for the treatment of epilepsy.[14] The pathology, which was originally diagnosed as a "mixed oligoastrocytoma," was later shown to be a DNET. The patient received postoperative radiation therapy. One year later MR imaging showed the formation of a cyst that was drained via a craniotomy. After this procedure the patient underwent a 6-week course of chemotherapy. Three years later, his seizure activity resumed and a tumor recurrence was found. The patient underwent a third surgery, and the pathologic diagnosis of the lesion was consistent with progression to an anaplastic astrocytoma.

Three other studies also suggest the potential for transformation or progression of a DNET. Josan et al. reported a 3-year-old girl with seizures who was found to have a DNET. She was managed conservatively.[9] At the age of 14 years, follow-up MR imaging showed a large cystic lesion, which was resected. The lesion was diagnosed as a pilocytic astrocytoma within a surrounding DNET. In a 9-year-old with seizures, Sampetrean et al. described a DNET with a small ring-enhancing core; the size of the lesion tripled in 3 months.[15] Surgical resection confirmed the diagnosis of DNET. Five years after surgery, the patient remained seizure free without a recurrence. Jensen et al. reported a 46-year-old patient who had medically refractory seizures with a nonenhancing, low-intensity lesion in the mediotemporal lobe.[8] The patient opted for conservative management until the tumor developed contrast enhancement after 15 years. Surgical pathology revealed a DNET without atypical changes. These findings suggest that on imaging these tumors can show progression that does not necessarily imply malignant transformation.

Because DNETs have only been discovered within the last 20 years, their natural history is not yet completely defined. The literature, however, suggests that these lesions hold the potential for malignant change. It is possible that the discovery of a higher-grade lesion within a histologically proven DNET is simply coincidental. Given that some DNETs display high mitotic activity based on the Ki-67 proliferation labeling index, it seems likely that these tumors arise from neoplastic cells within the DNET itself.[2] These findings support the argument that a DNET is at least partially a neoplastic lesion, although its nature is still debated. Although some of these tumors progress, most are stable and rarely recur after surgery. Possibly, a subset of these tumors yet to be identified has the propensity

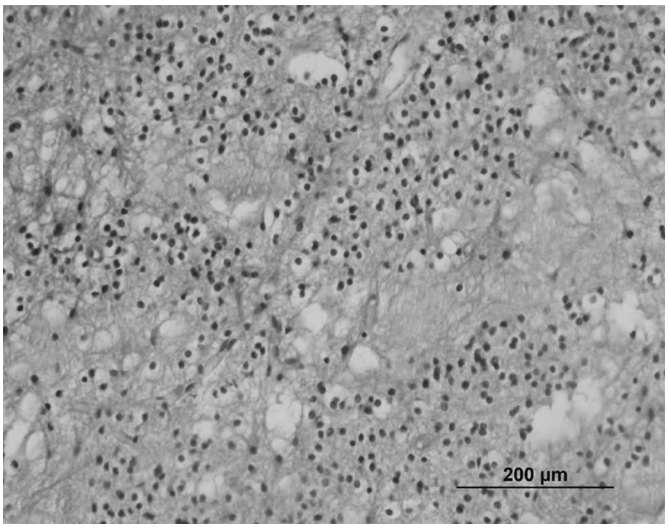

Figure 4. Low-power view of oligodendrocyte-like cells with prominent perinuclear halos embedded in a background of abundant basophilic mucin (hematoxylin and eosin, original magnification x200).

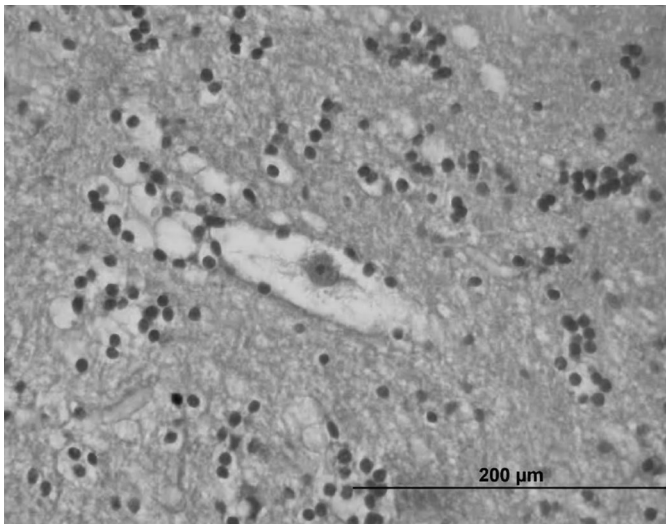

Figure 5. High-power view of a floating neuron (hematoxylin and eosin, original magnification x400).

for malignant transformation. When the natural history of these tumors is better defined with longer follow-up, we also may find that a greater percentage progress to more aggressive lesions than previously thought. For now these reports demonstrate the importance of regular follow-up, both clinical and radiographic, for patients who harbor DNETs.

Conclusion

Since their discovery in 1988, much has been learned about the characteristics and clinical course of DNETs. It is widely accepted that patients with seizures attributable to these lesions are excellent surgical candidates who achieve good outcomes and low recurrence rates without the use of adjunct therapies. Although most DNETs are benign, low-grade lesions, it is becoming increasingly apparent that a small number will progress to more aggressive lesions. Consequently, we recommend that these patients have regular follow-up examinations to identify progression at its early stages. As the natural history of DNETs is better defined, it should become increasingly possible to tailor treatments and follow-up regimens to individual patients.

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Neurosurgical Management of *Bipolaris*-Specific Skull Base Allergic Fungal Sinusitis: Diagnostic Criteria and Outcome

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Skull base allergic fungal sinusitis is a rare but important neurosurgical entity that can be mistaken for a skull base tumor during preoperative assessment. Due to the significantly variable clinical presentation of and preoperative evaluation for this disease, clinicians are often surprised when the diagnosis becomes apparent during surgery or thereafter. However, SBAFS must be differentiated from malignancy and invasive fungal disease because this allergic disease does not require aggressive, complete resection or potentially toxic antifungal medications. We report six cases of SBAFS to illustrate the neurosurgical management of this rare disease.

Key Words: allergic fungal sinusitis, *Bipolaris*, skull base

Abbreviations Used: AFS, allergic fungal sinusitis; CT, computed tomography; GMS, Gomori methenamine silver; MR, magnetic resonance; SBAFS, skull base allergic fungal sinusitis

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Over the past decade, the incidence of fungal infections has increased dramatically. Fungal paranasal sinus disease, a large component of fungal infections, is common and is defined by the host and the host's response to the fungus. Invasive fungal sinusitis occurs in immunocompromised hosts and can manifest as acute, fulminant, and life-threatening or as a more manageable chronic/granulomatous indolent form. However, the hallmark of invasive disease is the presence of large amounts of the fungal element in the associated pathology without immune containment.

In contrast, noninvasive fungal sinusitis occurs in immunocompetent individuals. It exists in two forms, both characterized by the host's response to the fungal agent. With the first, mycetoma, the host's immune response is inadequate and the fungal agent proliferates as an encapsulated mass. The second, AFS, the subject of this report, occurs when the host provides an overly exuberant immune response to the antigens of the fungus.

Skull base allergic fungal sinusitis, a term first introduced by Kinsella et al., denotes the specific condition in which AFS extends intracranially.[10] Ten to 20% of patients with AFS have an intracranial extension.[13] Once SBAFS is encountered, neurosurgical intervention is required. Because of their variable presentation and rarity, these lesions are seldom expected preoperatively.[15] Consequently, SBAFS is often mistaken for a malignancy,[11,12,18,27] and patients may receive overly aggressive therapy. Because SBAFS is noninvasive, surgical debulkment is standard therapy; radical resection or toxic med-

Table 1. Clinical Summary of Six Patients with *Bipolaris* SBAFS

Case	Age/ Sex	Presenting Symptoms†	Presenting Signs	Medical History	Surgery	Bacterial Isolate‡	Neurological F/U
1	31/M	HA, OD vision loss, OS blurring	OD blindness/RAPD, Dysconjugate gaze	NP, asthma, chronic sinusitis	TNTS	*Staphylococcus*	resolved
2	25/F	OS vision loss	OS vision loss	NP, allergies, chronic sinusitis	SLTS	*Staphylococcus*	resolved
3	20/F	HA, N/V	OD proptosis and vision loss	NP, asthma	TNTS	*Staphylococcus*	resolved
4	36/M	Chronic nasal drainage	CN 6 paresis	NP, allergies, chronic sinusitis	SLTS§	*Haemophilus*	resolved
5	75/F	Tremor, falling, HA, decreasing memory	Head and upper extremity tremor	NP, allergies	TNTS	*Staphylococcus*	resolved
6	19/M	OD proptosis and blurring	Diplopia on left lateral upward gaze	NP, allergies, asthma	BCC	*Staphylococcus*	resolved

†No patient had presenting symptoms consistent with pituitary malfunction. ‡All cases cultured *Bipolaris* heavily; bacterial isolate represents coincident culture. §Complicated by aseptic meningitis. F/U = follow-up, HA = headache, N/V = nausea and vomiting, OD = right eye, OS = left eye, RAPD = relative afferent pupil defect (nonreactive pupil), NP = nasal polyps, CN = cranial nerve, TNTS = transnasal transsphenoidal, SLTS = sublabial transsphenoidal, BCC = bicoronal craniotomy.

ical regimens are unnecessary. We present six patients with *Bipolaris*-specific SBAFS to highlight the neurosurgical management of this rare clinical entity.

Clinical Materials and Methods

Bipolaris-Specific SBAFS

The records of six patients (3 men, 3 women; mean age, 34 years; age-range, 19 to 75 years) who underwent resection with pathologic verification of AFS and culture-proven *Bipolaris* from January 1989 to August 2004 were analyzed retrospectively. The criteria for pathologic verification were allergic mucin-containing eosinophils, Charcot-Leyden crystals, cellular debris, and sparse hyphae. To evaluate the invasive nature of this disease, all cases of *Bipolaris*-specific AFS were identified by querying our microbiology database from January 1998 to August 2004.

Most patients became symptomatic with visual complaints or headache of gradually increasing intensity (Table 1). On examination, the most frequent sign was ocular defect. All patients had a history of atopy, including polyps and at least one other indicator of atopy.

Bipolaris-Specific AFS

Between January 1998 and August 2004, 28 cases of culture-proven *Bipolaris*-specific AFS were treated at our institution. There were 20 men and 8 women (mean age, 30 years; range, 13 to 80 years). Three patients had an intracranial extension consistent with SBAFS (invasion rate, 10.7%). Of these 28 cases, only 1 had fungal elements identified on a KOH preparation. Eleven had concomitant positive cultures for bacteria. Three patients who underwent surgery were not included in the microbiology database because they predated its establishment.

Results

Radiology

Bipolaris-specific SBAFS lesions were isointense on T1-weighted MR images relative to brain tissue (Table 2). T2-weighted MR images lacked lesional or perilesional hyperintensity, suggesting no inflammation. All but one lesion was isointense to brain parenchyma; the exception was hypointense (Table 2). Four cases showed intense uptake on gadolinium-enhanced MR imaging, and another lesion was considered ring enhancing. There was no gadolinium enhancement in the remaining case. In all cases CT showed increased attenuation and bony destruction with expansion of its associated sinus or sella without evidence of hyperostosis. The location of the pituitary in relation to the tumor varied across the cases.

Treatment

Five cases consisted of a primary sphenoidal extension and were treated through a transsphenoidal approach (Table 1). A tumor that originated from the frontal sinus and extended into the anterior cranial fossa was approached through a bicoronal craniotomy. In all cases a coincident positive culture of bacterial isolate (nasopharyngeal flora) was also treated (Table 1). Postoperatively, one patient was diagnosed with aseptic

Table 2. *Bipolaris* SBAFS Imaging Characteristics

Case	MRI†		Gadolinium Uptake	Attenuation†	CT Bone Destruction	Pituitary Location‡
	T1	T2				
1	Isointense	Isointense	Intense	Increased	+	Posterior
2	Isointense	Isointense	Intense	Increased	+	Elevated
3	Isointense	Isointense	Ring enhancing	Increased	+	Posterior
4	Isointense	Isointense	Intense	Increased	+	Anterior
5	Isointense	Isointense	No uptake	Increased	+	Posterior
6	Isointense	Hypointense	Intense	Increased	+	None

†Relative to brain parenchyma. ‡Relative to mass and sella.

meningitis. The resulting transient recurrent sixth cranial nerve palsy resolved with treatment. Whether this complication was related to surgery is unclear. After surgical decompression neurologic symptoms resolved in all cases (range of follow-up, 2 months to 15 years). All patients received postoperative steroids from 2 weeks to 4 months. Three patients also received 2 weeks of antifungal therapy. There were no recurrences.

Illustrative Case

Patient History

A 31-year-old African-American man was transferred from an outside hospital with the radiographic diagnosis of a skull base tumor for further evaluation. The patient reported an 8-month history of headache and progressive loss of vision. The headache consisted of constant throbbing frontal pain. It gradually progressed from low-grade pain to an intensity of 10 on a 1 to 10 scale. Photophobia was present, but there was no evidence of nausea, vomiting, transient visual scotoma, or flashing lights. With the right eye, the patient could only see shadows. Vision in his left eye was beginning to blur. His history included evidence of significant atopy, nasal polyposis, chronic sinusitis with eight previous sinus surgeries, and childhood asthma.

Physical Examination

On neurologic examination the patient was alert and oriented. His right pupil was nonreactive to light; his left pupil was miotic but briskly reactive. Vision was full to confrontation in the left eye. Extraocular movements were intact bilaterally; however, gaze was dysconjugate. Evaluation of pituitary function was unremarkable.

Radiological Examination

Noncontrast head CT showed a hyperattenuating mass occupying the sphenoid sinus and sella (Fig. 1). The bony confines were expanded, and multiple calcified foci were present within the lesion without evidence of hyperostosis or perilesional edema. On T1- and T2-weighted MR images, the lesion was isointense relative to brain parenchyma (Fig. 2). Gadolinium-enhanced MR images showed a large, avidly enhancing lesion with its isocenter in the sphenoid sinus. It extended to the planum sphenoidale inferiorly and abutted the clivus posteriorly. Furthermore, there was evidence of an intracranial extension into the anterior cranial fossa beneath the frontal lobes. Moreover, involvement of the optic nerve suggested chiasmopathy and involvement of the perichiasmal segment (Fig. 3).

Treatment

The patient began steroid therapy and his vision subsequently improved. He then underwent frameless stereotactic transnasal-transsphenoidal debulking of the lesion. A firm white mass intermingled with fibrous tissue, which had eroded the planum sphenoidale and anterior and basal sellar floors, was encountered. Its adherence to the sellar diaphragm and frontal fossa dura made its removal difficult. An intraoperative frozen-section biopsy was consistent with an inflammatory process. The lesion was debulked without complication.

Histopathology

Hematoxylin and eosin staining revealed inflammatory infiltrate without dysplasia. Sparse fungal elements with the rare yeast were present on Fontana and GMS stains. By Day 10, intraoperative cultures were positive for *Bipolaris*.

Outcome

The patient recovered on steroid therapy without complications. At discharge his visual function had normalized, and his headaches had improved significantly.

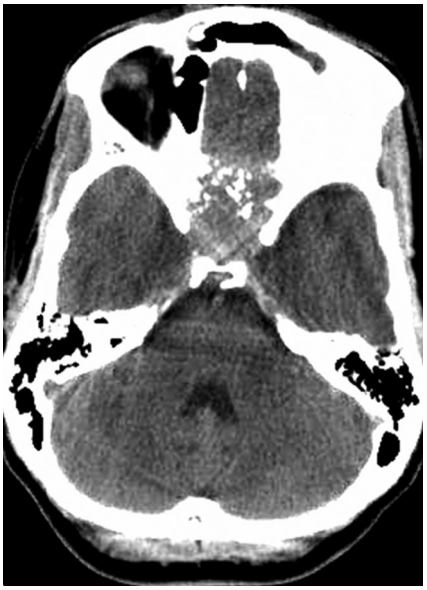

Figure 1. Noncontrast head CT shows a hyperattenuating lesion occupying the sphenoid sinus and sella, with evidence of expansion of these fossae and bony destruction.

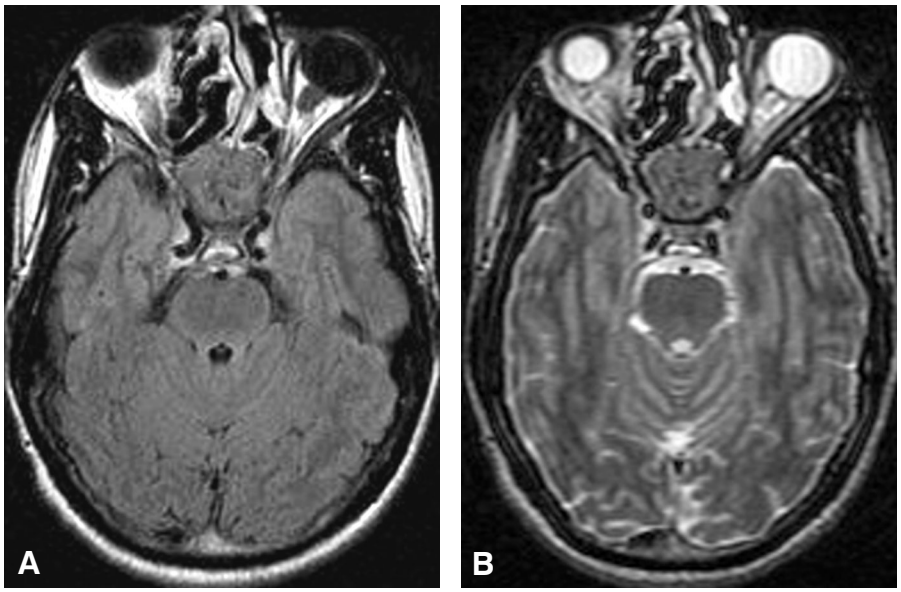

Figure 2. (*A*) T1- and (*B*) T2-weighted MR images show an isointense lesion occupying the sphenoid sinus and sella.

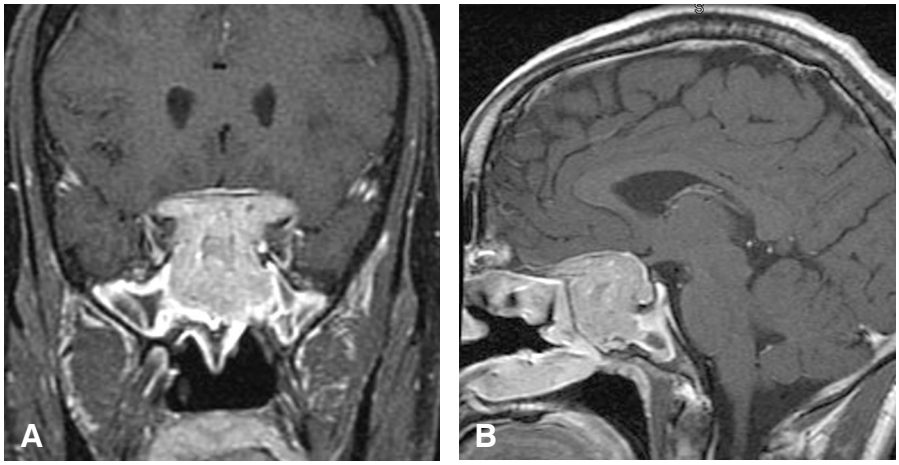

Figure 3. T1-weighted gadolinium-enhanced (*A*) coronal and (*B*) sagittal MR images show chiasmopathy and impressive expansion of the sella. On the sagittal MR image (*B*), an intracranial extension into the anterior cranial fossa resembles a dural tail.

Discussion

Natural History

AFS accounts for 7% of all fungal sinus disease. Dematiaceous fungi, most prominently *Bipolaris*, account for 81% of AFS. The remaining cases are primarily caused by *Aspergillus*. *Bipolaris* is found in dust and soil and on plants. Many cases of *Bipolaris* occur in hot, arid climates with mild winters such as the southern United States and Middle East.[10,17,24,25]

AFS caused by *Aspergillus* and fungal agents of the dematiaceous family, *Bipolaris*, represent different entities. Many *Aspergillus*-associated cases of AFS have been associated with immunodeficiency such as chemotherapy for acute lymphoblastic leukemia, renal failure, or long-standing diabetes. Therefore, we excluded such cases. However, all cases reviewed and all cases reported as *Bipolaris* SBAFS fit the atopic pattern of young, immunocompetent patients, suggesting that this group is homogeneous. Patients with aspergillosis AFS may have elements of invasive disease and should not be considered to have AFS.[19]

The mean age of patients with AFS ranges between 21 to 26 years. Our patients, however, averaged 30 to 34 years old.[4,14] There was no difference in the incidence of SBAFS patients by gender, but the 2:1 male-to-female ratio in our AFS population is consistent with published reports.[14] All had nasal polyps with at least one other atopic finding, which is also consistent with previous reports. None of our patients had stigmata of immunoincompetency. Many patients with SBAFS have proptosis or visual defects.[5,22,28] Five of our six surgical patients had an ocular defect. Almost 11% of the 28 AFS patients we treated had an intracranial extension, a finding consistent with the literature.[13]

In addition to those proposed by Kinsella et al.,[10] we support the following criteria for the diagnosis of *Bipolaris* SBAFS (Table 3). (1) Evidence of intracranial extension by radiographic, surgical, or pathologic means must be present. (2) Histopathologically, the lesion must be consistent with AFS. *Aspergillus* should be excluded. (3) Finally, many reports suggest that species such as *Drechslera* and others are separate microbial agents, but this is not the case.

Curvularia, *Brachycladium*, *Drechslera*, and *Helminthosporium* are obsolete synonyms of *Bipolaris*. *Cochliobolus* is also a teleomorph. Therefore, all of these microbes should be reported as *Bipolaris*.

Diagnostic Imaging

The most remarkable aspect of SBAFS is the consistency with which findings on preoperative imaging are considered to be a malignancy, as occurred in our patient. Preoperative radiographic diagnoses often include chordoma, meningioma, chondrosarcoma, and head-and-neck squamous cell carcinoma. Such misdiagnoses can result in an overly aggressive surgical and/or medical intervention. However, reported imaging characteristics are relatively uniform. In early case reports, sinus expansion was uniformly noted on CT.[3,30] As in our patient, bony erosion with residual bony spiculation without hyperostosis has been reported in all cases of SBAFS.[6]

The finding of a hyperattenuating lesion (45-60 Hounsfield units) is also uniform. Sinus expansion and bony destruction may be related to pressure atrophy, and hyperattenuation may be related to the high residual content of metallic ions in the lesion. Moreover, these lesions appear as areas of diminished signal intensity on both T1- and T2-weighted MR images. As in our patient, the lesions often enhance with the administration of gadolinium.[2,16,23] CT evidence of a lesion extending from a paranasal sinus associated with bony expansion, erosion, and hyperattenuation should prompt suspicion of an SBAFS. When this diagnosis is doubtful, MR imaging can be useful. The lesion should appear iso- to hypointense on both T1- and T2-weighted MR imaging. Transnasal sampling under CT guidance is possible.[20]

Treatment

Because the pathophysiology of AFS is of an allergic nature and the disease is noninvasive,[14] complete removal is unnecessary. The goals of surgery should be to provide tissue for pathologic verification (via intraoperative frozen section, permanent section, and microbial culture), debulkment, and aeration of sinuses. Several authors describe aggressive approaches such as facial degloving. Such radical approaches reflect preoperative uncertainty about malignancy. Aggressive surgical approaches can be associated with complications such as granulomatous encephalitis or cerebrospinal fluid leakage. No case of dural invasion in histiologically confirmed SBAFS has been described. No postoperative complications were associated with conservative treatment in our patients.

Whether postoperative antifungal therapy should be used is also uncertain. No differences have been reported in recurrence rates between cases of SBAFS treated with or without antifungal medications.[26,31] In most early cases of SBAFS, culture of a fungus was followed by treatment with systemic amphotericin B, ketoconazole, or itraconazole. These agents were initiated despite limited in vitro or in vivo activity of these drugs against *Bipolaris*. If treatment for the fungal agent was warranted, systemic corticosteroids, which are usually prescribed with the antifungal agent, would be contraindicated. However, patients usually respond to systemic steroid therapy rather than to antifungal medication. Several cases of recurrent AFS after antifungal therapy alone have been reported.[9,31] No cases of AFS appear to have recurred after appropriate corticosteroid therapy. However, cases of recurrent AFS treated with corticosteroids have resolved.[1,7,8,21,26,29] Although three of our patients with SBAFS received antifungal therapy after surgery, it is most likely not useful and may even be harmful due to the toxicity of systemic antifungal agents. Moreover, postoperative corticosteroid therapy may be necessary for complete resolution.[10] Definitive treatment for SBAFS is surgical debridement with adjunctive steroid therapy.

The prognosis of SBAFS is good. After adequate surgical debridement and aeration of the sinuses, complete neurologic resolution can be expected, as in our 6 cases. Close follow-up care is important. CT, MR imaging, or both are adequate for following SBAFS. The long-term use of topical steroids controls relapses, and systemic steroids may be warranted for a recurrence.

Table 3. Diagnostic Criteria for SBAFS

Skull base involvement
Radiographic evidence of sellar or anterior cranial fossa invasion.
Surgical evidence of intracranial spread
Pathologic abutment of dura
Pathology
Inflammatory reaction to fungus with "sporadic fungal elements"
No fungus ball collection (i.e., mycetoma)

Conclusions

Although *Bipolaris* SBAFS associated with a skull base extension is rare, this diagnosis should be considered when a paranasal sinus mass is present in a young atopic patient. CT findings of a hyperattenuating mass extending from the paranasal sinuses with bony erosion and isointense to hypointense lesions on T1- and T2-weighted MR images are consistent with *Bipolaris* SBAFS. These findings should raise suspicions of this entity in patients living in hot, arid climates. Definitive treatment consists of conservative surgical debulkment with aeration of the sinuses and pre- and postoperative use of corticosteroids. Postoperatively, antifungal medications are not required and complete neurologic recovery can be expected.

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Diskal Cyst: An Unusual Cause of Lumbar Radiculopathy

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Diskal cyst is a rare cause of radiculopathy. We describe the presentation, imaging, surgical management, and outcome of a 24-year-old man who presented with classic L5 radiculopathy. After conservative management failed, he underwent a standard L4/5 microdiskectomy with resection of the cyst. His symptoms improved after surgery

Key Words: cyst, disk, lumbar, radiculopathy, spinal surgery

Abbreviations Used: MR, magnetic resonance

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Lumbar disk herniation, a frequent cause of lower back pain and radiculopathy, is one of the most common indications for spinal surgery. Occasionally, other disease processes may mimic disk herniation. One such entity, diskal cysts, has rarely been reported. We therefore discuss the presentation, imaging, surgical management, and outcome of a 24-year-old man with a diskal cyst that caused L5 radiculopathy.

Case Report

A 24-year-old man had experienced 14 months of lower extremity pain on the left side in the distribution of the L5 nerve root. His strength was graded as 5/5 in all muscle groups. His reflexes and light touch were normal. His ipsilateral straight leg raise was positive. His symptoms had a rapid onset and were resistant to conservative management, including steroids and physical therapy. MR imaging of the lumbar spine showed a mass lesion arising from the L4-5 disk and impaction of the left L5 neural foramen (Fig. 1). In August 2007, the patient elected to undergo an L4-5 microdiskectomy.

Surgical Management

The patient underwent a standard approach for a left-sided L4-5 microdiskectomy. The left L5 pedicle, foramen, and nerve root were identified. No disk bulge was observed at the level of L4-5. However, the L5 nerve root was elevated dorsally. After further exploration, we found a cystic structure arising from the L4-5 disk space compressing the L5 root. The cyst was adherent to the ventral aspect of the L5 nerve root and di-

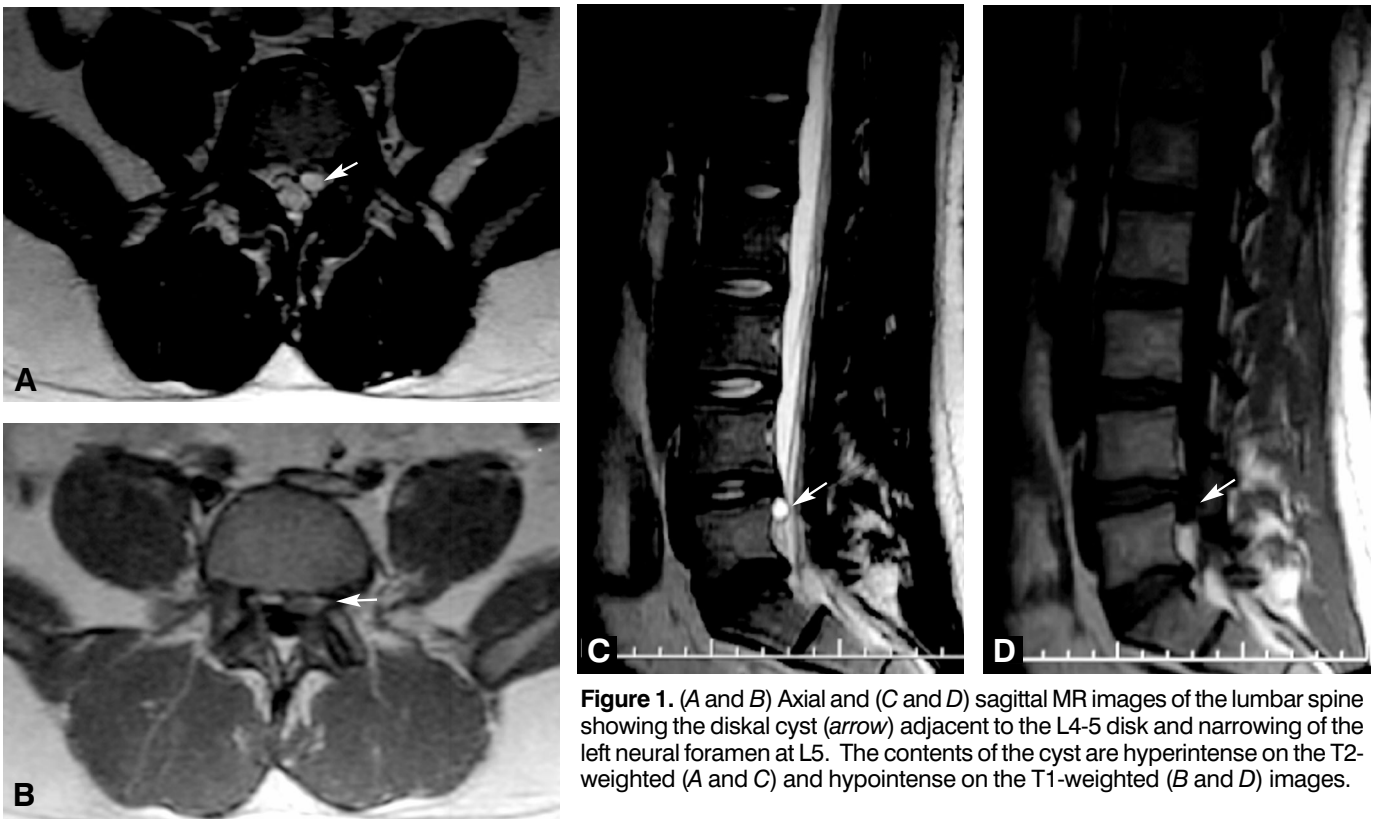

Figure 1. (*A* and *B*) Axial and (*C* and *D*) sagittal MR images of the lumbar spine showing the diskal cyst (*arrow*) adjacent to the L4-5 disk and narrowing of the left neural foramen at L5. The contents of the cyst are hyperintense on the T2-weighted (*A* and *C*) and hypointense on the T1-weighted (*B* and *D*) images.

rectly communicated with a small annular tear in the caudal aspect of the annulus. The cyst was carefully dissected free and removed. Conservative exploration of the disk space via the annular tear revealed no free fragments. A conservative foraminotomy was performed, and the nerve root was noted to be decompressed adequately. The wound was closed in a standard fashion.

Postoperative Course

After surgery the patient reported resolution of his symptoms. His neurological examination was normal, and he was discharged home the same day. At his 2-month follow-up examination, he reported that his radiculopathic pain had improved significantly compared to his preoperative status. However, he still experienced some recurrent pain (rated as 4 on a scale of 1 (least) to 10 (most)) in the left L5 distribution. His strength and sensory examinations were normal. MR imaging at that time was unremarkable. He was tapered from steroids and underwent a 1-month course of physical therapy. At 6 months his radiculopathy had resolved and he had occasional back pain. At 24 months he had no recurrence of radiculopathy and occasional back pain.

Discussion

Diskal cysts are characterized by radiculopathy, which is clinically indistinguishable from a disk herniation. These cysts are extradural and arise ventrally within the spinal canal. Unlike other intraspinal cysts, diskal cysts exist in direct continuity with the corresponding intervertebral disk. Cystic contents are hypointense on T1-weighted MR imaging and hyperintense on T2-weighted MR imaging and can therefore be distinguished from the imaging characteristics of herniated disks.

The pathogenesis of diskal cysts is unknown and the subject of debate. The finding of blood products in some cysts has led to speculation that diskal cysts emerge from a resolving hematoma caused by an initial injury to the disk. Others propose a degenerative mechanism similar to that underlying the development of ganglion cysts. Diskal cysts have also resolved spontaneously without surgical intervention.[2]

In 2001 Chiba et al.[1] published the largest case series of diskal cysts (eight relatively young patients). Their patients' symptoms, which consisted of pain in a single nerve root distribution, resolved immediately after the cyst was removed. Kishen et al.[3] described similar findings in a 13-year-old girl with S1 radiculopathy, which was relieved completely by surgical decompression. Most recently Nabeta et al.[4] reported five males with diskal cysts, all of whom presented with radiculopathy indistinguishable from a ruptured disk. After surgical treatment all five patients had immediate, durable resolution of their symptoms.

Initially, our patient described complete relief of his symptoms. In retrospect, he may have had some residual radiculopathy. We have no direct evidence, but we postulate that the cystic contents

irritated the nerve and may have been responsible for his persistent radiculopathy. For this reason, we chose to treat him with steroids.

Conclusion

A diskal cyst should be considered in the differential diagnosis of mass lesions causing radiculopathy, particularly if imaging characteristics are consistent with a cystic structure attached to the disk space. Microsurgical management is similar to microdiskectomy and can improve or resolve the associated symptoms.

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Miliary Tuberculosis Presenting with Neurological Symptoms

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TB continues to be an important cause of morbidity and mortality around the world. It is also reemerging in developed nations. Only about 1% of patients with TB develop intracranial tuberculomas, usually as part of miliary TB that arises from extracranial spread. Tuberculomas are usually seen in patients with extracranial signs and symptoms. The authors report the case of a 14-year-old Kenyan boy who presented in the United States with encephalopathy and signs of meningeal inflammation. Investigation revealed multiple brain tuberculomas from miliary TB. This case is unusual because the patient was young and presented with CNS symptoms rather than pulmonary symptoms despite the advanced stage of his disease. This case illustrates that this rare entity can be found even in developed countries. Rapid identification of lesions, biopsy, and treatment are essential to maximize outcomes for patients.

Key Words: cerebral tuberculosis, meningitis, tuberculomas, tuberculosis

Abbreviations Used: CNS, central nervous system; CT, computed tomography; DNA, deoxyribose nucleic acid; MR, magnetic resonance; TB, tuberculosis

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Tuberculosis continues to be a major worldwide health threat. Presently, it is reemerging in industrialized nations because of the relative ease of travel from endemic areas, the increasing incidence of infections with the human immunodeficiency virus, and the emergence of multiple drug-resistant *Mycobacterium* strains of tuberculosis.[6] Considering the increased prevalence of TB, it is not surprising that extrapulmonary spread is also becoming more common. Interestingly, however, the incidence of cerebral TB in children as old as 14 years is quoted as being as low as 0.00005%.[3]

Several recent articles have delineated the cerebral spread of miliary TB, which occurs in only about 1% of TB patients.[1,4,5] We present the unique case of an adolescent boy who presented to the hospital with encephalopathy and was found to have multiple infratentorial and supratentorial lesions without the expected pulmonary manifestations of *Mycobacterium* tuberculosis infection.

Case Illustration

A 14–year-old Kenyan boy presented to an outside hospital with encephalopathy, worsening headaches, and photophobia. Lumbar puncture revealed 500 white blood cells/ml^3 (80% lymphocytes), 25 red blood cells/ml^3, protein 307 mg/dL, and glucose 70 mg/dL. Intravenous vancomycin and ceftriaxone were started as empiric therapy. He quickly defervesced. His cerebrospinal fluid cultures remained negative so the antibiotics were discontinued. After 48 hours, he began spiking temperatures again and was returned to the emergency department at the outside hospital. There, he was

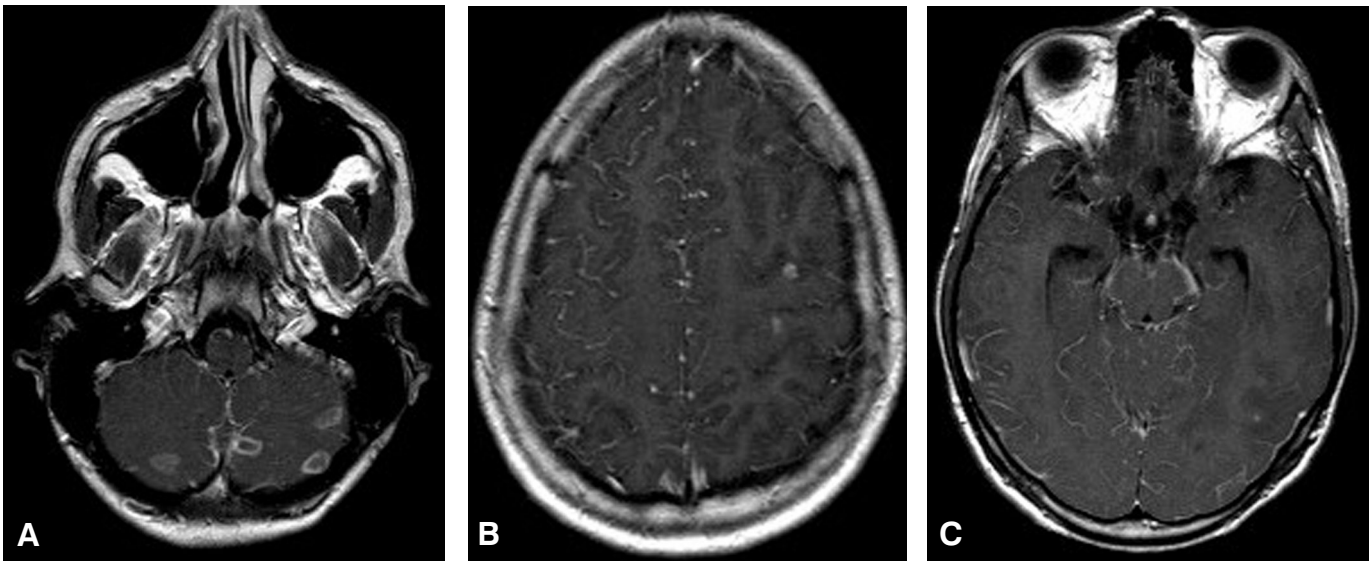

Figure 1. Contrast-enhanced T1-weighted axial MR images showing (*A*) multiple ring-enhancing lesions in the cerebellum, (*B*) multiple enhancing cortical granulomas, and (*C*) perimesencephalic leptomeningeal enhancement consistent with basilar meningitis.

given intravenous fluid hydration and antiemetics and discharged home with the diagnosis of influenza.

He continued to feel ill and returned for evaluation in the emergency department complaining of his mind "feeling blank." He subsequently became confused and developed rapid speech over the next several hours. Due to his altered mental status, contrast-enhanced CT of the head was performed. The study showed multiple ring-enhancing lesions in the cerebellum, brainstem, and gray-white junction bilaterally in the frontal, parietal, and occipital lobes. MR imaging of the brain showed multiple ring-enhancing lesions measuring about 5 mm in diameter throughout the cerebellum and cerebrum (Fig. 1). The largest lesion, approximately 8 mm in diameter, was in the brainstem (Fig. 2). A chest radiograph showed an ill-defined opacity in the right upper lobe, which was interpreted as right upper lobe aspiration or pneumonia. A right hilar opacity was interpreted as mild atelectasis.

A left suboccipital craniotomy was performed for excisional biopsy of the largest cerebellar lesion. Via microdissection, the lesion was carefully circumscribed, removed intact, and sent to pathology and microbiology for analysis. Biopsy revealed caseating granulomas

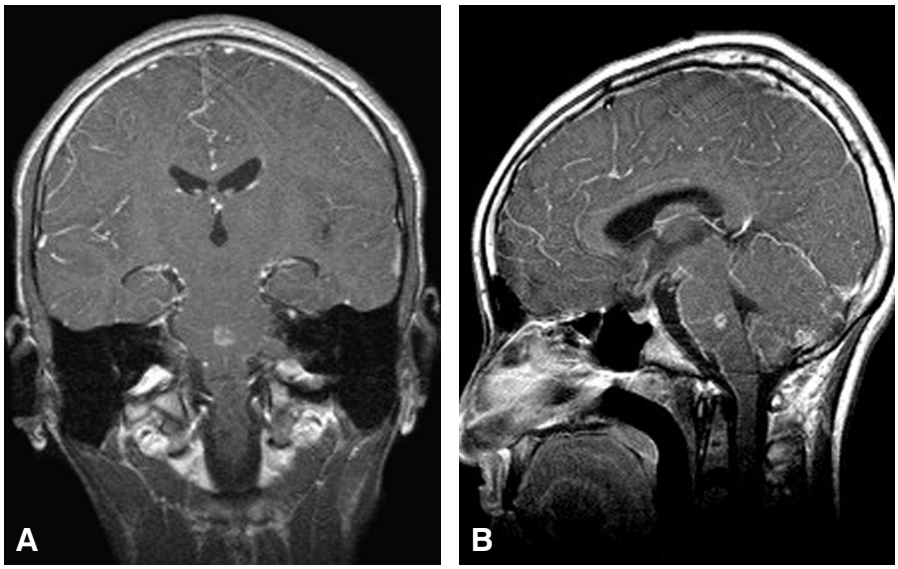

Figure 2. Contrast-enhanced T1-weighted (*A*) coronal and (*B*) sagittal MR images showing a large pontine lesion.

with acid-fast organisms consistent with tuberculoma. On further inspection, the arachnoid at the cisterna magna was noted to be thickened focally and milky consistent with basal meningitis. Biopsy of this arachnoid material showed caseating granulomas, as did the basal arachnoid specimen. This finding was consistent with TB meningitis.

Purified protein derivative skin testing resulted in a 34-mm induration on the forearm. Given these findings as well as the biopsy results, further imaging, including CT of the neck, chest, abdomen, and pelvis, was performed. Isoniazid, rifampin, pyrazinamide, and streptomycin (which was later changed to ethambutol) were started as treatment.

CT of the neck showed two mildly enlarged necrotic lymph nodes in the left carotid jugular chain. CT of the chest demonstrated pulmonary cavitation and nodularity bilaterally as reticular-nodular opacities in the upper lobe, tree-in-bud

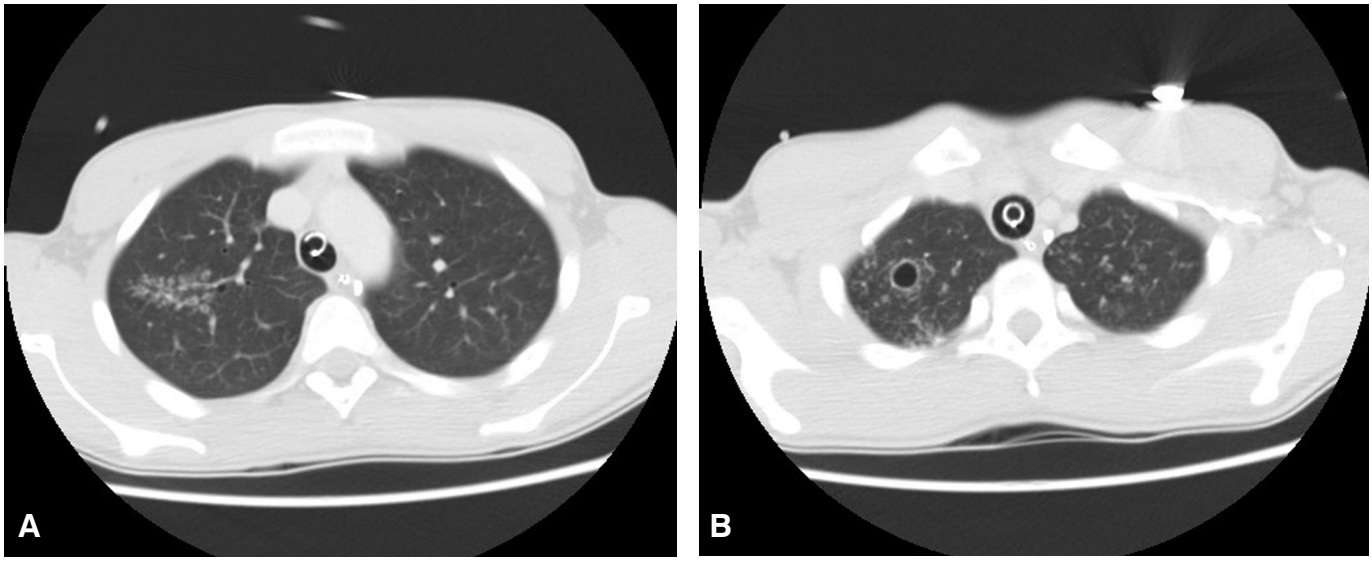

Figure 3. CT scans of the chest showing (*A*) reticular-nodular opacities, tree-in-bud opacities and (*B*) cystic bronchiectasis mostly involving the right lung.

opacities, and cystic bronchiectasis of the lungs (Fig. 3). CT of the abdomen and pelvis showed no abnormalities.

The microbiological analysis found growth from the brain sample consistent with pan-sensitive *Mycobacterium* tuberculosis, which was later confirmed by DNA probing. Spine radiographs were performed to rule out Pott's disease. No bony erosion was seen.

The patient had no history of ill contacts or other infectious diseases, such as human immunodeficiency virus. He had moved from Kenya 21 months before his hospitalization and likely contracted the TB before his move to the United States.

Discussion

Tuberculomas are avascular, spherical caseating granulomas that consist of epithelioid cells surrounded by lymphocytes and Langerhans giant cells. The centers of these lesions contain the caseous necrotic areas in which the *Mycobacterium* tuberculosis organisms reside. They tend to be located infratentorially in the pediatric population and supratentorially in adults. Lesions deeper in the neural parenchyma enlarge to form a tuberculous abscess. Within the CNS, these small tuberculomas initially develop in the subpial or subependymal surface of the brain or spinal cord. They can rupture into the subarachnoid and intraventricular spaces resulting in tuberculous meningitis.[3] Furthermore, this patient's cerebrospinal fluid findings, which showed a lymphocytic pleocytosis, were typical for TB meningitis.

The CNS becomes involved with TB in the form of tuberculous meningitis and tuberculomas. Ring-enhancing lesions with perilesional edema suggest tuberculomas.[7] Clinical signs and symptoms are initially silent, but symptoms gradually worsen.

The most important factor affecting the prognosis of cerebral TB is initiation of treatment. In our case, the patient had a definitive diagnosis within 18 hours of arriving at the hospital, and a regimen of antituberculosis medications was initiated immediately thereafter.

Numerous intracranial lesions were found in our patient. However, tuberculomas are usually solitary lesions. Studies have shown that 15% to 34% of cases present with multiple lesions.[2] Because of their high vascular supply, these lesions usually occur in the cerebral and cerebellar hemispheres. Rarely do these lesions develop in the brainstem. Interestingly, one of the largest lesions seen in our patient was in the brainstem.

Tuberculomas should be differentiated from tuberculous abscesses. The latter tend to present acutely, and patients appear quite ill, with fevers and chills, bad headaches, and focal neurological deficits. Tuberculous abscesses also tend to occur in the supratentorial space.

TB has been an important cause of morbidity and mortality in underdeveloped countries and now is in the United States as well. Cerebral TB usually manifests with extracranial signs and symptoms. However, it is important to recognize that even in the setting of significant pulmonary disease from a TB infection, the presenting symptoms can be purely neurological, as documented by our case. A high level of suspicion for infection should be maintained for atypical infections such as TB, which are becoming more prevalent in developed countries. However, our patient's TB infection likely was contracted while he lived in Kenya, where he had spent most of his life. Furthermore, the prevalence of disease is high in Kenya. The numerous intracranial tuberculomas also support this notion. The prevalence of TB is greatest in subSaharan Africa and southeast India. Furthermore, the development of tuberculomas is rare in the United States.[4]

Once the diagnosis of intracranial tuberculoma is suspected, antituberculosis therapy should be initiated as soon as possible. The choice of empiric therapy should be based on sensitivities. Combination therapy usually includes isoniazid, rifampin, pyrazinamide, and a fourth agent such as an aminoglycoside, ethambutol, or ethionamide. Adjuvant corticosteroid therapy (i.e., prednisone 2–4 mg/kg/day for 1 month) is recommended for patients with tuberculous meningitis. It also should be considered in children with pleural or pericardial lesions, severe miliary disease, and endobronchial disease.[4]

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