

Oligoastrocytoma presenting with intractable epilepsy

Girish K. Hiremath¹, William E. Bingaman¹,
Richard A. Prayson², Dileep Nair³

¹ Department of Neurosurgery

² Department of Anatomic Pathology

³ Department of Neurology, Cleveland Clinic Foundation, Cleveland, Ohio, USA

Received November 21, 2006; Accepted May 3, 2007

ABSTRACT – Objective. Oligoastrocytomas (OA) are mixed gliomas with distinct oligodendroglial and astrocytic neoplastic components. Very little about OA has been reported in the intractable epilepsy population. **Methods.** We undertook a retrospective review of 923 patients who underwent resective surgery for intractable epilepsy between 1996 and 2004. **Results.** 6/923 (0.7%) patients were diagnosed with OA. Five patients were female, one was male. Median age at diagnosis was 25 years (range 19-44 years). Tumors arose from the left side in all patients and from the temporal lobe in five patients. Three patients had complex partial seizures. Median length of refractory epilepsy prior to surgery was 10.5 years (range 1-28 years), and the median number of antiepileptic drugs used was 2 (range 1-10). Preoperative WADA testing for language and memory localization was done for three patients; preoperative stereotactical localization was done for three patients. Surgical pathology revealed low-grade OA (WHO II) in five patients, and anaplastic OA in one. There were no surgical complications, clinical or radiographic tumor recurrence at a mean follow up period of 3.2 years (range 2-8). Excellent seizure freedom was achieved in 5/6 patients. **Conclusion.** As a result of our small sample size, general conclusions may be imprecise, but this review suggests that OA behave similar to other tumors related to intractable epilepsy: they usually have a preoperative seizure course of many years, an excellent rate of seizure-freedom following surgery, and are in general, low-grade tumors with an indolent course for which serial imaging is sufficient follow-up.

Key words: oligoastrocytoma, intractable epilepsy, epilepsy surgery, tumor

An oligoastrocytoma (OA) is a mixed glioma with distinct oligodendroglial and astrocytic neoplastic components. The diagnosis of OA remains problematic, as controversy exists regarding the requirements for the precise pathologic definition of the lesion.

When initially described as a distinct entity in 1974, two patterns of mixed glioma were described by Hart *et al.* (1974). In one pattern, there were geographically distinct areas of oligodendrogloma and astrocytoma in the

same tumor. Most pathologists still recognize this pattern as mixed glioma; however, there is no uniform agreement about the required percent of the minor cell component that is necessary to make a diagnosis of mixed glioma versus pure oligodendrogloma or astrocytoma. The second pattern of mixed glioma described is one in which the two cellular components of the tumor are admixed together. This also has difficulties from a diagnosis standpoint in that recognition of this pattern is somewhat obser-

Correspondence:

Girish K. Hiremath
Department of Neurological Surgery,
Cleveland Clinic Foundation, S-80,
9500 Euclid Avenue,
Cleveland, OH 44195
USA
Tel.: (216) 444-5539
Fax : (216) 445-6801
<hiremag@ccf.org>

ver dependent. It is not unusual in a predominantly oligodendrogloma or astrocytoma tumor to find occasional intermixed cells of the other tumor type. With the more recent recognition that certain molecular findings, particularly deletions on chromosomes 1p and 19q, are associated with the oligodendrogloma phenotype (and with chemoresponsiveness and better outcome), evaluation of the markers in "mixed gliomas" have provided some guidance in a subset of tumors that show both deletions. The literature has also been marked by articles, which have either failed to specifically define what is meant by mixed glioma, or studies which have lumped the mixed gliomas together with oligodendroglomas, making it difficult to get a true sense on how these tumors behave.

Compared with pure astrocytomas, whose incidence rate is 3.69 per million population per year, and pure oligodendroglomas, whose incidence rate is 2.22 per million population per year, the incidence of OA's is 1.02 per million population per year (Beckmann and Prayson 1997). According to the Norwegian Cancer Registry, in a group of 596 patients with low-grade gliomas diagnosed between 1982 and 1993, 13.8% were OA's (WHO grade II) (Johannesen et al. 2003). Tortosa and colleagues found that anaplastic (WHO grade III) OA's represent approximately 17% of all anaplastic gliomas (Tortosa et al. 2003). Seizures occur in 63-85% of patients with OA as the initial presenting symptom (Tortosa et al. 2003; Buhl et al. 2004). Other common presenting symptoms included memory changes, headache, and speech difficulties (Buhl et al. 2004).

Very few studies have evaluated in any significant detail, the correlation between OA and patients who suffer from intractable epilepsy, necessitating neurosurgical excision of seizure foci. We present the findings of six patients with a histological diagnosis of OA from our series of 923 patients operated at the Cleveland Clinic for resection of seizure foci for the treatment of intractable epilepsy between November 1996 and December 2004.

Methods

A review of all of the patients in the epilepsy surgery database of the principal author (WEB) was undertaken after approval by our institutional review board. We found that between November 1996 and December 2004, a total of 1254 patients underwent procedures for intractable epilepsy. Of this group, 225 patients underwent procedures related to vagal nerve or deep brain stimulators for control of seizures, without the excision of seizure foci. One hundred patients underwent other neurosurgical procedures that did not include resection of epileptogenic foci—this included removal of subdural electrodes without resection of cortical tissue, in addition to procedures for management of postoperative complications such as hydrocephalus and wound infections. Six patients under-

went radiosurgical treatment of epileptogenic foci. As a result, 923 patients remained from the initial group. Out of this group of 923 patients, pathological analysis revealed hippocampal sclerosis in 26% of samples, cortical dysplasia in 23%, gliosis in 17%, neoplasm in 12%, vascular etiology in 13%, and nonspecific changes or other rare entities in 9%. In the subgroup of neoplasm, 23% showed ganglioglioma, 13% of samples showed low grade astrocytoma, 12% showed dysembryoplastic neuroepithelial tumor (DNET), 12% showed oligodendrogloma, 2% showed primitive neuroectodermal tumor (PNET), 2% showed meningioma, and other low grade gliomas comprised 32%. OA comprised 4% of all neoplasms in this population. 0.7% of patients (6/923) had OA on surgical pathology using the most current World Health Organization Classification (Smirniotopoulos 1999). The diagnosis of OA was made when, in a mixed glioma, the minority cell type exceeds 20% of the proportion of the total tumor (Beckmann and Prayson 1997, Mueller et al. 2002). Charts, computerized records, and imaging of all six patients were reviewed. In addition, details of each patient's demographic information, seizure semiology, electroencephalogram (EEG) findings, imaging findings, length of antiepileptic drug use, type of surgery, surgical complications and postoperative course, status at follow-up, and surgical pathology reports were collected. The patient's seizure semiology are described using the semiologic classification used at our institution (Luders et al. 1989).

Case reports

Patient 1

This 16 year old white female presented to us with a one year history of seizures. The seizures began with an abdominal discomfort that was often associated with tingling of her right hand. This then evolved into a chill spreading throughout her body and into the right leg. This would last a few minutes without disturbing her level of awareness and would tend to cluster at an interval of 10-12 seizures in a 24 hour period. These seizures were daily occurring both during the day as well as during the night. The initial seizure at the time of the onset of her symptoms consisted of a glazed look, loose awareness then evolving into twitching of her limbs. This seizure only occurred once at the time of her presentation. The patient underwent a video-EEG evaluation during which interictal spikes were recorded in the left temporal region maximum T7(T3). This population consisted of 100% of the interictal spike activity. She had 9 seizures recorded in a cluster over 2 hours. These seizures were classified as abdominal aura evolving into a right hand somatosensory aura. There was no loss of consciousness or awareness during these seizures. The ictal EEG was classified as regional left temporal with repetitive theta spiking involving the left temporal region, maximum T7. She was placed on phenytoin with good

control of seizures, but developed signs of raised intracranial pressure such as headache, nausea and emesis, prompting magnetic resonance imaging (MRI) one year after the onset of seizures. MRI revealed a 6 X 4.3 X 4.5 cm heterogenous, cystic mass, with enhancement in the left temporal lobe, causing mild uncal herniation. She underwent preoperative evaluation with WADA for language and memory testing. This patient underwent resection of the mass *via* awake craniotomy for language mapping. As the mesial structures were found to be uninvolving, tumor resection proceeded upto, but not including this area. Pathology revealed anaplastic OA (WHO III). At a follow up of two years, this patient remains at Engel Class II with no radiological evidence of tumor recurrence.

Patient 2

This 43 year old white female presented with a 28 year history of intractable epilepsy. Her initial seizures consisted of a stare with an alteration of consciousness. One year later she experienced her first secondary generalized seizure. The seizures at the time of evaluation consisted of a feeling in her stomach that rises to her head and then her entire body. This is also associated with a feeling of fear. She then begins to feel her body start to tremble then loses awareness. Observers at this point state that she appears to be staring and is unresponsive. She has some manual automatisms. The seizure lasts for a few minutes followed by a return to baseline after five minutes of confusion. She feels very nauseous at the end of her seizures. Her seizures tend to cluster around her menses with 1-5 seizures immediately before her menses or after the cessation of her menses. Her secondary generalized seizures occur more infrequently at a frequency of approximately one per year. She had a history of being struck in the head at the age of 12 years by a swing and reportedly lost consciousness for about 30 minutes but returned to baseline after 24 hours. She underwent a video-EEG evaluation during which interictal spikes were recorded from the left mesial temporal electrode (SP1) and consisted of 100% of the interictal spike population. She also had two seizures recorded which were classified as aura evolving into a dialeptic seizure followed by right versive seizure then generalized tonic-clonic seizure. Both ictal EEG were classified as regional left temporal with a rhythmic theta pattern seen developing over the left temporal region. MRI revealed a non-enhancing, hyperintense lesion of the left superior temporal gyrus on T2 weighted imaging, with central CSF-appearing characteristics. This patient underwent a stereotaxis-guided volumetric resection of the left superior temporal gyrus lesion. Pathology revealed low-grade OA. At a follow up of two years, this patient remains at Engel Class I, with no radiological evidence of tumor recurrence.

Patient 3

This 21 year old white male presented with a three year history of seizures. The initial seizure consisted of a sudden loss of consciousness with observers stating that his head turned to the right followed by shaking of his extremities. These seizures have persisted at a frequency of two per year. His more frequent seizures consist of a feeling as if he is "losing his train of thought." He also gets a feeling of "something about to come on" or an indescribable distortion of his vision and on occasion he sees stars and gets a chill sensation. He is able to maintain his awareness during all these feelings but has difficulty thinking and often does not make sense when he talks. Observers state that his speech is garbled during this time but is able to continue with motor activities in a purposeful manner. The seizure lasts for 1-3 minutes and occur 2-3 times per week. He underwent a video-EEG evaluation during which two populations of interictal spikes were recorded. One was regional left parieto-occipital, maximum PO3/POz consisting of 60% of the total interictal epileptiform discharges. The other population was seen regional left centroparietal, maximum C5/T7 consisting of 40% of the interictal epileptiform population. A total of ten seizures were recorded of which nine were just auras and one that began with an aura but evolved into an automotor seizure then right versive seizure followed by a generalized tonic-clonic seizure. Of the auras six consisted of a feeling in his head as if he couldn't think straight and 4 consisting of a feeling in his stomach like excess gas associated with nausea. In one aura there was no clear EEG change. In all the rest of the seizures the ictal EEG was classified as regional left parieto-occipital with low amplitude semirhythmic sharply contoured activity in the alpha frequency arising from the O1,P7,PO7, and P3 electrodes. MRI revealed a non-enhancing, hyperintense mass of the left inferior parietal lobule measuring 2.5 X 1.4 X 2 cm. He underwent preoperative evaluation with WADA for language and memory testing. This patient underwent stereotaxis-guided volumetric resection of this lesion. Pathology revealed low-grade OA. At a follow of two years, this patient remains at Engel Class I, with no radiological evidence of tumor recurrence.

Patient 4

This is a 17 year old white female with a 10 year history of seizures that begins on occasion with an aura in which she sees colors or sometimes sees a snake wrapped around her arm. These auras evolve into a loss of consciousness but can occur in only 10-20% of her seizures. Most of her seizures consists of a fall, generalized stiffening of her body a head turn towards one side or spinning of her body in one direction. The seizures last from 1 to 2 minutes and occur 10 to 12 times a day and more frequently during her menses. Following the seizure she had difficulty with word finding which can last for 1 hour. She underwent a video-

EEG evaluation during which interictal spikes were seen in the left parietal region, maximum P7 (70% of the total spike population), left temporal region, maximum FT9 (20% of the spike population), and right temporal region, maximum FT10 (10% of the spike population). She also had 5 seizures recorded which were classified as complex motor seizure evolving into a right ictal seizure followed by a generalized tonic-clonic seizure. The ictal EEG in all these seizures were classified as regional left fronto-central with a rhythmic beta activity seen maximum in the F3>C3 electrodes. She then underwent an invasive video-EEG evaluation with the aim to tailor the resection of the lesion and spare eloquent cortex with extraoperative cortical mapping. She underwent a subdural grid placement in which an 8X8 grid was placed over the left lateral parietal lobe and posterior-superior temporal lobe (A plate); a 4X4 subdural grid placed over the left posterior inferior frontal lobe (B plate); and two 1X6 strip electrodes placed over the left anterior basal temporal region (C plate), and left basal posterior temporo-occipital region (D plate). Interictal spikes were seen over regions of the left lateral temporal area (40%), left mesial temporal area (45%), and left parietal area (15%). Three clinical and 12 subclinical seizures were recorded. The clinical seizures were classified as aura evolving into a dialeptic seizure. The ictal EEG onset occurred 4-19 seconds prior to clinical onset and was classified as regional left temporoparietal as a paroxysmal fast activity seen over regions of the A plate close to the cystic margins of the tumor. Cortical stimulation to map posterior language function was carried out and large area of cortex near the vicinity of posterior superior temporal gyrus was identified as language areas (producing difficulties in reading, difficulties in understanding verbal or written commands, or difficulties in naming). MRI revealed a 2.6 X 2.8 X 2.0 cm solid and cystic, enhancing posterior left temporal lobe mass that extended to involve the ependymal surface of the temporal horn of the lateral ventricle. She underwent preoperative evaluation with WADA for language and memory testing. The patient underwent subdural grid evaluation to more precisely define the epileptogenic area. Following this procedure, she underwent a resection of the tumor, without resection of mesial structures, as this was found to be free of disease upon visual inspection intraoperatively. Pathology revealed low-grade OA. At a follow up period of three years, this patient remains at Engel Class I, with no radiological evidence of tumor recurrence.

Patient 5

This is a 43 year old white female with a 19 year history of seizures. In 1988, she initially underwent a left anterior temporal lobectomy with removal of tumor and sparing of the amygdala and hippocampus, which was found to be OA at pathology. Her presurgical evaluation at that time showed left temporal sharp waves and left temporal seizures. Her seizures were classified as aura evolving into an

automotor seizure. However, the patient continued to have seizures immediately after surgery with no change in her semiology. Her seizures consisted of an aura which was described as a "weird feeling or hot flashes." This then would evolve into a stare with unresponsiveness associated with lip smacking or picking movements of her hands. The seizures lasted for minutes and were occurring 5-15 times per month. She did have a history of secondary generalization in the past but had not had any for the past 10 years. Her repeat video-EEG evaluation showed interictal sharp waves regional right temporal, maximum SP2 (consisting of 50% of the total interictal epileptiform discharges) and left temporal, maximum T7 (50% of the total epileptiform discharges). She had a total of 8 seizures recorded of which five were auras not associated with any EEG changes. The other three seizures evolved into a right face clonic then generalized tonic-clonic seizure which showed an ictal pattern classified as regional left temporal with rhythmic theta/delta pattern maximum T7. Her neuroimaging initially was found to have hyperintense changes in the mesial structures, which were not removed during this initial surgery. Following the repeat evaluation, she underwent a resection of the mesial structures. This patient has been at Engel Class I for eight years without radiological evidence of tumor recurrence. Pathology continued to reveal OA.

Patient 6

This is a 29 year old Hispanic female with a 21 year history of seizures which were initially described as beginning with an aura of fear lasting for about 2 minutes before losing consciousness and falling to the floor. At that point she would have a shaking of her body affecting more the right side of her body. At this point she had only routine and one ambulatory EEG which did not capture any of her seizures. There was interictal epileptiform activity recorded at that time which was seen regional temporal frontotemporal (F7/T7). MRI revealed a cystic neoplasm of mesial structures of the left temporal lobe. She underwent a left temporal lobectomy with resection of mesial structures and tumor. Pathology revealed low-grade OA. This patient was seizure-free for eight months following surgery, but then began having recurrent seizures. She, however, did have worthwhile improvement in her seizure burden compared to her preoperative status. She remains at Engel Class 3 without radiological evidence of tumor recurrence at a follow up of 2 years. Her seizures after surgery had a different semiology. She began to experience an aura in which she heard voices (usually someone yelling at her) at which point she would feel fear then lose consciousness. Observers state that she stares, is unresponsive, and fumbles with her clothes. Her seizures now last 3-4 minutes and occur once per week. She had a video-EEG evaluation at that point which recorded left midtemporal spikes, maximum T7/TP7 consisting of 100% of the interictal epileptiform activity. She had one

Table 1. Summary of patients diagnosed with oligoastrocytoma.

Pt #	Age	Sex	Seizure type, duration of seizures	MRI findings	Surgery	Pathology
1)	16	F	1. Abdominal Aura->Right hand somatosensory aura, 2. Dialectic seizure -> GTC 1 year	Cystic left temporal lobe mass	Awake craniotomy with resection of tumor	AOA (WHO III) 1p,19q intact Ki-67: 9-10%
2)	43	F	Abdominal Aura -> Dialectic seizure -> GTC, 28 years	Focal T2 hyperintensity of left STG	Stereotactic resection of left STG lesion	OA (WHO II) 1p, 19q intact Ki-67 < 1%
3)	21	M	Aura -> Automotor seizure -> Right versive -> GTC, 3 years	Focal T2 hyperintensity in left parietal region	Stereotactic resection of left parietal tumor	OA (WHO II) 1p,19q intact Ki-67 < 1%
4)	17	F	Aura -> Complex motor seizure -> Right versive -> GTC, 10 years	Cystic left temporal lobe mass with enhancement	SD grids with cortical mapping, followed by resection of tumor	OA (WHO II) 1p,19q intact Ki-67 < 1%
5)	43	F	Aura-> Automotor seizure -> Right face clonic-> GTC,, 19 years	Hypoattenuation of left amygdala and hippocampus	1988: left anterior temporal lobectomy with partial resection of mesial structures; 1998: reoperation and further resection of mesial structures stereotactically	OA (WHO II) 1p,19q intact Ki-67 < 1%
6)	29	F	1.Auditory aura -> automotor seizure -> GTC, (after surgery) 2. Fear aura -> Generalized tonic-clonic (before surgery) 21 years	Cystic mass involving mesial structures of left temporal lobe	Left temporal lobectomy with resection of tumor and mesial structures	OA (WHO II) 1p,19q intact Ki-67 < 1%

Key: F = female; M = male; CPS = complex partial seizures; GTCS = generalized tonic-clonic seizures; STG = superior temporal gyrus; SD = subdural; AOA = anaplastic oligoastrocytoma.

seizure recorded classified as an auditory aura evolving into a generalized tonic-clonic seizure. The ictal EEG was classified as left temporal onset with a rhythmic theta activity seen maximum at F7. Further presurgical testing was advised with invasive recordings to map ictal onset zones and function mapping. She is continued to be followed but her surgical work up was placed on hold due to a pregnancy.

Results

Patient demographics are summarized in *table 1*. Of the six patients, five were female, and one was male.

The median age for each patient was 25 years (range 19-44 years). The median length of medically refractory epilepsy prior to surgery was 10.5 years (range 1-28 yrs). The median number of antiepileptic drugs used was 2 (range 1-10). Please refer to *table 2* for details of surgical management.

There were no immediate surgical or postoperative complications for any of these six patients. No patient had seizures during the immediate postoperative period, and five of six have remained seizure-free. The average length of follow-up was 3.2 years. *Figures 1A,B, 2A,B* are representative preoperative and postoperative MRI's of this group.

Table 2. Surgical management.

Patient	Tumor Location	Preoperative WADA	Stereotaxis	Intraoperative Studies/cortical mapping	Lesionectomy Only
1	Left Anterior TL	Yes	No	Awake language examination	Yes
2	Left STG	No	Yes	No	Yes
3	Left Parietal	Yes	Yes	No	Yes
4	Left Inferior TL	Yes	No	SD Grids, followed by resection	Yes
5	Left Amy/Hip	No	Yes	No	No
6	Left Mesial TL	No	No	No	No

Key: TL = temporal lobe; STG = superior temporal gyrus; SD = subdural; Amy/Hip = amygdala, hippocampus.

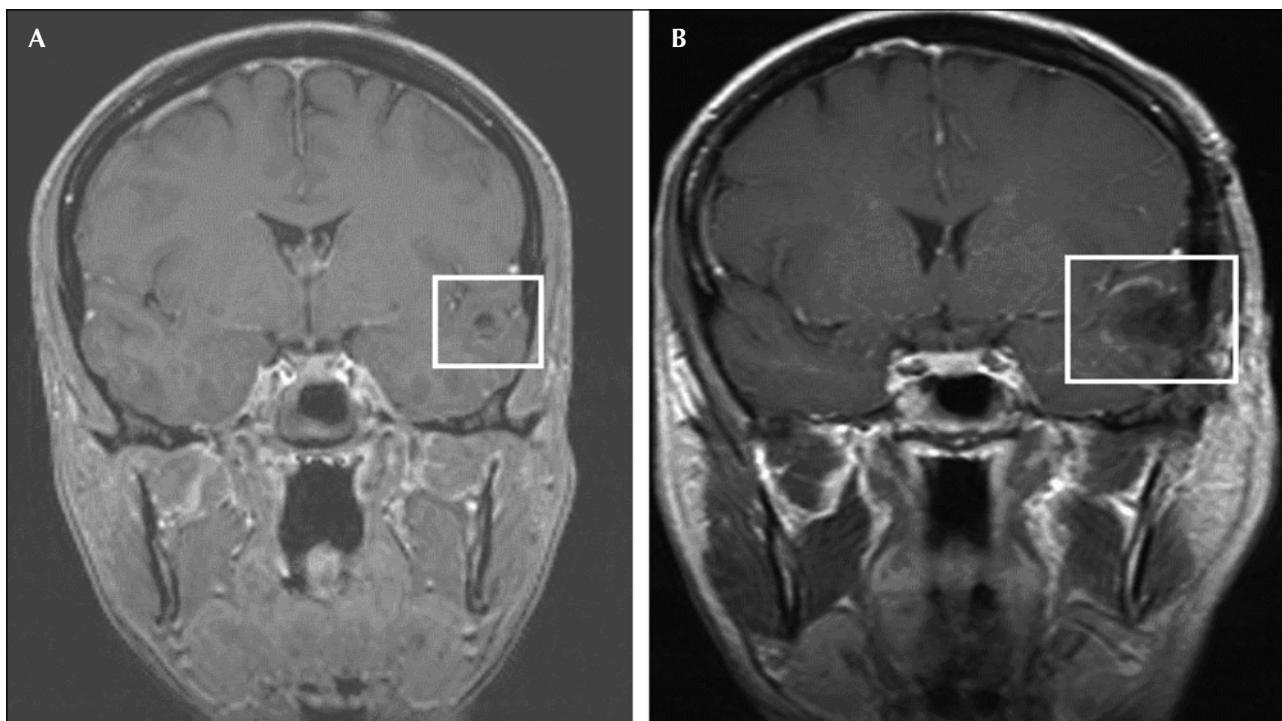


Figure 1. Left temporal lobe OA pre-(A) and post-(B) resection.

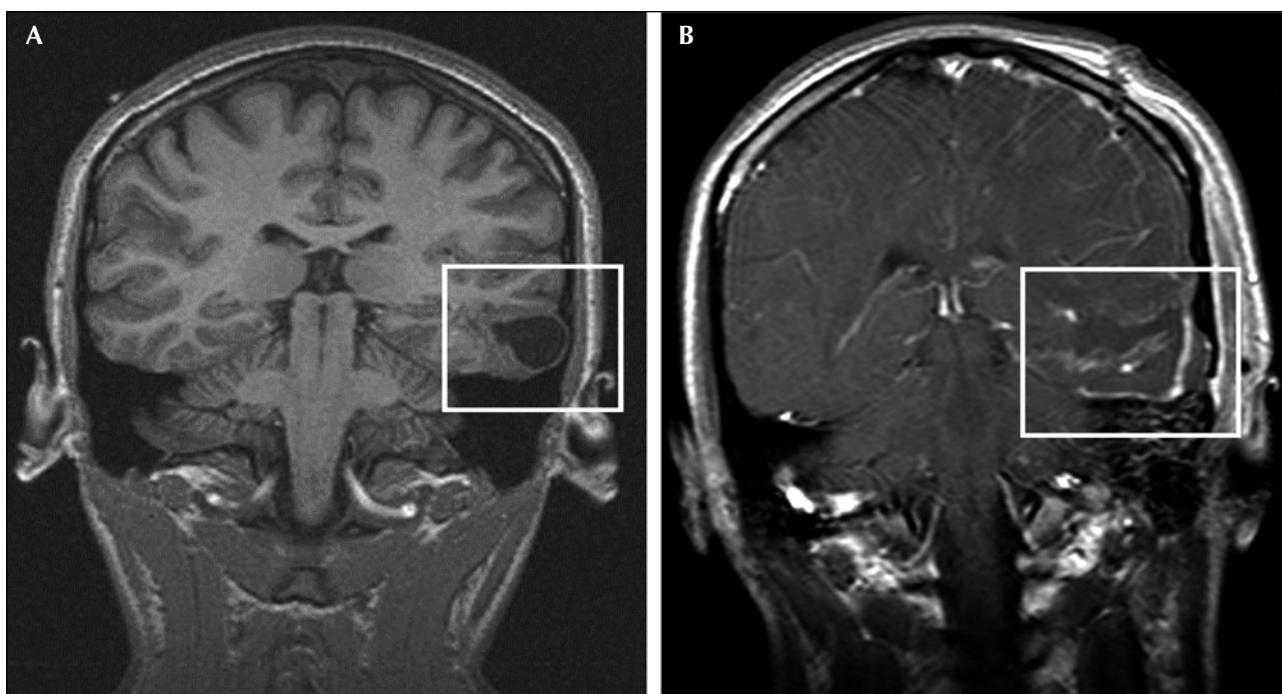


Figure 2. Predominantly cystic left temporal lobe OA pre-(A) and post-(B) resection.

Five of the six patients (patients 2-6) were found to have low-grade (WHO Grade II) OA on surgical pathology. None of these five patients have undergone adjunctive

chemotherapy or radiation therapy. One patient was found to have anaplastic (WHO Grade III) OA marked by increased cellularity and nuclear pleomorphism,

increased mitotic activity (up to five mitotic figures per high power field), focal vascular proliferation and necrosis. This patient underwent radiation therapy and chemotherapy with Temozolomide®. None of the six patients, at a mean follow-up of 3.2 years (range 2-8) show any radiological evidence of tumor recurrence.

All patients had chromosomal analysis of surgical pathology specimen, and were found to have intact chromosomes 1p, and 19q. Ki-67, a cell proliferation index, was < 1% for all of the patients with low-grade oligoastrocytoma (WHO Grade II), but was 9-10% in the one patient with anaplastic oligoastrocytoma (WHO Grade III). Immunostaining with antibody to p53 (DO-7 clone) was performed on all tumors and the results demonstrated < 10% positivity.

Discussion

We present a series of patients suffering from intractable epilepsy in whom diagnosis of resected epileptogenic brain was OA; we find that in this patient population, this diagnosis is a relatively rare one, affecting only 0.7% of surgically treated patients with epilepsy over an 8 year period. As mentioned before, very little has been reported with regard to the presentation of OA in the intractable epilepsy population. Perhaps the largest series of OA in the intractable epilepsy population is that of Plate *et al.* (1993) who performed a retrospective pathological analysis on specimen collected after selective amygdalohippocampectomy, and found that 126 out of 224 (56%) specimens were involved with tumor, and that 12 of the 126 (10%) tumor specimens was involved with OA (Plate *et al.* 1993). The proportion of patients who had OA in this series was much higher than in ours, or in other series. Plate *et al.* did not describe their classification scheme for the diagnosis of OA, and it is possible that their scheme does not conform to the classification scheme established in the most recent WHO classification as mentioned above, at least partially explaining the significant difference noted. Oda *et al.* (1998) studied surgical specimens from thirty patients with intractable epilepsy, and found only one patient with OA. Wolf *et al.* (1993) studied the chronic epilepsy population whose seizures arose from non-temporal origin, and found one OA in a consecutive series of 63 patients. In our own series of 133 consecutive resections for extra-temporal lobe based epilepsy, only one patient was diagnosed with OA (Frater *et al.* 2000). In the present series, five out of the six patients were female, and all five of them harbored temporal lobe seizure foci. Female predominance however, with respect to OA has not been shown in a review of the literature (Beckmann and Prayson 1997, Buhl *et al.* 2004, Okamoto *et al.* 2004, Whittle and Beaumont 1995). Interestingly, all tumors in this population were located on the left side. As may be expected in this population, most of the six pa-

tients harbored OA in the temporal lobe (83%). The median age at diagnosis of OA in this population was 25 years, which is lower than the mean age at diagnosis for all patients presenting with OA—the mean age at diagnosis for OA WHO grade II was 39 years and for OA WHO grade III was 44 years according to Buhl *et al.* (2004). In our own series of OA in the general brain tumor population (Beckmann and Prayson 1997), the average age of presentation was 37 years.

The median preoperative course, 10.5 years, was long compared to other OA series (Beckmann and Prayson 1997, Buhl *et al.* 2004, Johannessen *et al.* 2003, Whittle and Beaumont 1995). It has been established that patients suffering from tumor-related intractable epilepsy have a generally good prognosis, with an indolent course of their tumors. In addition, there is a high probability of being seizure-free postoperatively (Morris *et al.* 1993, Zentner *et al.* 1997). In the series presented by Zentner *et al.* (1997) the mean preoperative course of medically refractory seizures was 14 years; in the series of Morris *et al.* (1993) the mean preoperative course was 10.5 years. Patient 1 in our group had the shortest preoperative course of one year—this patient was also the only patient harboring an anaplastic OA. This finding further supports the argument that patients with tumor-related intractable epilepsy generally have low-grade tumors with a preoperative course of many years—and that the clinical presentation of the one patient with anaplastic OA in our series may parallel that of those harboring OA not associated with intractable epilepsy (Zentner *et al.* 1997).

Electrocorticography (ECOG) is an intraoperative technique used to maximize the extent of neocortical seizure focus resection, while allowing the mapping of adjacent eloquent cortex. Controversy exists with regard to whether tumor resection should involve the use of intraoperative ECOG to resect additional cortical tissue that may be epileptogenic. However, there has been no definitive evidence stating that the use of ECOG substantially changes the patient's chance of being free of seizures postoperatively (Pilcher *et al.* 1993, Whittle and Beaumont 1995). In addition, resection of non-tumoral tissue, especially in this patient population may contain risks of damage to eloquent cortex, with resultant neurological deficits (Whittle and Beaumont 1995).

With regard to chromosomal analysis, no patients in our group demonstrated deletions on chromosomes 1p and 19q—findings that are observed in over half of oligodendrogliomas. Smith *et al.* (2000) found that combined loss of 1p and 19q are identified as predictors of prolonged overall survival among patients with pure oligodendroglomas, but not for patients with OA. As can be expected in our patient population, most lesions arose in the temporal lobe, leading to the symptoms of epilepsy of temporal lobe onset. Interestingly, Mueller *et al.* (2002) have studied temporal, and non-temporal OA, and have found that OA's in the temporal lobe have a low rate of allelic

loss of chromosomes 1p and 19q. Further, loss of heterozygosity of 1p and 19q were noted to be inversely associated with p53 mutations (Mueller *et al.* 2002). However, other studies have found no obvious association with the presence of p53 mutations in OA and tumor grade or behavior (Beckmann and Prayson 1997).

Shaw *et al.* (1994) found that the median survival for OA's WHO grade II is approximately 6.3 years, and for OA WHO grade III is approximately 2.8 years. Mean follow-up for our patients is 3.2 years, and no patients have been found to have radiological or clinical recurrence. It will be interesting to see if, upon longer-term follow-up, the survival of this patient group parallels those with OA with deletions of chromosomes 1p, and 19q.

Conclusion

OA is a rare cause of medically intractable epilepsy. When present, surgical resection of the tumor led to an excellent seizure-free outcome in the majority of our cases. As a result of our small sample size, other general conclusions regarding the long term outcome of OA would be difficult to make. However, we draw certain similarities between OA, and other forms of tumors related to intractable epilepsy. Like other tumors in the intractable epilepsy population, OA in this population seems to be an indolent disease, and its prognosis may be better than OA in the general brain tumor population. Therefore, in this group of patients, serial imaging for grade II OA may be sufficient follow-up, with adjuvant therapies reserved for higher grade OA's Awad *et al.* 1991. □

Acknowledgments. We would like to thank Ann Warbel, RN for helping us with the epilepsy patients' database and imaging.

References

- Awad IA, Rosenfeld J, Ahl J, Hahn JF, Luders H. Intractable epilepsy and structural lesions of the brain: mapping, resection strategies, and seizure outcome. *Epilepsia* 1991; 32(2): 179-86.
- Beckmann MJ, Prayson RA. A clinicopathological study of 30 cases of oligoastrocytoma including p53 immunohistochemistry. *Pathology* 1997; 29: 159-64.
- Buhl R, Hugo HH, Stark AM, Mihajlovic Z, Gottwald B, Mehndorn HM. Clinical experiences with oligoastrocytomas WHO grade II and III. *Neurosurg Rev* 2004; 27: 218-23.
- Frater JL, Prayson RA, Morris HH, Bingaman WE. Surgical pathological findings of extratemporal-based intractable epilepsy: A study of 133 consecutive resections. *Arch Path Lab Med* 2000; 124(4): 545-9.
- Hart MN, Petito CK, Earle KM. Mixed gliomas. *Cancer* 1974; 33: 134-40.
- Johannesen TB, Langmark F, Lote K. Progress in long-term survival in adult patients with supratentorial low-grade gliomas: a population-based study of 993 patients in whom tumors were diagnosed between 1970 and 1993. *J Neurosurg* 2003; 99: 854-62.
- Luders H, Hahn J, Lesser RP, et al. Basal temporal subdural electrodes in the evaluation of patients with intractable epilepsy. *Epilepsia* 1989; 30: 131-42.
- Morris HH, Estes ML, Gilmore R, Van Ness PC, Barnett GH, Turnbull J. Chronic intractable epilepsy as the only symptom of primary brain tumor. *Epilepsia* 1993; 34(6): 1038-43.
- Mueller W, Hartmann C, Hoffmann A, et al. Genetic signature of oligoastrocytomas correlates with tumor location and denotes distinct molecular subsets. *Am J Pathol* 2002; 161: 313-9.
- Oda M, Arai N, Maehara T, Shimizu H, Kojima H, Yagishita A. Brain tumors in surgical neuropathology of intractable epilepsies, with special reference to cerebral dysplasias. *Brain Tumor Pathol* 1998; 15(1): 41-51.
- Okamoto Y, Di Patre PL, Burkhardt C, et al. Population-based study on incidence, survival rates, and genetic alterations of low-grade diffuse astrocytomas and oligodendrogiomas. *Acta Neuropathol (Berl)* 2004; 108: 49-56.
- Pilcher WH, Silbergeld DL, Berger MS, Ojemann GA. Intraoperative electrocorticography during tumor resection: impact on seizure outcome in patients with gangliogliomas. *J Neurosurg* 1993; 78(6): 891-902.
- Plate KH, Wieser, Yasargil MG, Wiestler OD. Neuropathological findings in 224 patients with temporal lobe epilepsy. *Acta Neuropathol (Berl)* 1993; 86: 433-8.
- Shaw EG, Scheithauer BW, O'Fallon JR, Davis DH. Mixed oligoastrocytomas: a survival and prognostic factor analysis. *Neurosurgery* 1994; 34: 577-82.
- Smirniotopoulos JG. The new WHO classification of brain tumors. *Neuroimaging Clin N Am* 1999; 9(4): 595-613.
- Smith JS, Perry A, Borell TJ, et al. Alterations of Chromosome Arms 1p and 19q as predictors of survival in oligodendroglomas, astrocytomas, and mixed oligoastrocytomas. *J Clin Oncol* 2000; 18: 636-45.
- Tortosa A, Vinolas N, Villa S, et al. Prognostic implication of clinical, radiologic, and pathologic features in patients with anaplastic gliomas. *Cancer* 2003; 97(4): 1063-71.
- Whittle IR, Beaumont A. Seizures in patients with supratentorial oligodendroglial tumors-clinicopathological features and management considerations. *Acta Neurochir (Wien)* 1995; 135: 19-24.
- Wolf HK, Zentner J, Hufnagel A, et al. Surgical pathology of chronic epileptic seizure disorders: experience with 63 specimens from extratemporal corticectomies, lobectomies and functional hemispherectomies. *Acta Neuropathol (Berl)* 1993; 86: 466-72.
- Zentner J, Hufnagel A, Wolf HK, et al. Surgical treatment of neoplasms associated with medically intractable epilepsy. *Neurosurgery* 1997; 41(2): 378-87.