AJNR

Intracranial Oligodendrogliomas: Imaging Findings in 35 Untreated Cases

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The radiographic findings in 35 cases of untreated intracranial oligodendrogliomas were reviewed. The mean age of the patients was 34.6 years, and seizure disorder and headache were the most frequent presenting symptoms. Slightly less than two-thirds of the tumors were histologically pure and almost half were low-grade. Most lesions were cerebral and peripheral in location, and the majority were in the frontal lobes. On CT the tumors were usually hypo- or isodense. Contrast enhancement of tumor occurred in nearly half the cases, and was usually mild and poorly defined. Tumor calcification often occurred, and hemorrhage or cystic formation was not infrequent. Occasionally, calvarial erosion was associated with the tumors because of their peripheral location and slow-growing nature. The lesions were usually sharply demarcated and without edema. MR most frequently revealed hypointense lesions on T1-weighted images and abnormal hyperintensity on T2-weighted scans. In regard to grading or purity of oligodendrogliomas, no significant correlations were found except for a suggestion that higher-grade and mixed tumors tend to enhance more often on CT.

The radiographic features of oligodendroglioma are quite characteristic but not pathognomic. A high preoperative suspicion might lead to more appropriate tumor management. MR, although less sensitive in detecting tumor calcification, is superior to CT in defining the tumor extent, which is beneficial for surgical and postsurgical radiotherapy planning.

Oligodendrogliomas are relatively uncommon primary brain neoplasms and account for 4–7% of all primary intracranial gliomas [1, 2]. They occur more frequently in young adults and tend to involve the frontal lobes of the cerebrum. Oligodendrogliomas often contain other glial elements, and approximately 50% of the tumors generally classified as oligodendrogliomas consist of mixed-cell forms [1]. The presence of a mixed-cell population and the absence of characteristic cytoplasmic clearing in frozen biopsy material make the intraoperative diagnosis of oligodendroglioma challenging [3]. Furthermore, the higher cellularity and nuclear/cytoplastic ratio as well as the nonprognostic increased mitotic activity of oligodendrogliomas may lead to misdiagnosis of more malignant anaplastic astrocytoma, which might alter or defer a proper surgical resection. A high index of suspicion on preoperative imaging studies may contribute to a proper frozen section diagnosis. With the advances in neuroimaging in recent years, the diagnostic capability of brain tumor imaging has vastly improved. We review the CT and MR features of intracranial oligodendrogliomas and attempt to correlate these with the histologic tumor purity and grading.

Materials and Methods

The pretreatment imaging studies of 35 patients with surgically proved oligodendrogliomas were reviewed retrospectively. All patients had pre- and postcontrast CT, which was performed on a variety of scanners. Most of the studies were obtained on high-resolution scanners. More recently, 11 patients also had preoperative MR, which was performed on

TABLE 1: Intracranial Oligodendrogliomas (n = 35)

	Location (No.)	Tumor Margin (No.)	Tumor Matrix				Ca++ (No.)	Hemorrhage (No.)	Cystic Formation (No.)	Calvarial Erosion (No.)	Edema (No.)
			CT Density (No.)	Enhancement (No.)	T1-MR (No.)	T2-MR (No.)					
1. Pure oligodendrogliomas (n = 23)											
Low-grade (n = 15)	Frontal (9), Temporal (2), Parietal (1), Frontoparietal (1), Parietooccipital (1), Thalamus (1)	Sharp (11), Poor (4)	Hypodense (11), Isodense (1), Hyperdense (1), Mixed (2)	(3)	Hypointense (6), Mixed (1)	Hyperintense (7)	(6)	(3)	(1)	(3)	Present (2), Absent (10), Unknown (3)
Intermediate (n = 8)	Frontal (6), Parietal (1), Parietooccipital (1)	Sharp (6), Poor (2)	Hypodense (4), Isodense (2), Hyperdense (1), Mixed (1)	(4)	Hypointense (2)	Hyperintense (2)	(3)	(2)	(2)	(1)	Present (4), Absent (4)
2. Mixed oligodendrogliomas (n = 12)											
Low-grade (n = 2)	Frontal (2)	Sharp (1), Poor (1)	Hypodense (1), Isodense (1)	(1)	–	–	(0)	(0)	(1)	(0)	Present (1), Unknown (1)
Intermediate (n = 9)	Frontal (5), Parietal (3), Frontoparietal (1)	Sharp (6), Poor (3)	Hypodense (4), Isodense (3), Mixed (2)	(7)	Hypointense (1), Hyperintense (1)	Hyperintense (2)	(4)	(2)	(3)	(1)	Present (4), Absent (2), Unknown (2)
High-grade (n = 1)	Temporal (1)	Sharp (1)	Isodense (1)	(1)	–	–	(1)	(0)	(1)	(1)	Present (1)

either a 1.5-T GE Signa unit or a 0.35-T Diasonics MT/S scanner with images obtained with spin-echo T1-weighted, proton-density, and T2-weighted pulse sequences. Slice thickness ranged from 5 to 10 mm, and the majority of studies were done using a 5-mm slice thickness.

All of the pathologic specimens were collected from subtotal or total resections. Tumor composed of at least a 75% oligodendroglial element was categorized as a pure oligodendroglioma, with a mixed tumor containing less than 75% oligodendroglioma. Mixed gliomas with predominant nonoligodendroglial elements were excluded from this study. Histologic grading of oligodendroglioma was modified after Smith's classification [4]. In low-grade oligodendroglioma, the neoplastic cells are fairly uniform, with round or polygonal shapes, and there is a characteristic retraction artifact of the cytoplasm, which forms a clear halo that surrounds the nuclei. The nuclear/cytoplasmic (N/C) ratio is less than one-third. There is no vascular endothelial proliferation or necrosis. In intermediate-grade (or anaplastic) oligodendroglioma, there is an increased N/C ratio and mild nuclear pleomorphism. Increased cell density may produce a "back-to-back" appearance. Vascular endothelial proliferation may be present but necrosis is not seen. In high-grade oligodendroglioma (glioblastoma multiforme with oligodendroglial features), the tumor is very cellular and highly pleomorphic, with a high N/C ratio. Necrosis is present along with abundant vascular endothelial proliferation.

Medical records were reviewed for patient's gender, presenting symptoms, interval between initial symptoms and diagnosis, and age at time of diagnosis.

The radiographic parameters studied for the tumors were size, configuration, location, CT density and contrast enhancement of tumor matrix, tumor intensities of T1- and T2-weighted MR images, tumor calcification, hemorrhage, cystic formation, and associated calvarial erosion. The definition of tumor margins and associated edema was decided by MR when available.

Results

Table 1 presents a summary of the following findings.

The patients ranged in age from 2 to 71 years, with a mean age of 34.6 years. There were 17 males and 18 females. Seizure was the most frequent presenting symptom, occurring in 26 patients (74.3%), followed by headache (23%) and neurologic deficit of sudden onset (17%). The interval between initial symptoms and diagnosis of tumor was remarkably variable, with the shortest span being a few days and longest more than 15 years. In thirteen patients (37%) tumor was detected within 1 month of onset of symptoms, in five patients (14%) tumor was detected between 1 month and 6 months, in six patients (17%) between 6 months and 1 year, in eight patients (23%) between 1 and 5 years, and in three patients (9%) beyond 5 years.

Histopathologically, there were 23 pure oligodendrogliomas (66%) (15 low-grade, and eight intermediate-grade) and 12 mixed tumors (34%) (two low-grade, nine intermediate-grade, and one high-grade). All the mixed tumors contained minor elements of astrocytoma or anaplastic astrocytoma. All tumors were cerebral and peripheral in location, except for one that occurred in the thalamus (Fig. 1). In no case was tumor found in the cerebellum. The tumors were confined to or partially involved the frontal lobes in 24 cases (69%). The next most frequent site was the parietal lobe (20%). There was no true intraventricular case in our series. Four cases were misdiagnosed as anaplastic astrocytoma in intraoperative frozen material.

The tumors tended to be round or oval and rarely multilobulated (Fig. 1), with the size ranging from 2 × 2 × 2 cm to 8
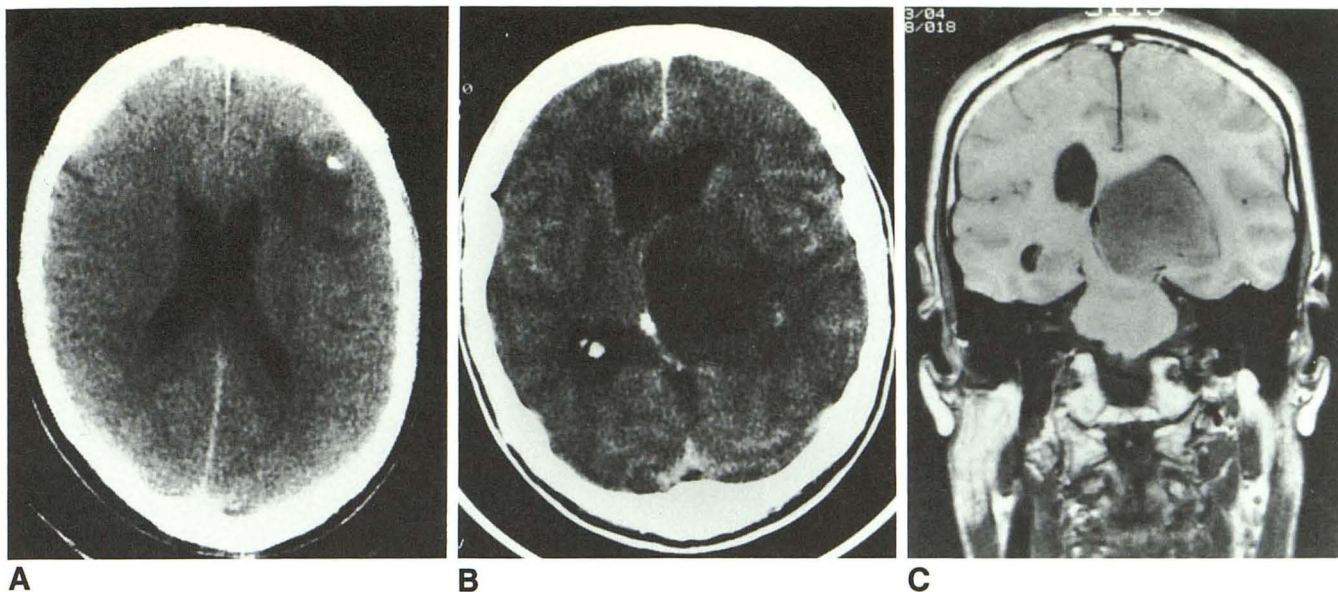
Fig. 1.—*A*, Peripheral, pure low-grade oligodendroglioma. Hypodense nonenhancing characteristics of tumor matrix with a fleck of calcification.

B and *C*, Central pure low-grade oligodendroglioma. MR image (600/25) clearly demonstrates the absence of intraventricular extension of this subependymal thalamic tumor.
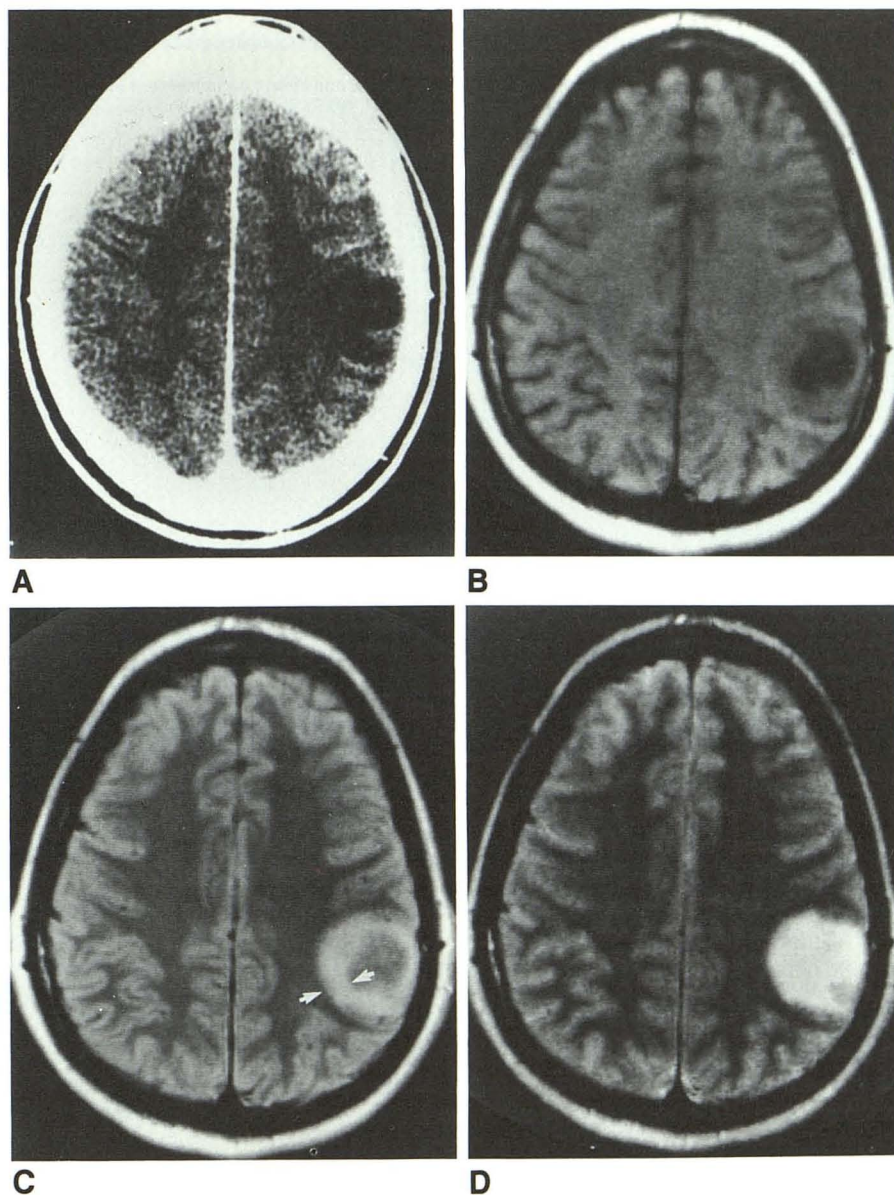

Fig. 2.—Mixed intermediate-grade oligodendroglioma.

A, Postcontrast CT shows hypodense nonenhancing tumor peripherally in left parietal lobe with poorly defined borders.

B–D, MR images (500/30, 2000/30, and 2000/90, respectively). Tumor margins are sharply delineated, with demonstration of a central cystic component; the best demarcation of tumor (*arrows* in C) from surrounding normal tissue and cyst is on the proton-density image (*C*, 2000/30).

A   B   C
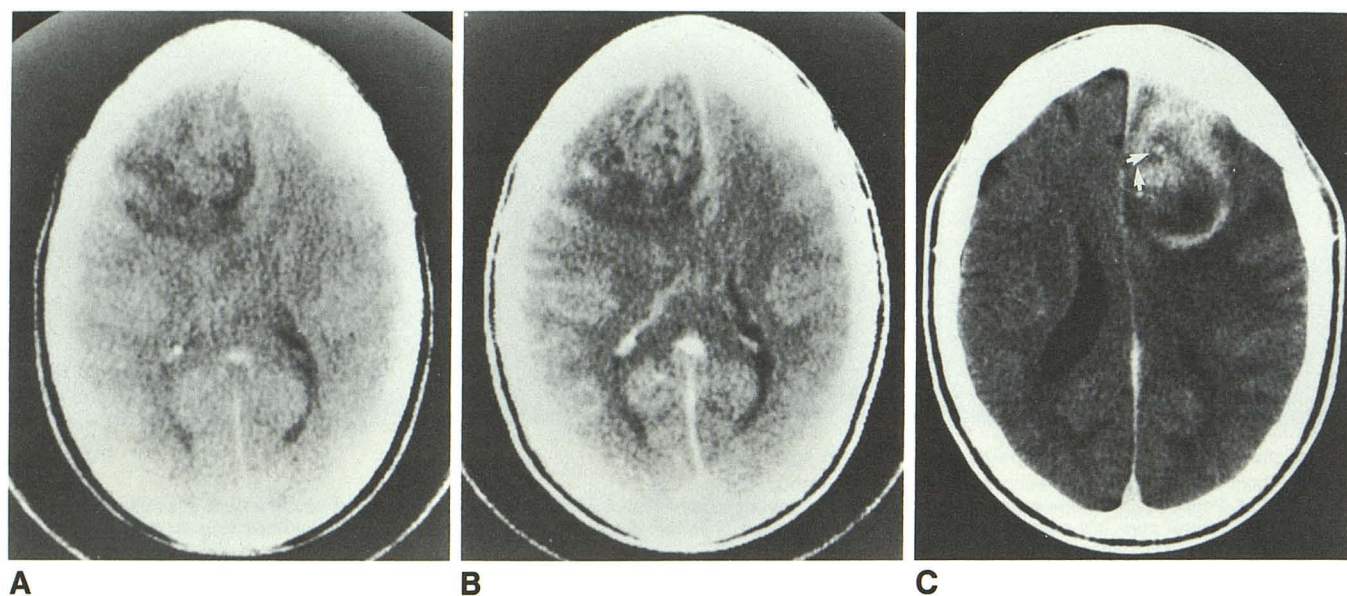
Fig. 3.—A and B, Pre- (A) and post- (B) contrast CT of a pure intermediate-grade oligodendroglioma. Contrast enhancement of the tumor is mild and poorly defined.
C, Postcontrast CT of a mixed intermediate tumor with uncommon strong enhancement of the solid portion of the tumor. Note minute matrix calcifications (arrows) and cystic formation.

A   B   C
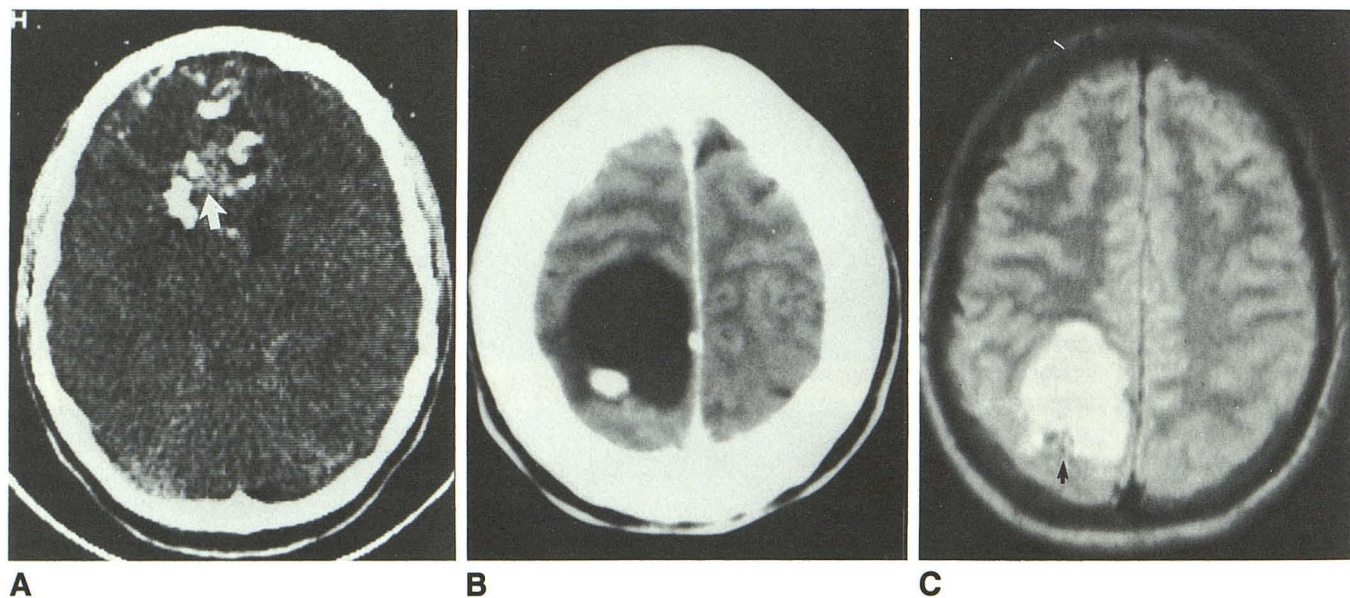
Fig. 4.—A, Extensive scattered calcifications in a mixed intermediate-grade oligodendroglioma. Poorly defined tumor enhancement (arrow) is noted.
B and C, Noncontrast CT (B) and MR, 2000/56, (C) of a pure low-grade tumor. Note poorly defined low signal at tumor calcification (arrow in C), which is clearly demonstrated on CT.

× 7 × 6 cm. On CT the tumor margins were sharp in 17 cases (49%) and poorly marginated in 18 (51%). Indistinct tumor margins on CT became sharply marginated on MR in eight of nine cases (Fig. 2).

On the noncontrast CT scans the tumor matrix was hypodense to brain parenchyma in 20 cases (57%) and isodense in eight (23%). Two were extremely hyperdense due to extensive tumor hemorrhage, and five were mixed. CT contrast enhancement of tumor was noted in 16 patients (46%) and was faint and poorly defined in all but two (Fig. 3). Sixteen cases had no definite tumor enhancement, and two could not be evaluated due to extensive tumor hemorrhage. Of the 15

Fig. 5.—Postcontrast CT of a hemorrhagic pure intermediate-grade oligodendroglioma. The large acute hematoma obscures the underlying tumor.
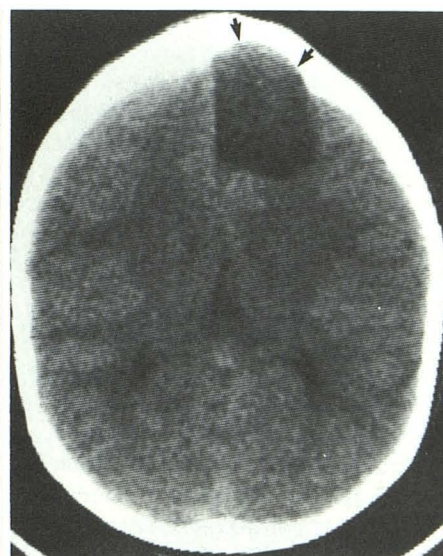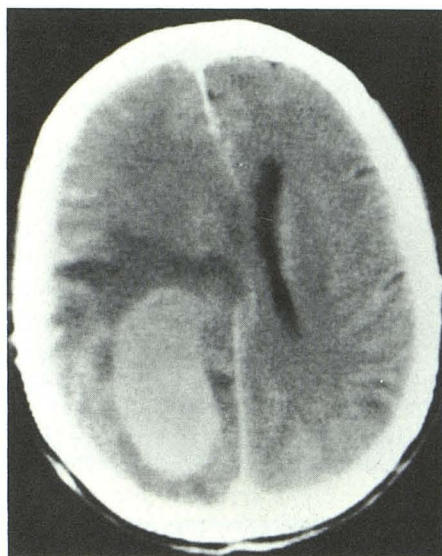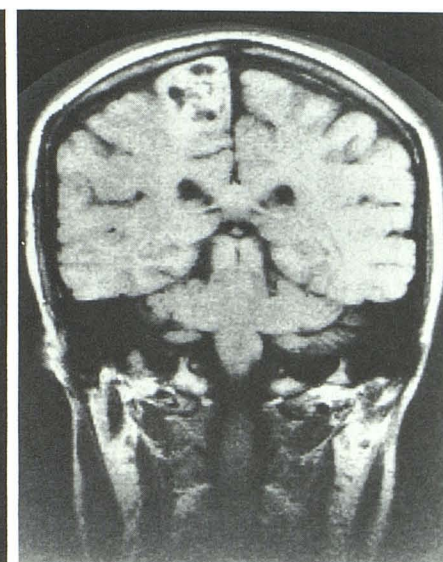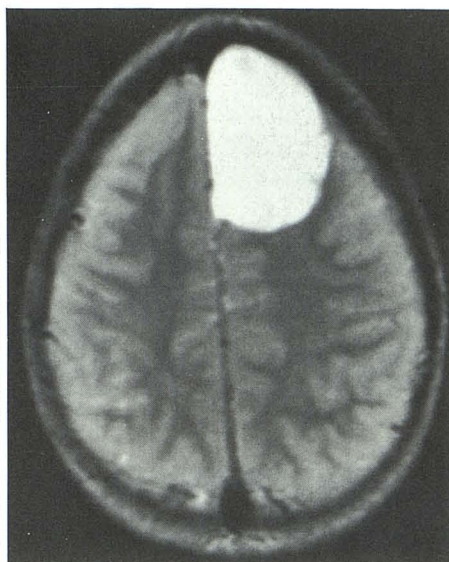
Fig. 6.—Pure low-grade oligodendroglioma. Note erosion of overlying calvarium (*arrows*) from this peripheral tumor, which was oval, hypodense, and nonenhancing.

5　　　　　6

A　　　　　B　　　　　C

Fig. 7.—*A* and *B*, T1-weighted, 450/25, (*A*) and T2-weighted, 2500/100, (*B*) MR images of the patient shown in Fig. 6. Typical but nonspecific hypointensity on T1-weighted image and hyperintensity on T2-weighted image. Also clearly shown is the extension of tumor into the diploe of overlying frontal bone.

C, Uncommon hyperintense tumor with areas of signal void created by matrix calcification on T1-weighted MR image (500/40) of a mixed intermediate-grade oligodendroglioma.

pure low-grade oligodendrogliomas, three enhanced on CT, as did four of eight pure intermediate-grade tumors. Among the 12 mixed oligodendrogliomas, all enhanced except for one low-grade and two intermediate-grade tumors. There was a tendency for mixed- or higher-grade tumors to have contrast enhancement.

Tumor calcifications were identified on CT in 14 patients (40%), appearing as clumps in six and as flecks in eight (Fig. 4). Known calcifications were undetectable on MR in two

cases. Calcifications were seen in 40% of pure low-grade tumors, 38% of pure intermediate-grade tumors, 44% of mixed intermediate-grade tumors, and in the only mixed high-grade tumor. Tumoral hemorrhage was noted on CT in seven patients (20%). Two were so extensive that a nonhemorrhagic part of tumor could not be identified (Fig. 5). Hemorrhage was seen in three pure low-grade, two pure intermediate-grade, and two mixed intermediate-grade tumors. A cystic component was seen in seven oligodendrogliomas (20%). There was

no consistent correlation of tumoral calcification, hemorrhage, or cystic formation with tumor purity or grading.

Owing to tumor hypodensity and absence of contrast enhancement, assessment of possible associated edema could not be made on CT in 12 patients. In the remaining 23 patients, edema was absent in 14 and present in nine. In 11 MR studies, edema was present in three and absent in four of seven cases of hypodense, nonenhancing tumors with uncertainty of associated edema on CT. Therefore, in a total of 30 patients the presence of edema could be correlated with histopathologic findings. Among 20 pure oligodendrogliomas (12 low-grade, and eight intermediate-grade), six were associated with edema (30%). Six of 10 mixed tumors (one low-grade, eight intermediate-grade, and one high-grade) were positive for edema (60%). Edema was present in three of 13 low-grade tumors (23%) and nine of 17 more malignant (intermediate- or high-grade) tumors (53%).

Associated calvarial erosion, caused by the peripheral location and slow-growing character of tumor, was present in six cases (17%) (Fig. 6). This was seen in three pure tumors that were low-grade, one pure intermediate-grade, one mixed intermediate-grade, and one mixed high-grade lesion.

Of the 11 cases that had MR imaging (Fig. 7), seven were pure low-grade oligodendrogliomas. Six of these were hypointense on T1-weighted images and one had mixed areas of hypo- and hyperintensity. Two pure intermediate-grade tumors also were hypointense. There were two mixed tumors with one demonstrating hypointensity and the other mixed intensity on T1-weighted scans. Hyperintensity of tumor was observed on T2-weighted images in all 11 cases. No significant differences in T1 or T2 intensity were noted regarding the purity or grading of the tumors. Late-echo images to a TE

of 100 were obtained in four patients and did not provide additional information.

Discussion

Oligodendroglioma is a relatively slow-growing primary brain tumor, and the diagnosis is usually preceded by a long history of symptoms, frequently a seizure disorder or headaches [2, 5, 6]. However, with easy access to modern noninvasive neuroimaging techniques, such as CT or MR, the interval between initial presentation and diagnosis of tumor has been greatly reduced. As shown in our series, slightly over half the cases (51%) were diagnosed within 6 months from the onset of symptoms.

Histologically, the oligodendroglioma is often in a mixed form [1]. In our series about one-third were mixed tumors that also contained minor components of astrocytoma or anaplastic astrocytoma. It should be mentioned that the high-grade oligodendrogliomas, either pure or mixed, are often categorized as glioblastoma multiforme because of the presence of necrosis, and therefore the reported incidence of higher-grade oligodendrogliomas may not be accurate.

As also described in the literature, almost all the lesions in this series, either pure or mixed, are located peripherally in the cerebrum, with a definite propensity for the frontal lobe [2, 5]. Intraventricular and posterior fossa lesions are very rare [7, 8], and neither one was found in our series. Oligodendrogliomas are often round or oval in shape and frequently are sharply marginated. A significant number of cases with poorly defined tumor margins on CT demonstrated sharp margination on MR. Furthermore, MR provided better delineation of tumor in the anatomic sites where inherent computer
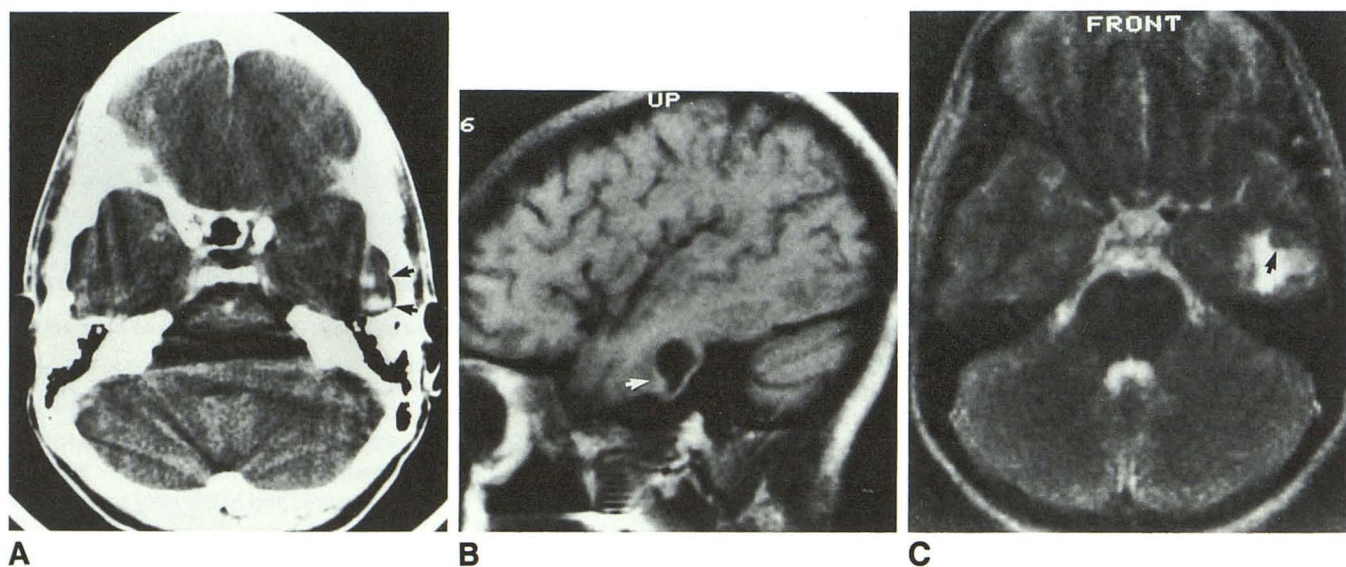

A   **B**   **C**

Fig. 8.—*A–C*, Contrast CT (*A*), T1-weighted, 500/30 (*B*), and T2-weighted, 2500/90, (*C*) MR images of a pure low-grade oligodendroglioma. Tumor calcifications (*arrows* in *A*) are far better appreciated on CT. However, the tumor margins and cystic component, obscured by computer artifacts on CT, are clearly shown on MR. Solid tumor nodule (*arrows* in *B* and *C*), proved at surgery, is sharply demonstrated.

Fig. 9.—Left pure low-grade oligodendroglioma.

A, Precontrast CT shows no definite abnormality.

B, Postcontrast CT after infusion of 300 ml of 30% iodinated contrast. A small poorly defined enhancing mass is identified in the medial aspect of left frontal lobe.

C, Repeat study after infusion of 200 ml of 76% iodinated contrast. The lesion becomes better defined and larger.

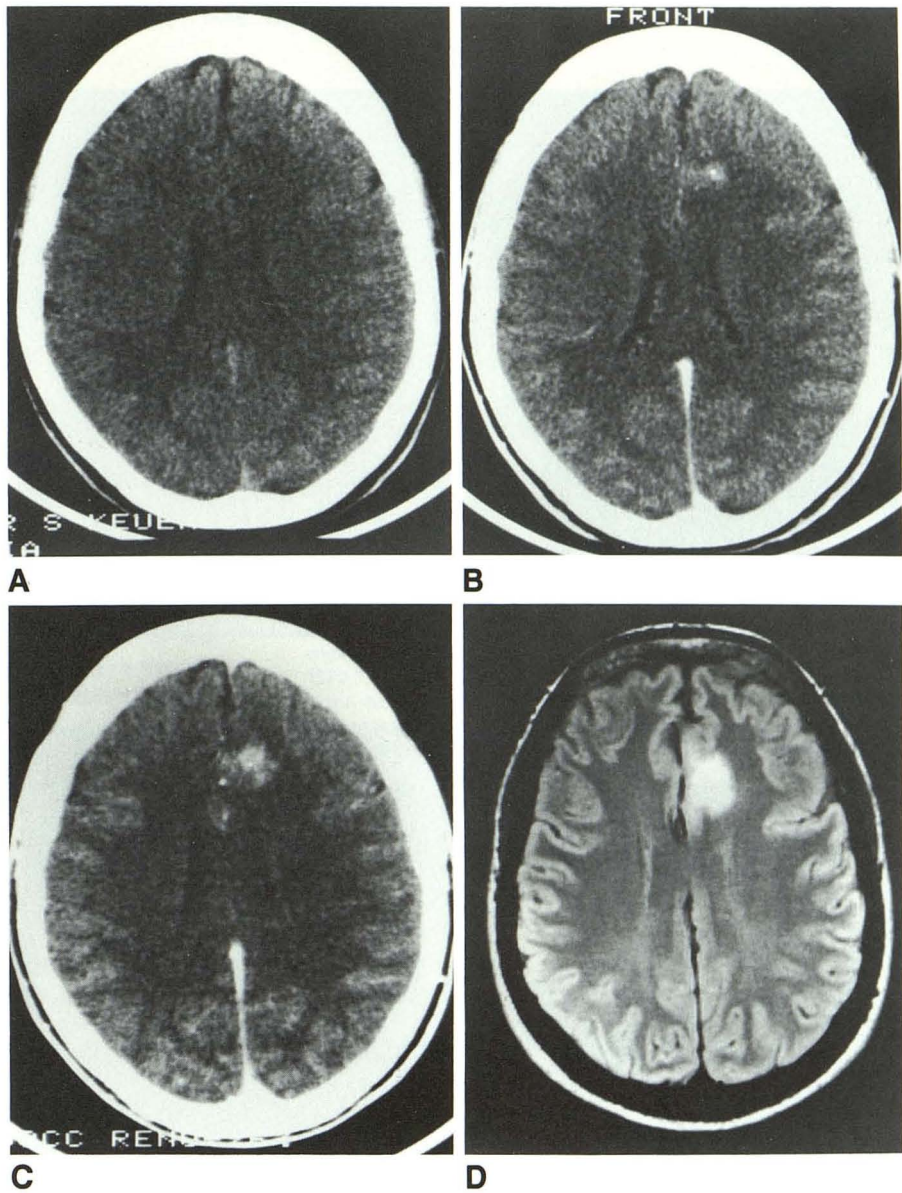*D*, MR image (2000/20) best demonstrates the tumor borders.

A

B

C

D

Fig. 10.—27-year-old woman with sudden-onset grand mal seizures.

A, Initial contrast CT. A poorly marginated hypodense nonenhancing mass is identified in left frontal lobe with minimal mass effect. Patient refused surgery and radiotherapy after becoming symptom-free with anticonvulsant medication.

B, Contrast CT 5 years later, after patient developed severe frontal lobe dysfunction. The tumor did not progress in size and the matrix remained hypodense and nonenhancing; however, tumor calcifications (*small arrows*) and cystic formation (*large arrow*) have occurred. Pure intermediate-grade oligodendroglioma.
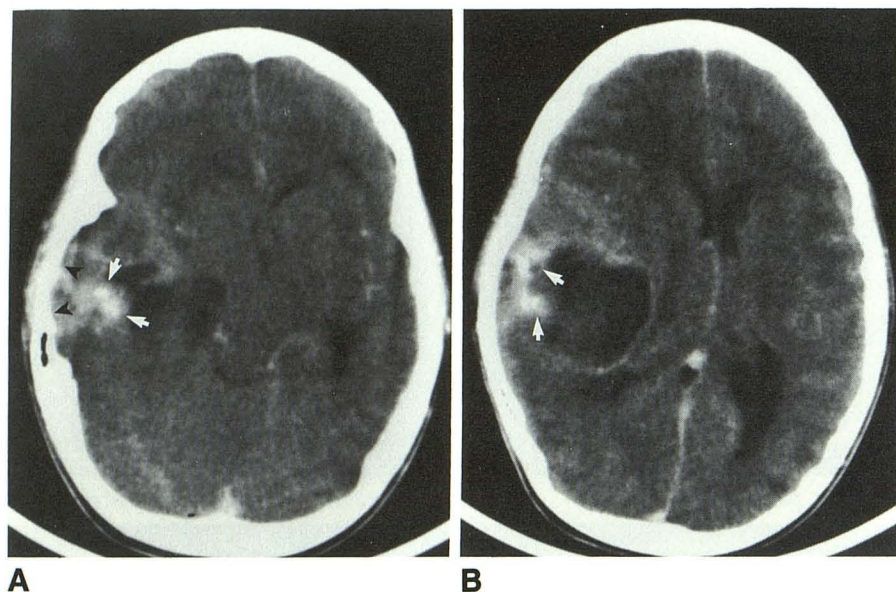

A

B

A   B
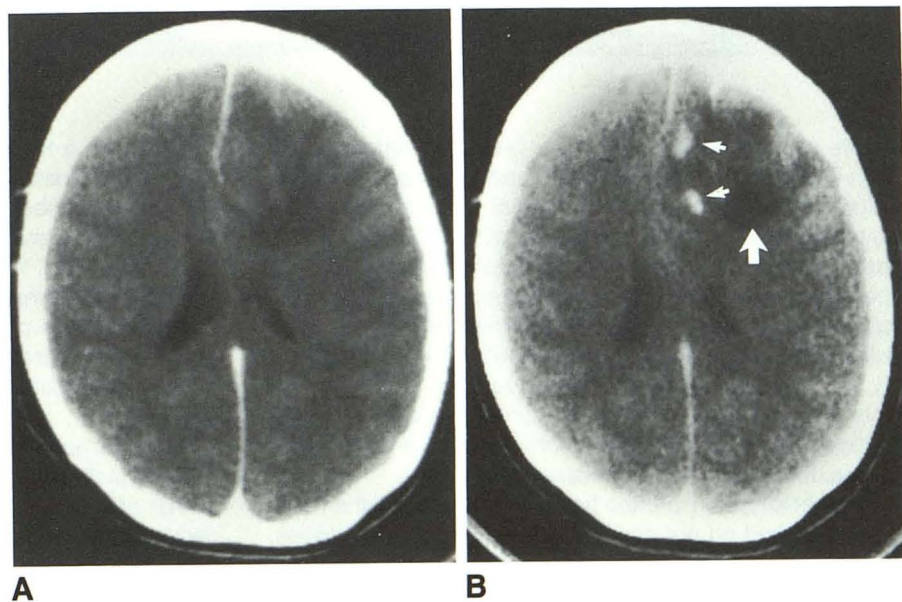
Fig. 11.—Mixed high-grade oligodendroglioma.
A and *B*, Postcontrast CT shows multilobulated temporal mass with large cystic or necrotic component, compatible with a glioblastoma multiforme. However, the presence of tumor calcifications (*arrows*) and calvarial erosion (*arrowheads* in *A*), with minimal surrounding edema, favors a lower-grade malignancy and suggests oligodendroglioma.

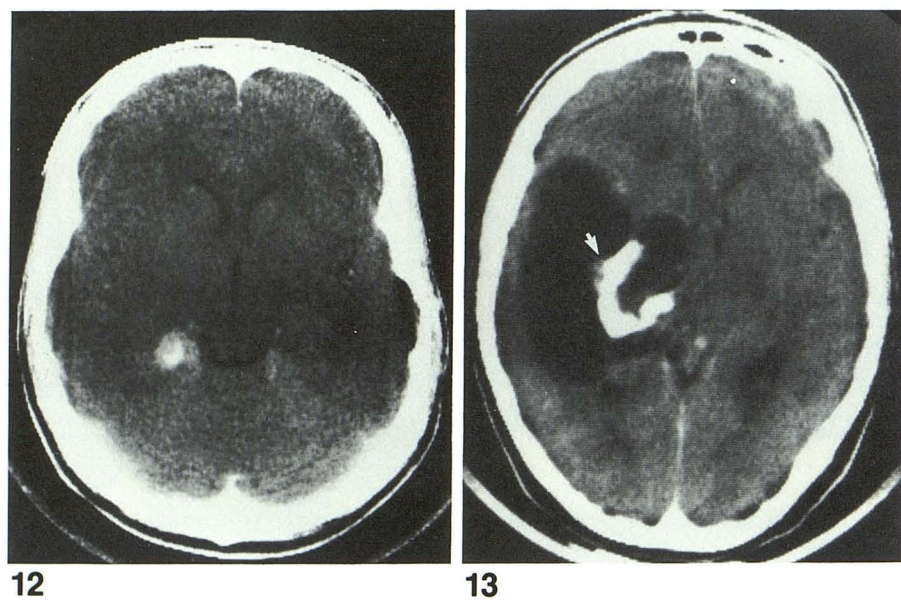12   13

Fig. 12.—Postcontrast CT shows typical ganglioglioma presenting as a calcified and enhancing mass in the right posterior medial temporal lobe.

Fig. 13.—Postcontrast CT shows large cystic mass with dense calcification and minimal enhancement (*arrow*). Surgery revealed an astrocytoma with xanthochromic cystic fluid from old hemorrhage.

artifacts and limited imaging planes precluded detailed evaluation (Fig. 8). This improvement of tumor delineation should facilitate not only presurgical planning of tumor resection, but also postsurgical radiotherapy if needed [9]. On CT the tumor matrix is often either hypo- or isodense, and occasionally hyperdense due to tumoral hemorrhage. Nearly half the tumors enhanced on CT after IV administration of contrast medium. The tumor enhancement tended to be poorly defined and heterogeneous. Pathologic correlation revealed that higher-grade and mixed tumors more often demonstrated enhancement on CT. CT tumor enhancement is often better with the double contrast technique (Fig. 9).

Tumor calcification is often better defined on CT than MR; however, based on our observations in this series of cases, it seems to have no direct correlation with the purity or the grade of the tumors. The same observation is made with respect to tumor hemorrhage. A cystic component has been said to have a significant correlation with the malignancy of oligodendroglioma [10]. This observation was not made in our series. Instead, there is a suggestion that time may play a role in the development of this finding as well as the tumor calcification (Fig. 10). As expected, edema is less often observed in the pure or low-grade oligodendrogliomas. Occasionally noted is calvarial erosion in association with slow-growing, peripherally located oligodendrogliomas. This observation also appeared to be independent of the tumor purity or grade.

With the application of high-resolution CT and MR, the differential diagnosis of oligodendroglioma is relatively limited to that of a few primary brain tumors. The high-grade oligodendroglioma may be difficult to differentiate from the more frequent glioblastoma multiforme. However, the presence of tumor calcification, a peripheral location, and the sometimes associated calvarial erosion might indicate a lower malignancy

of the tumor and suggest the proper diagnosis (Fig. 11). Ganglioglioma, an even more indolent tumor, will frequently present as calcified mass and cause diagnostic difficulty [11]; however, its propensity to involve the temporal lobe and deep cerebral tissue may provide a differentiating clue (Fig. 12). Occasionally, astrocytoma with dystrophic calcification from old hemorrhage may also look like an oligodendroglioma (Fig. 13). The most difficult lesion to differentiate is astrocytoma or low-grade anaplastic astrocytoma presenting as a hypodense, nonenhancing mass on CT. However, these astrocytic tumors tend to be deeper in location and to extend along the fiber tracts, and usually lack calcifications.

The diagnosis of oligodendroglioma on frozen section can be challenging. The high cellularity and high nuclear/cytoplasmic ratio of some oligodendrogliomas, with the absence of classic cytoplasmic halos in frozen material, might cause a misdiagnosis of anaplastic astrocytoma. Since the usual prognosis of oligodendroglioma is somewhat better than that of anaplastic astrocytoma, a high index of suspicion of the former on the presurgical CT and MR may prompt a correct histologic diagnosis, leading to more appropriate management of the tumor.

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