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# Late Recurrence of Intractable Epilepsy Associated with MRI-occult Pilocytic Astrocytoma in the Temporal Lobe Nine Years after Initial Removal: A case report with surgical and late-seizure recurrence observations

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## ABSTRACT

A 28-year-old male who presented a relapse of intractable epilepsy consisting of complex partial seizures with occasional secondary generalizations at the age of 26, had undergone removal of a left mesial temporal lobe tumor at another hospital at 18 years old. Pathological examination at that time revealed a low-grade astrocytoma, and the tumor was further treated by complementary adjuvant irradiation therapy. Magnetic resonance imaging (MRI) findings on admission portrayed a post-operative cavity anterior to the atrophied hippocampus on the left side with hyperintense in fluid-attenuated inversion recovery (FLAIR) images. There were no enhanced lesions in T1-weighted gadolinium images. As it was diagnosed as left mesial temporal lobe epilepsy with preoperative evaluations, the patient underwent left anterior temporal lobe resection (TLR). Intraoperative findings revealed that a small lump of grey tissue was attached to the anteromesial side of the sclerotic hippocampus. We surgically removed this and the tissue was a pilocytic astrocytoma. The patient has since remained seizure-free for 2.5 years. Seizure outcomes at postoperative 1-2 years are highly predictive of long-term outcomes after TLR for temporal lobe epilepsy (TLE). Late-seizure recurrence (> postoperative 2 years) with an initially successful outcome rarely occurs in TLR patients. This case report suggests that recurrence of even benign pilocytic astrocytomas may occur when seizure recurs in long-term follow-up.

***Key words:*** *Temporal lobe tumoral epilepsy, Late recurrence, Pilocytic astrocytoma*

Hippocampal sclerosis is the most common cause of intractable TLE which has highly responded to temporal lobe resection (TLR) for seizure control[8,10-12]. Most chronic epilepsy associated with tumors is also of temporal origin (temporal lobe tumoral epilepsy)[6,13]. Several studies on patients with temporal lobe tumoral epilepsy have reported some risk factors (i.e., residual tumor, additional hippocampal sclerosis, and multiple EEG foci) which may be attributed to surgical failure of seizure control in the 1-year postoperative period[5-7]. The probability of seizure-freedom continuation is high when patients have a 1- or 2-year postoperative period of complete seizure-freedom[5,6,13]. Late seizure recurrence, which indicates seizure relapse (> 2 years after surgery with initial successful outcome), rarely occurs in such patients. However, the risk factors specific to this phenomenon are as yet unidentified[7]. We report a case with late recurrence of intractable TLE nine years after the initial removal of the mesial temporal lobe tumor. MRI-occult pilocytic astrocytoma was found to be attached to the sclerotic hippocampus. We discuss an etiology and mechanism of late seizure recurrence in this rare case with temporal lobe tumoral epilepsy.

## CASE REPORT

A 28-year-old right-handed male was referred to our hospital with a relapse of seizures since the age of 26. He started taking antiepileptic drugs for atonic seizure at the age of 13 years. At age 14, he was diagnosed with a left mesial temporal lobe tumor on MRI at the hospital where he underwent tumor removal at age 18. Pathological examination revealed a low-grade astrocytoma in the temporal lobe, and the tumor was further treated by complementary adjuvant irradiation therapy with an extended local dose of 52 Gy. He remained thereafter seizure-free for 9 years (off-medication for the last 4 years). As seizures relapsed and

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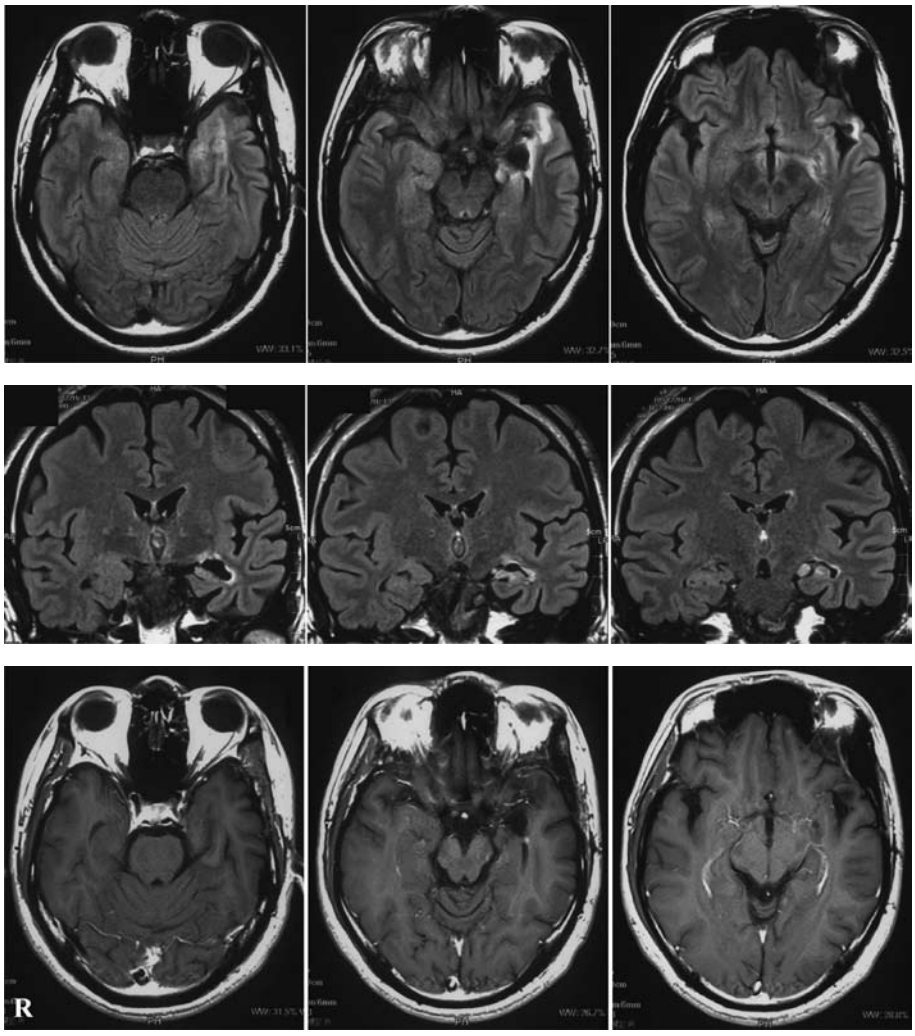


**Fig. 1.** Magnetic resonance imaging (MRI) performed prior to operation attempt 2. Axial (A) and coronal (B) fluid-attenuated inversion recovery (FLAIR) images showed hyperintensive hippocampal atrophy on the left side adjacent to a cavity of the initially operated site. A gadolinium (Gd)-treated axial T1-weighted image (C) did not portray any enhanced lesion.

increased in frequency even after treatment with multiple antiepileptic drugs from age 27, he was referred to our department for further observation and special treatment.

On admission, he had complex partial seizures (1-2 times/week) consisting of impaired consciousness, staring with facial grimacing on the right side, accompanied by right-arm stiffening with occasional secondary generalizations. He was treated with zonisamide, valproic acid and clonazepam. MRI findings portrayed a post-operative cavity anterior to the atrophied hippocampus on the left side with hyperintense in FLAIR and T2-weighted images (Fig. 1A, 1B). T1-weighted gadolinium (Gd) images revealed no enhanced lesions surrounding the mesial structure (Fig. 1C). Interictal iomazenil SPECT demonstrated bilaterally cumulative decreases (left-sided predominance) in the mesial temporal regions. Although neuropsychological examination by the revised Wechsler Memory Scale revealed substandard IQ scores: (FIQ: 81, verbal IO: 81, performance IQ: 85), his memory function was unaffected (verbal memory: 112, nonverbal: 114). The Wada test revealed left hemisphere speech/language dominance.

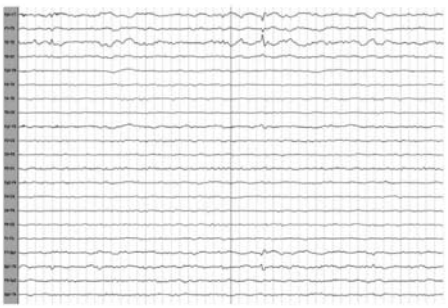

**Fig. 2.** Interictal scalp-sphenoidal EEG-recording.

Intermittent spikes intermingled with focal slowing were observed over the left anterior to mid temporal and subtemporal regions with phase reversals at F7-T3 and Sp1.

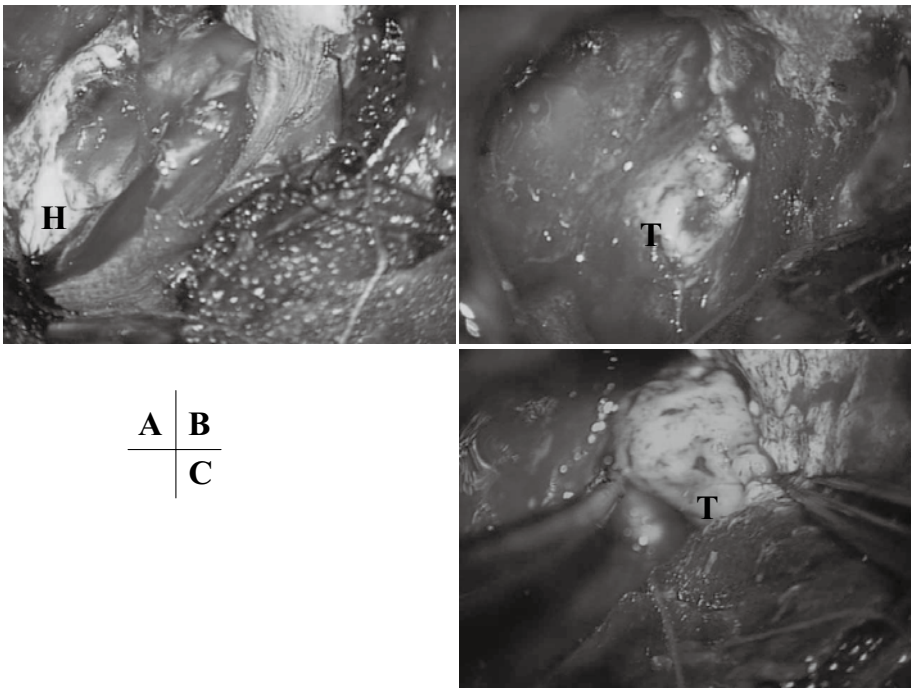


**Fig. 3.** Intraoperative views. Sclerotic hippocampus (H) seen in the inferior horn after anteriorlobectomy (A), A small grayish white tumor (T) was found after removal of the hippocampus, which was suppressing the pedunculus of the midbrain without an intervening arachnoid membrane (B, C).

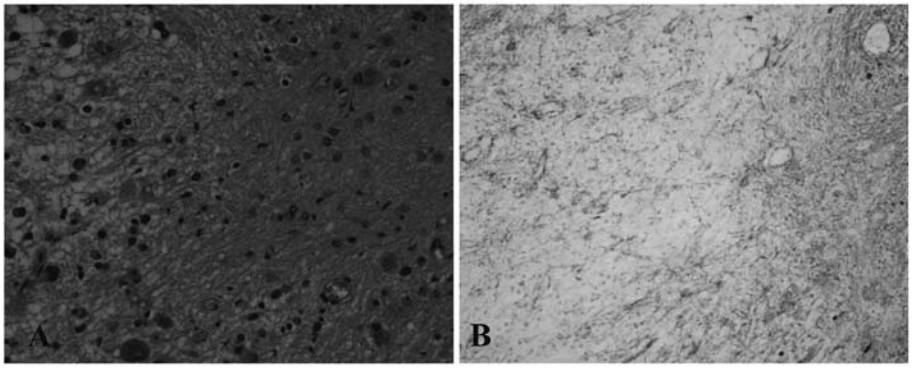


**Fig. 4.** Pathological findings: Pathological specimens showing differently textured glioma matrixes with Rosenthal fibers and eosinophilic granular bodies with low mitotic activity. Vascular proliferation and necrosis were not indicated with hematoxylin-eosin staining (× 100) (A). Tumor cells were stained positive with antibodies against the glial fibrillary acid protein (GFAP, × 200) (B).

We recorded 5 habitual seizures during 8-day video-scalp EEG monitoring with sphenoid electrodes: all seizures were clinically and electrographically identical. The seizure semiology consisted of complex partial seizures with (2 episodes) and without (3 episodes) secondary generalization. Electrographically the ictal onset was localized to the left, anterior to middle temporal regions and at the right subtemporal region. The interictal scalp EEG frequently demonstrated spikes in a region analogous to the site of an ictal onset (Fig. 2).

As the seizures were diagnosed as left mesial TLE, the patient accordingly underwent left anterior TLR. Intraoperative findings revealed that a small lump of grey tissue was attached to the anteromesial side of the sclerotic hippocampus. We surgically removed the affected hippocampus and the grey tissue (protruding to the pedunculus of midbrain) without an intervening arachnoid membrane (Fig. 3). Subsequent pathological examination revealed that the tissue was a pilocytic astrocytoma (Fig. 4). Although affected by transiently mild hemipareses in the right extremities after operation attempt 2, the symptoms were completely relieved one month after operation, and the patient has since remained seizure-free for 2.5 years.

## DISCUSSION

Only a limited number of studies have attempted to examine predictors or risk factors related to long-term outcomes in patients with intractable

epilepsy-associated tumors in the temporal/extratemporal lobe[6,13]. Gross or complete tumor resection is one of the common approaches for establishing postoperative seizure-free status in patients[6,13].

Hippocampal sclerosis, the most common cause of intractable temporal lobe epilepsy (TLE), responds favorably to temporal lobe resection (TLR) for seizure control[8,10-12]. A majority of tumor-associated chronic epilepsy cases are of temporal origin; i.e., temporal-lobe tumoral epilepsy (TLTE)[6,13]. The probability of maintaining a persistently seizure-free status is high when patients have experienced a complete seizure-free postoperative period of more than 1-2 years[5,6,13]. As postoperative cases with late-seizure recurrence (LSR) (i.e. seizure relapse in > postoperative 2 years) are rarely found once an initially successful outcome has been established, LSR-specific risk factors remain unidentified as yet[7].

According to the results of longitudinal follow-up of TLE patients with various etiologies, seizure outcome at postoperative 1-2 years is highly reliable for predicting long-term outcome (up to 9-10 years) after TLR[5,7]. Jutila et al have analyzed the long-term results of TLE surgery in 140 consecutive patients for a mean follow-up of 5.2 (range: 1.0-10.5) years: 83 of 140 (59%) patients had recurrent seizures during the follow-up period, and 86% (71/83 cases) of all seizure relapses occurred within postoperative 1 year[5]. In fact, postoperative results at postoperative 1 year were analogous to the long-term outcome. Late-seizure relapses (> postoperative 2 years) were observed in only 5% of all patients studied (n=7), and 8% of all recurrent cases were late relapses[5]. Once patients have established a seizure-free status, the long-term year-to-year seizure outcome is likely to remain substantially stable[6]. McIntosh et al have demonstrated that cases with excessively slow attrition of the seizure-free rate 2 years after operation[7] are rarely likely to experience LSR.

The etiology and/or mechanism of LSR may be different from that of surgical failure for postoperative residual seizure or the aforementioned early recurrence. Results analyzing a large patient-sample (n=325) with TLR and long follow-up (mean 9.6 ± 4.2 years) have indicated that LSR is not associated with any of the currently known risk factors[7].

Our case experienced LSR, though he had a 9-year seizure-free period after initial removal of the temporal lobe tumor. Although MRI before operation attempt 2 in our case located no visible/enhanced lesions (except for hippocampal atrophy adjacent to a cavity of the initially operated site), we did find a small tumor attached to the sclerotic hippocampus during the operation. Due to record misplacement, neither pathological information from the imaging findings nor accurate pathological results of the initial operation performed at the previous hospital was available for our reference. As a result, we could only speculate that the mechanisms relevant to LSR in our case were as follows: (I) Induction of hippocampal sclerosis precipitated by previous repeated seizures independent of tumor recurrence; (II) direct attachment effect of long-existing residual tumor or tumor recurrence in the hippocampus, and (III) adverse effect of radiation therapy after the initial operation. Apart from being a useful adjuvant therapy for tumor control[3,9], irradiation is also effective in reducing tumor-related epileptogenesis in the early stages[2]. Recently, stereotactic radiosurgery has been introduced to establish seizure control by irradiating epileptogenic hippocampus in TLE patients[1]. Although the presence or absence of hippocampal atrophy at the initial operation was unknown in our case, additional hippocampal sclerosis might have been one of the risk factors derived from surgical failures to establish seizure control[6]. Therefore, seizure intractability could have been maintained after the initial removal of tumor, and seizures might have relapsed earlier (i.e. within 1-2 years after surgery), if the hippocampal sclerosis had been preexistent[6]. Our patient was seizure-free and off-medication after the initial operation. However, hippocampal sclerosis might have developed after the initial operation. Furthermore, we believed that tumor recurrence or regrowth with residual tumor after the initial operation was most likely to be the factor that aggravated seizure intractability in our case, possibly due to the formation of hippocampal sclerosis (involvement of mechanism I; vide supra).

A complete surgical resection is considered most likely to be curative for the majority of pilocytic astrocytomas[4]. A tumor may display late recurrence even after complete or total gross resection[3,9]. Stuer et al have reported that one in 19 macroscopic total resections performed for benign pilocytic astrocytomas indicates tumor recurrence over a long-term (mean: 76; range: 1-227 months) follow-up period[9]. In cases of subtotal resection or biopsy, the rate of late tumor recurrence increases to as high as 30% of all patients with pilocytic astrocytomas[9], a far higher incidence than those reported in previous studies[3,9]. Furthermore, 13% of pilocytic astrocytoma cases show either no or only minimal image contrast-enhancement in MRI[9]. Thus, prudent monitoring is recommended for tumor recurrence, although the vast majority of patients remain stable after gross or subtotal resection[3,9].

## CONCLUSION

It is important to consider the possibility of tumor recurrence (even for benign pilocytic astrocytomas) as a cause for LSR induction even without

positive MRI findings in patients with a previous history of epilepsy-associated tumor surgery when repeated operations have been indicated for epilepsy.

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