

Epilepsy Surgery of the Cerebral Paragonimiasis

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Objective : The authors investigate appropriate evaluation and surgical methods in treatment of the cerebral paragonimiasis accompanying epilepsy.

Methods : Thirteen patients with the cerebral paragonimiasis accompanying epilepsy were included for this study. Preoperative evaluation methods included history taking, skin and serologic tests for *Paragonimus westermani*, neurologic examinations, computerized tomography, magnetic resonance imaging, amytal test, PET or SPECT, and video-EEG monitoring with depth and subdural grid electrodes. Seizure outcome was evaluated according to Engel's classification.

Results : Surgical methods were temporal lobectomy including lesions in six, lesionectomy in five, and temporal lobectomy plus lesionectomy in two. Postoperative neurological complications were not noticed, and seizure outcomes were class I in 12 patients (92%), class II in one (8%).

Conclusion : In patients with a cerebral paragonimiasis accompanying epilepsy, further evaluation methods must be done to define the epileptogenic zone, and complete resection of the epileptogenic zone with different surgical methods should be performed for seizure control.

KEY WORDS : Epilepsy · Cerebral paragonimiasis · Epilepsy surgery.

Introduction

Paragonimiasis is a benign lung disease caused by trematodes of genus *Paragonimus*. More than 20 species of *Paragonimus* have been described throughout the world but the most important species is *Paragonimus westermani*. Brain involvement has been reported in 2~27% of patients with *Paragonimus westermani*. In that case, *Paragonimus westermani* mostly occurred in the occipital lobe and the temporal lobe. It causes epilepsy, hemiparesis, or other neurological deficits. It may result in death, mental retardation, or blindness. By far the most common initial manifestation of cerebral involvement by *Paragonimus westermani* is a seizure. In our cases, the lesions by *Paragonimus westermani* were relatively large (average 6×6 cm), multiple conglomerated round nodules.

Epilepsy could be highly associated with the gliotic tissues surrounding the calcific nodules in the cerebral paragonimiasis.

Authors tried to define the epileptogenic zone and control seizures with the different surgical procedures, in the cerebral paragonimiasis with relatively large size.

Materials and Methods

Patients

Thirteen patients with the cerebral paragonimiasis associated with epilepsy who underwent surgical treatment in our hospital, from January 1997 to January 2004, were included for this study.

Preoperative evaluations (Table 1)

Diagnosis for cerebral paragonimiasis was based on the clinical manifestations, history taking of eating undercooked freshwater crayfish or crabs, skin test and serologic test for *Paragonimus westermani*, and neuroimaging studies. Seven patients had CT scans, three had both CT scans and MRI, and the rest had only MRI. Preoperative evaluations for defining the epileptogenic zone included history taking, neurological examinations, MRI, amytal test, PET or SPECT, chronic video-EEG monitoring with surface electrodes. Invasive EEG recording with subdural grid electrodes and depth electrodes was done in one patient. Intraoperative speech mapping was per-

• Received : June 7, 2005 • Accepted : July 28, 2005

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Table 1. Patients profile, preoperative evaluation, extent of resection and surgical outcome

Patient No. and age/gender	Seizure			Preoperative evaluation								Postoperative outcome(Engel's classification)
	Age of onset (yrs)	Duration (yrs)	Frequency	Location of lesions in CT, MRI	FDG-PET	SPECT	EEG with Surface electrodes	EEG with depth electrodes and SDG	Amytal test	Intraoperative speech mapping	Surgery	
1(36/M)	14	22	10/month	Lt. T	—	—	Lt. T	—	L : Lt. m : Rt.	Wernicke's area	Lt. T. lobectomy	I
2(37/M)	3	33	13/month	Rt. F-T-O	bilateral T-P	—	Rt. F-T	—	L : Lt. m : Rt.	—	Rt. T. lobectomy	I
3(32/F)	10	1	10/month	Rt. T	—	—	Rt. T	—	—	—	Rt. T. lobectomy	I
4(34/F)	14	20	4/month	Rt. T-O	—	Rt. T	Rt. T	—	L : Lt. m : Lt.	—	Rt. T. lobectomy	I
5(31/M)	15	16	12/month	Lt. F-T-O	—	—	Lt. T	—	—	Broca's area	Lt. T. lobectomy	II
6(28/F)	12	16	10/month	Lt. T-O	Lt.T-P-O	—	Lt. T	—	L : Rt. m : Rt.	—	Lt. T. lobectomy	I
7(40/F)	40	2 weeks	4/month	Lt. F	—	—	—	—	—	—	Lt. F. lesionectomy	I
8(46/F)	28	16	10/month	Lt. P-O	bilateral T	—	Lt. P-O	—	L : Lt. m : both	—	Lt. P-O. lesionectomy	I
9(32/F)	27	5	10month	Lt. T	Lt. T	—	Lt. T	—	—	—	Lt. T. lesionectomy	I
10(36/F)	38	1	5/month	Rt. T-O	—	—	Rt. T	—	—	—	Rt. T-O. lesionectomy	I
11(38/F)	20	17	10/month	Rt. T-O	—	—	—	—	—	—	Rt. T-O. lesionectomy	I
12(44/F)	35	8	2/day	Lt.F- T	Lt. T	—	Lt. F-T	Lt.frontal & temporal	L : Lt. m : both	—	Lt. T. lobectomy & Lt.F. lesionectomy	I
13(33/M)	8	27	3-4/month	Lt. T-P-O	—	—	Lt. T-O	—	—	—	Lt.T. lobectomy & Lt.O. lesionectomy	I

No : number, M : male, F : female, Lt.: left, Rt.: right, T : temporal, P : parietal, O : occipital, yrs :years FDG-PET : fluorodeoxyglucose-positron emission tomography, SPECT: single photon emission computerized tomography, SDG: subdural grid, L: language, m: memory, MRI: magnetic resonance imaging, -: preoperative evaluation was not done

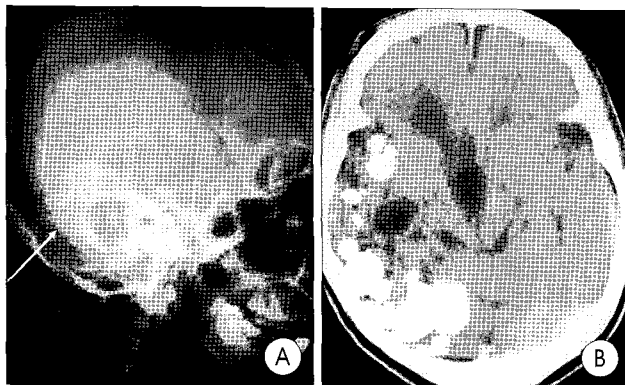


Fig. 1. A : Plain skull X-ray shows conglomerated calcified nodules in the right temporo-occipital area (white arrow). B : Brain computed tomography depicts pathognomonic findings of multiple, variable sized, round, calcified lesions in the right temporo-occipital area.

formed in two and neuropsychologic test was done in one.

The clinical manifestations were seizure, headache, and visual field defect. Visual field examination noticed a left homonymous hemianopia in two patients, and a right homonymous hemianopia in four patients. None of 12 patients had a memory of ingestion of freshwater crabs or crayfish in childhood. But these patients might reasonably have been forgotten their trivial event as eating these kinds food. Skin tests and serological study (ELISA) for *Paragonimus westermani* were negative

probably due to a long duration of possible infestation of the parasites. In blood test, however, eosinophilia in circulating blood beyond 10% was observed in one. Cerebral paragonimiasis was in chronic inactive stage in 12 patients, and acute stage in one.

Calcific nodules visible in plain skull X-ray is a radiological characteristic of the cerebral paragonimiasis (Fig. 1A). Brain computed tomography revealed pathognomonic findings of multiple, variable sized, round, calcified lesions surrounded by low density areas together with cortical atrophy in occipital, temporal, and parietal lobes (Fig. 1B). The cerebral paragonimiasis was identified in the temporal lobe in seven, right temporo-occipital lobe in two, left parieto-occipital lobe in one, right frontal and occipital lobe in one, and left premotor area in one in CT and MRI.

Epileptogenic zone was defined by prolonged video-EEG monitoring with surface electrodes in 11 patients, with depth and subdural grid electrodes in one. In one patient in acute stage, evaluation methods except MRI were not done. Ictal EEG onset was recorded in the temporo-occipital in 10, fronto-temporal in one, and parieto-occipital in one. In a patient with paragonimiasis in the left premotor cortex and hippocampal abnormality in MRI (Fig. 2A), invasive EEGs with depth electrodes in the left hippocampus and subdural grid on the

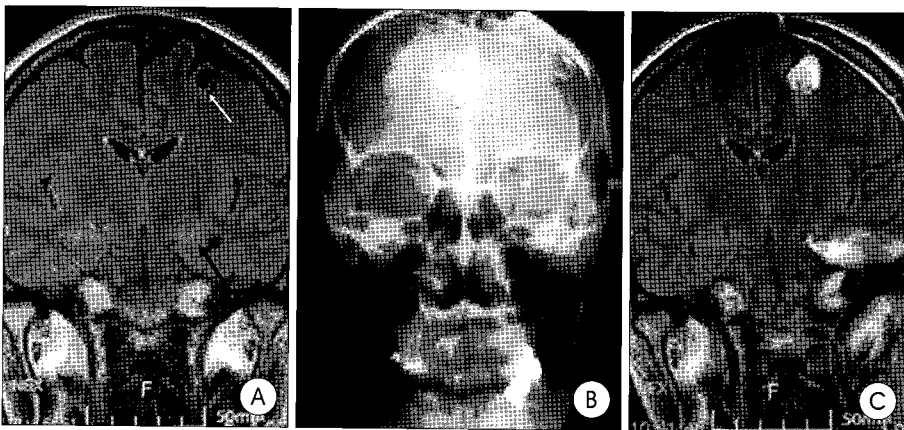


Fig. 2. A : Preoperative brain magnetic resonance FLAIR (fluid attenuated inversion recovery) image shows a lesion on left premotor cortex (white arrow), increased signal intensity of the left hippocampus, and dilatation of the temporal horn of the left lateral ventricle (black arrow). B : Plain skull antero-posterior view shows depth electrodes in the left hippocampus and subdural grid on the left cerebral convexity. C : Postoperative brain magnetic resonance FLAIR image shows a state of the left temporal lobectomy and lesionectomy in the left premotor area.

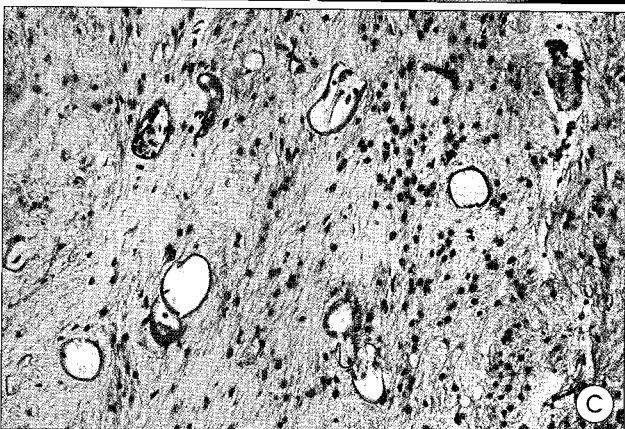
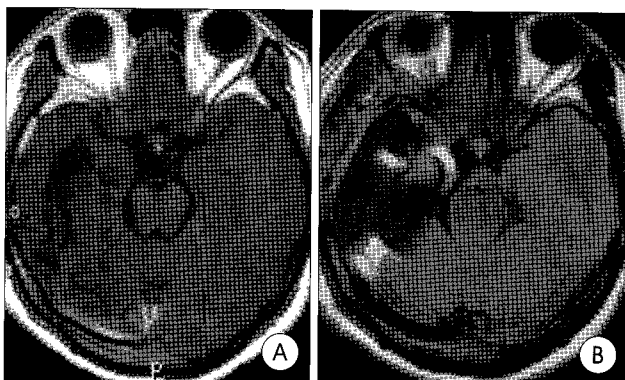


Fig. 3. A : Preoperative magnetic resonance image of the brain shows wide encephalomalatic change of the right temporo-occipital area, granulomatous lesion in the hippocampal body, and multiple ring-enhancing lesions in right temporal area in T1-weighted enhanced axial image. B : Postoperative MRI of the brain reveals state of right temporal lobectomy including mesial structures in T1-weighted axial image. C : The surgical specimen of the right temporal lobe is found to be replaced by numerous granulomatous and gliotic tissue and some eggs of *Paragonimus westermani* in cystic region (H&E, $\times 100$).

left cerebral convexity recorded ictal EEG from the left hippocampus and left premotor area (Fig. 2B). The invasive stu-

dy defined ictal onset zone in the left hippocampus and the irritative zone in the left premotor cortex. Prolonged video-EEG monitoring recorded repeated seizures starting with bizarre feeling evolving to head nodding, limb and orofacial automatism followed by generalized tonic seizure. Five patients had PET and one patient had SPECT. Hypometabolism was observed in unilateral temporal lobe in two, bilateral temporo-parietal in one, left temporo-parieto-occipital in one. Hypoperfusion was noticed in the right temporo-parieto-occipital area in

one. Hypometabolism in the unilateral temporal region was of value in localizing the epileptogenic zone in one patient with previous lesionectomy in the right temporo-occipital area. In Wada test, dominant hemisphere of language was in the left hemisphere in five patients and in the right hemisphere in one. Speech area was noticed in two patients by intraoperative speech mapping.

Surgical outcome

The surgical outcome was evaluated by using neurological examinations and Engel's seizure classification.

Results

Patients

The proportion of males to females was 4 : 9. The age of seizure onset was 3 to 40 years old (mean : 20.3 years old). The seizure duration was ranged from two weeks to 33 years (mean : 14.3 years). The seizure frequency before operation was four to five per month minimally, and twice a day maximally.

Operations

Three different types of the surgical procedure were performed for treatment of *Paragonimus westermani* and seizures, based on the results of preoperative evaluations. In six patients with the lesion limited in the temporal lobe accompanying typical temporal lobe seizure and ictal EEG onset from the temporal lobe, temporal lobectomy including hippocampectomy was done. In five patients with lesions in the temporo-parietal, temporo-occipital, parieto-occipital, and frontal area, a lesionectomy was done. Two patients had a temporal lobectomy plus lesionectomy. In one patient with previous lesionectomy in the right temporo-occipital area, additional temporal lobectomy

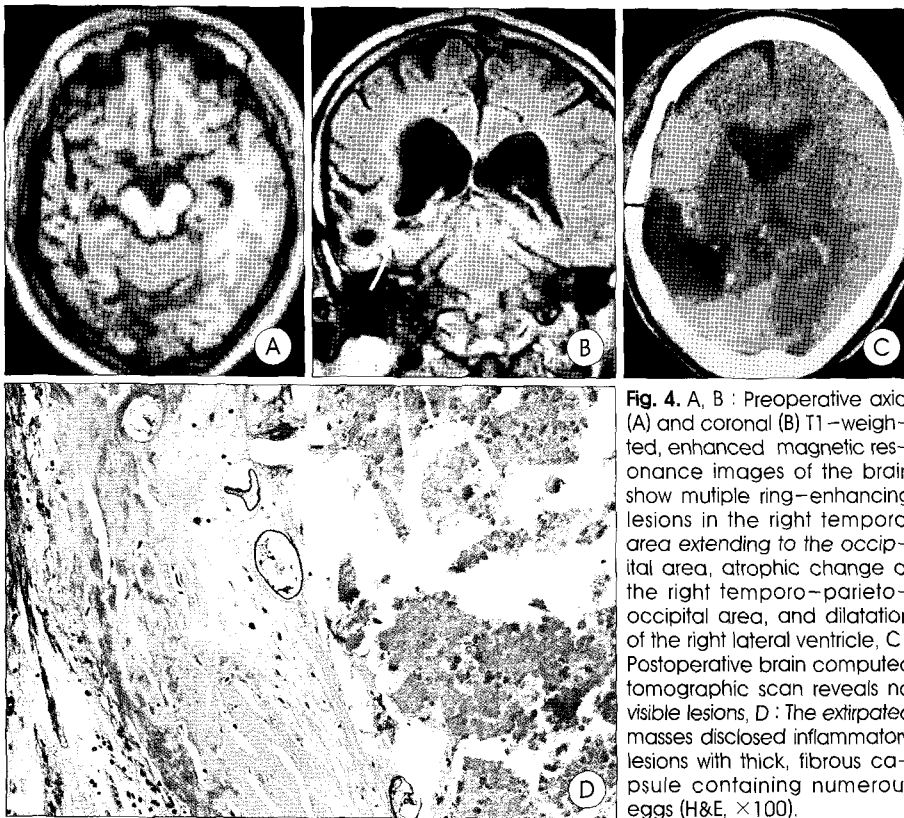


Fig. 4. A, B : Preoperative axial (A) and coronal (B) T1-weighted, enhanced magnetic resonance images of the brain show multiple ring-enhancing lesions in the right temporal area extending to the occipital area, atrophic change of the right temporo-parieto-occipital area, and dilatation of the right lateral ventricle, C : Postoperative brain computed tomographic scan reveals no visible lesions, D : The extirpated masses disclosed inflammatory lesions with thick, fibrous capsule containing numerous eggs (H&E, $\times 100$).

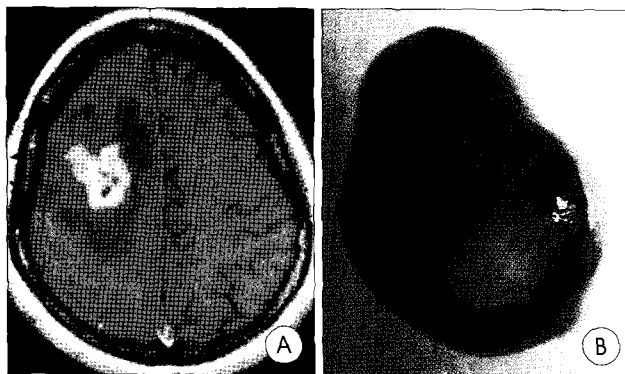


Fig. 5. A : Preoperative axial T1-weighted magnetic resonance image shows ring-enhancing large cystic mass with small eccentric nodule and wide peritumoral edema in the right cerebral convexity, B : Active form of *Paragonimus westermani* is identified.

including hippocampectomy was done due to persistent seizure attacks. Another patient showing cerebral paragonimiasis in the left premotor cortex and left hippocampal atrophy in MRI, temporal lobectomy including hippocampectomy and lesionectomy of cerebral paragonimiasis were performed simultaneously.

Surgical outcomes (Table 1)

At the average follow up period of 42.5 months (23~77 month), seizure outcomes were class I in 12 patients (92%) and class II in one patient (8%). Among six patients with temporal lobec-

tomy including the lesions in the temporal lobe extending to the mesial temporal portion, seizure outcome was class I in five patients and class II in one. All five patients with lesionectomy showed class I. One patients with previous lesionectomy of the paragonimiasis in the temporo-occipital area showed class I after additional temporal lobectomy. Seizures have not developed at all in a patient with simultaneous left temporal lobectomy and lesionectomy in the left premotor area (Fig. 2C). Postoperative wound infection occurred in one. Hemiparesis after wide lesionectomy in the frontal lobe occurred in one, which was relieved in two months. Histopathologic examination showed multiple cysts with thick fibrous wall and many eggs of *Paragonimus westermani* in cystic region, a central calcification surrounded by fibrous tissue, and reactive gliosis

in all patients. Hippocampal changes were revealed in patients who underwent temporal lobectomy.

Illustrative case 1 (patient No. 4)

A 34-year-old woman was admitted June, 2003 due to intractable seizures three to four times a month. Even though she had a previous operation for resection of the granulomatous lesions in the right temporo-occipital area in another hospital, magnetic resonance images(MRI) of the brain, on admission, revealed wide encephalomalatic change of the right temporo-occipital area, granulomatous lesion in the hippocampal body, and multiple ring-enhancing lesions in right temporal area (Fig. 3A). The first operation in another hospital could not control seizures in this patient. Recurrent seizures were probably due to resection of only the visible lesion of the right temporo-parietal region in MRI without any evaluation for epilepsy surgery. Semiology, according to the patient and her family, was highly suggestive of psychomotor seizure. Therefore, evaluation methods for definition of the epileptogenic zone were done. Chronic video-EEG monitoring recorded eleven complex partial seizures with ictal EEG onset from the right temporal region. Ictal SPECT showed hyperperfusion in the right temporal area including mesial temporal structures. Amytal test disclosed dominant hemisphere for memory and language in the left. According to these data, right temporal lobectomy including the mesial structures was carried out (Fig. 3B). The surgical specimen of the right temporal lobe was found to

be replaced by numerous granulomatous and gliotic tissue and some eggs of *Paragonimus westermani* in cystic region (Fig. 3C). And hippocampus showed neuronal cell loss in the CA1, CA2, CA3. Postoperatively, seizures have not developed.

Illustrative case 2 (patient No. 13)

A 33-year-old man with intractable seizures since eight years old was admitted on December 2000. He had suffered from seizures third a month. A plain skull film showed multiple calcifications in the right temporo-parietal region. Magnetic resonance images(MRI) of the brain showed multiple ring-enhancing lesions in the right temporal area extending to the occipital area, atrophic change of the right temporo-parieto-occipital area, and dilatation of the right lateral ventricle (Fig. 4A, B). Chronic video-EEG monitoring with surface electrodes recorded eight psychomotor seizures with ictal EEG onset from the right temporo-occipital area. The lesions in the right temporal lobe and the mesial temporal structures as well as the lesions in the occipital area were resected in December, 2001. The follow-up brain computed tomographic(CT) scans revealed no visible lesions (Fig. 4C). The histopathological findings were *Paragonimus westermani*. The extirpated masses disclosed inflammatory lesions with thick, fibrous capsule containing numerous eggs (Fig. 4D). Postoperative seizure outcome was class I.

Discussion

Paragonimiasis is a rare disease that is distributed throughout the Far East and Southeast Asia². The disease results from the ingestion of freshwater crabs or crayfish contaminated with the lung fluke, the genus *Paragonimus*. With the exception of the most common and usually primary site (the lung), paragonimiasis occurs most frequently in the brain^{6,9}. Brain involvement has been reported in 2~27% of clinical cases of all paragonimiasis¹. In the cerebral hemisphere, the reactions to the *Paragonimus* fluke are arachnoiditis, granulomas, and encapsulated abscesses. Although necrosis of the lesion and gliosis of the surrounding tissues due to arachnoiditis lead to local cerebral atrophy, almost all the granulomas and abscesses result in dense calcifications. Clinically, there are three stages : the initial stage of invasion and meningeal irritation, the stages showing features of a space-occupying lesion, and the late stage of arrest with sequelae. And radiologically, there are two stages ; early active stage and inactive chronic stage on MRI. MRI findings of cerebral paragonimiasis in early active stage are the presence of conglomerated, multiple ring-enhancing lesions with surrounding edema was the most characteristic¹. Multiple calcified and cystic granulomas with peripheral ring-like enhancement after gadolinium administration and surrounding local brain atrophy are considered to be characteristic findings in chronic inactive stage

of cerebral paragonimiasis¹¹.

In general, epilepsy and a variable neurologic disturbance may develop during this chronic inactive stage^{4,8,9}. The occipital and temporal lobes are the preferred cerebral site. In our cases, all but one patient had a long duration probably over 10 years of ingestion of uncooked crayfish or crab in their history taking. It occurred more frequently in the temporal lobe, and then, in the occipital lobe, the parietal lobe, the frontal lobe. In one case with sudden development of clustering attack of seizures and left hemiparesis two weeks after ingestion of uncooked crayfish, MRI showed ring-enhancing large cystic mass with small eccentric nodule and wide peritumoral edema in the right cerebral convexity (Fig. 5A). The cystic mass was extirpated to control increased intracranial pressure, neurologic disturbance, and seizure. During operation, active form of *Paragonimus westermani* could be identified in operative field (Fig. 5B).

In chronic inactive stage, the purpose of treatment of the cerebral paragonimiasis accompanying epilepsy is complete resection of the granulomatous lesion with surrounding gliotic tissues and control of seizures. Many authors have performed only lesionectomy to treat intractable epilepsy with small cerebral paragonimiasis^{1,3,5,6}. However, in terms of seizure control, possible epileptogenic zone including granulomatous lesion must be resected in cerebral paragonimiasis. Some authors reported that hippocampal change may be developed by the structural lesion in the temporal lobe or near the temporal lobe¹⁰. And these authors insisted that extrahippocampal lesion as well as hippocampus must be resected for good seizure control in patients with these kinds of pathologic substrate^{7,12}. In our cases, temporal lobectomy including hippocampectomy was done in eight patients with large paragonimiasis in the temporal lobe. In the cases of the lesions in the temporal lobe extending to the occipital lobe, we did a temporal lobectomy including hippocampus, and a lesionectomy in the temporal region extending to the extratemporal area. In patients with paragonimiasis granuloma mainly in the parietal or occipital lobe, lesionectomy was carried out. Interestingly, in one patient with small granulomatous lesion in the left premotor cortex, obvious hippocampal atrophy was identified in MRI. Chronic video-EEG monitoring with surface electrodes was done and recorded eight seizures with simultaneous ictal EEG onset from the left fronto-temporal region. Subdural grid electrodes were implanted on the left frontal region including granulomatous lesion and depth electrodes were contacted in the left hippocampus, to clarify the epileptogenic zone. Invasive EEG recorded 10 seizures with ictal EEG from the left hippocampus in eight and from the left premotor cortex in two. Based on these data, left temporal lobectomy and lesionectomy of the granuloma in the premotor cortex were done. Seizure has not developed after surgery. In this case, different epileptogenic zone was

presented in the distant area from the paragonimiasis granuloma. This result suggests that even though the lesion is identified in MRI, variable evaluation methods must be done for exact localization of the epileptogenic zone and better outcome in seizure control.

Conclusion

The relationship between structural lesions to epilepsy is not always simple or clear-cut. In patients with a cerebral paragonimiasis accompanying epilepsy, the variable evaluation methods were necessary for exact localization of the epileptogenic zone, and different surgical methods, including temporal lobectomy, lesionectomy and temporal lobectomy plus lesionectomy, must be done for complete resection of the lesion as well as the possible epileptogenic zone.

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Commentary

The authors reviewed the surgical results of 13 cases of cerebral paragonimiasis combined with intractable epilepsy. Although the treatment of acute parasitic lesions involving the central nervous system has well been established with effective anti-helminthic chemotherapy, the management of cerebral calcification or other chronic lesions from cerebral neurocysticercosis or paragonimiasis is yet to be clarified due to the lack of information regarding its clinical significance. While recent studies has suggested calcified chronic lesions may be linked with epilepsy or focal neurologic problems in the case of neurocysticercosis¹⁾, which is the most common parasitic condition involving the central nervous system, insufficient clinical data are available for chronic lesions of cerebral paragonimiasis except sporadic anecdotal reports. The causal relationship of the calcification in a patient with epilepsy could be one of three; 1) causal, implying that the lesion is the cause of focal epilepsy, 2) non causal, in which calcification and seizures merely co-exists independently, or 3) dual pathology. The authors had reasonably evaluated the causal relationship between the lesion and epileptogenesis and accordingly had accomplished excellent result in each case.

There was one patient who had been suspected in active stage of the disease in this study. The mechanism underlying seizures in active stage may be related to inflammatory reaction both in neurocysticercosis and cerebral paragonimiasis. Considering that anti-helminthic medication is generally effective for focal neurological symptoms including seizures in active stage of disease, it may need discretion to analyze active and chronic cases in one clinical series without subgrouping.

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