

A rare disease: a single-center experience of cerebral alveolar echinococcosis in 12 operated patients

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Abstract. – OBJECTIVE: In this study, we have evaluated 12 patients with cerebral alveolar echinococcosis (AE). All patients underwent surgery for cerebral AE. We aimed to demonstrate the relationship between the demographic properties of patients and surgical outcomes as well as surgical suggestions about surgical approaches.

PATIENTS AND METHODS: Patients were analyzed according to demographic properties, hepatic/ pulmonary AE lesion existence, symptoms, neurological and radiological examination, histopathological findings, and outcome after treatment.

RESULTS: Preoperative diagnosis based on the history of the patient, neurological examination, serological tests, and radiology. When enhanced radiological imaging like MR-Tractography and intraoperative neuromonitoring is combined with precision surgical methods cerebral AE is treatable. Ten of twelve cerebral AE patients had favorable outcomes after surgery.

CONCLUSIONS: AE of the brain is a rare but life-threatening parasitic disease. Wherever the primary focus is, surgery for cerebral involvement of AE is challenging but safe with appropriate surgical techniques and the help of radiological examination.

Key Words:

Echinococcus multilocularis, Cerebral alveolar echinococcosis, Cerebral surgery, Zoonotic diseases, Metastasis.

Introduction

Echinococcus multilocularis causes a parasitic disease in the liver known as alveolar echinococcosis (AE), one of the most dangerous zoonotic diseases seen in the northern hemisphere. AE has

the potential of metastasizing to the brain, lungs, and other extrahepatic areas, but cerebral metastasis is very rare at a rate of 1%^{1,2}. Although AE is often considered to be a benign disease, cerebral involvement may cause serious morbidity and mortality³. Despite all possible risks, the surgical approach is the standard treatment method for cerebral AE⁴.

The clinical diagnosis of cerebral AE is based on medical anamnesis and neurological examinations, serological tests, and radiology. Although direct craniography and angiography were used in radiological examinations in the past, magnetic resonance imaging (MRI) is the best radiological method for the diagnosis of cerebral AE today⁵. In the past, the Casoni skin test was used for *Echinococcus*, and in today's practices, specific IgG antibodies are evaluated in serological ELISA testing (Abbott Laboratories, Abbott Park, IL, USA)⁶.

Patients and Methods

The study protocol was approved by the Ethics Committee of the Faculty of Medicine of the Ataturk University and was conducted in accordance with the principles of the Declaration of Helsinki (B.30.2.ATA.0.01.00/664, 27.10.2022/8:48). This study included 12 patients with cerebral AE who were operated on in our clinic. Informed consent was obtained from all patients included in the study. All patients were evaluated according to demographic characteristics, presence of hepatic/ pulmonary AE lesions, symptoms, neurological and radiological examination results, histopathological findings, and outcome after treatment.

Serological tests were positive for *E. multilocularis* in all cases. In radiological examinations, computer tomography (CT) and/or MRI was performed. Surgical approaches were planned according to the localization of AE for each patient. Neuromonitoring records were obtained during surgery to avoid eloquent areas. Histopathological examination was performed under light microscope with hematoxylin and eosin (H&E) and periodic acid-Schiff (PAS) staining. Postoperative radiological imaging was performed to verify the resectioning of AE. Postoperative clinical statuses of the patients were evaluated with the Glasgow Outcome Scale. All patients used albendazole for up to 2 months during hospitalization and after discharge. The follow-up period for this patient cohort was 2-36 months.

Statistical Analysis

Analyses were conducted with IBM SPSS v. 20 (IBM Corp., Armonk, NY, USA). Data were presented as mean, standard deviation, median, minimum, maximum, percentage, and number. The normal distribution of continuous variables was evaluated with the Shapiro-Wilk W test and the Kolmogorov-Smirnov test. In 2×2 comparisons between categorical variables, the expected value (>5) was calculated using the Pearson Chi-square test. If the expected value was within the range of 3-5, the Yates Chi-square test was applied, and for expected values of <3, Fisher's exact test was applied. In comparisons of two quantitative variables, if the criteria for normal distribution were satisfied but the Pearson correlation was not significant, the Spearman correlation test was used.

Results

Of the 12 considered patients who were diagnosed with and operated on for cerebral AE, 2 were female and 10 were male. The mean age was 41.5±16.3 (13-64) years. All patients were from rural areas of the Eastern Anatolian Region of Turkey. Albendazole at 400 mg b.i.d was administered to each patient before and after surgery. The most common presentation of the patients was headache at 58.33% (n: 7), followed by hemiparesis at 50% (n: 6) and elevated intracranial pressure symptoms at 33.3% (n: 4). The neurological findings were consistent with the anatomical localizations of the AE masses. The lesions were located in the left hemisphere in 66% of cases and there was no difference in localization between

genders ($p=0.515$). There was no statistically significant difference between localizations (right/left hemisphere) and outcome scores ($p=0.056$), but there was a statistically meaningful correlation between age and localization ($p<0.01$). A summary of the patients' data is given in Table I.

In CT scans, the AE lesions were seen as hypo-isodense masses. In T2W MRI, lesions were seen as heterogeneous hypointense masses, while in T1W contrast-enhanced MRI, lesions were irregularly contrasted. Diffusion-weighted MRI revealed lesions with hypointense centers and hyperintense peripheries (Figure 1). MRI spectroscopy confirmed elevated lipid levels. Excluding only one patient, all patients were serologically positive. Ten patients had liver AE lesions (91.7%) and 2 patients (16.7%) had both liver and lung AE lesions. In one case, the serology results were positive but internal organ invasion was not observed.

Total resection of the lesions was achieved for all operated patients. Intraoperatively, AE was defined by the presence of rigid and non-mobile gray-yellow lobulated masses (Figure 2). In histopathologic evaluations, acellular membranes were seen by PAS staining and granuloma formation was seen by H&E, confirming that all resected lesions were cases of AE (Figure 3). We did not observe any germinative membranes or larvae in the resected specimens.

Spearman correlation tests showed that there were no correlations between age or localization of the cases and postoperative outcome scores ($p=1.00$).

Discussion

Rausch and Schiller⁷ confirmed that AE caused by *E. multilocularis* is a different medical condition from hydatid disease. Unlike cystic echinococcosis, AE is a rare medical condition, and it is still a potentially life-threatening infectious disease despite the administration of anthelmintic drugs, especially in Turkey, Iran, Alaska, Canada, Siberia, France, and alpine regions⁸. Brain involvement in cases of AE is rare, being reported at rates of less than 1% in the literature^{9,10}. However, Guo et al¹ reported the findings of more than 30 patients with AE and found brain involvement in 9 cases for a rate of 27%.

When AE spreads to the brain, the areas that feed the middle cerebral artery and the supratentorial parts of the cerebrum are usually

Table I. Summary of patients.

No.	Age/sex	Clinical presentation	Location of AE	Hepatic/pulmonary invasion	Serology	Treatment	Follow-up	Glasgow outcome
1	55/M	HA, L- weakness	R- post-parietal	+/-	Casoni +	TR	42 months	4
2	50/M	Dysarthria, R hand - Jacksonian sz	L- temporo-parietal	-	Casoni -	TR	36 months	5
3	40/M	HA, nausea, vomiting	L- parietal	+/-	Casoni +	TR	48 months	4
4	26/M	HA, L- weakness	L- parietal	+/+	Casoni +	TR	36 months	5
5	35/F	HA, R- weakness	L- thalamic	+/-	Ind hae +	TR	36 months	5
6	25/M	R- weakness	L- thalamic	+/-	Ind hae +	TR	42 months	4
7	64/M	Dysphasia,	R - temporal	+/-	Ind hae +	Temporal and parietal TR	4 months - exitus	1
8	27/F	HA, nausea and vomiting, altered consciousness	Left parietal	+/-	Ind hae +	TR	32 months	5
9	13/M	R- weakness	L- parieto-occipital	+/+	Ind hae +	TR	36 months	5
10	62/M	L- weakness	R- fronto-parietal	+/-	IgG +	TR	1 month - exitus	1
11	49/M	HA	R- parieto-occipital	+/-	IgG +	TR	36 months	5
12	52/M	HA	L- temporal, R- frontal	+/-	IgG +	R- frontal TR	24 months	5

qRT-aAE: Alveolar echinococcosis, M: male, F: female, R: right, L: left, HA: headache, Sz: seizure, Ind hae: indirect hemagglutination, IgG: immunoglobulin G, TR: total resection. PCR, quantitative Reverse-Transcription Polymerase Chain Reaction.

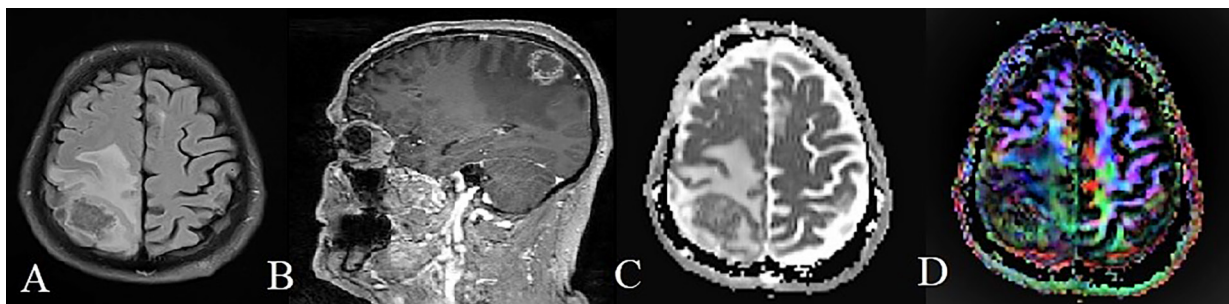


Figure 1. Preoperative radiological imaging of AE. **A**, T2W MRI heterogeneous hypointense lesion, **(B)** Ring-like contrasting pattern, **(C)** Diffusion-weighted MRI showing edema around the lesion, **(D)** MR-tractography image showing fibers surrounding the lesion.

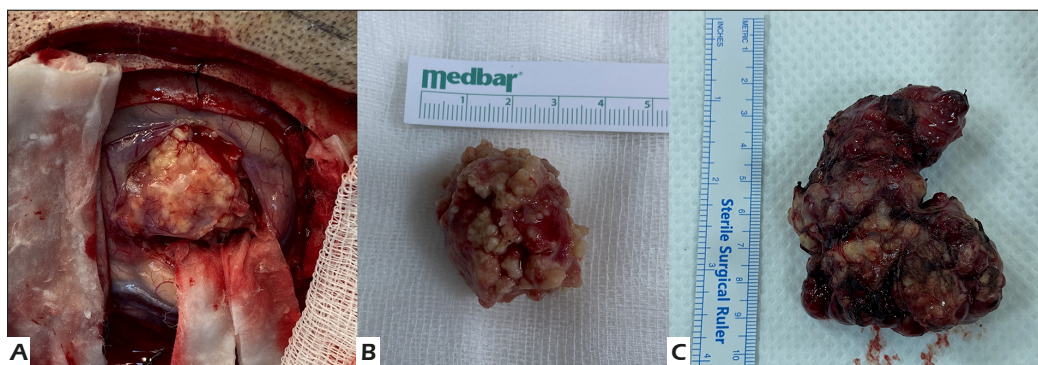


Figure 2. Macroscopic view of AE. **A**, After cortical dissection the AE lesion resembles Swiss cheese, **(B)** Total resected AE mass, **(C)** Largest sample of an AE mass resected piece by piece.

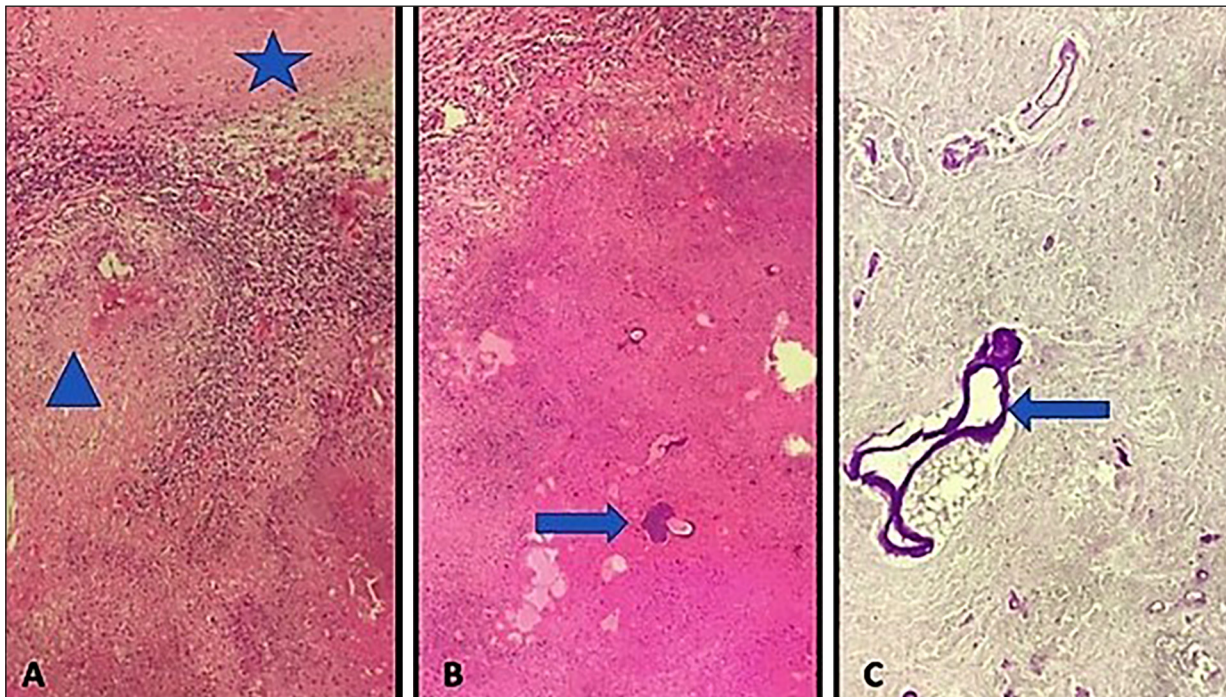


Figure 3. Histological evaluation of cerebral AE specimen. **A**, Granuloma structure (*triangle*) near glial tissue (*star*) (H&E, 10×), **(B)** Acellular membrane structure (*arrow*) inside a wide necrotic area (H&E, 10×), **(C)** PAS-positive acellular membrane structure (PAS staining).

most affected. These lesions can be solitary or multifocal^{11,12}. Because AE lesions behave like brain tumors, medical and surgical treatment of these cases is critically important. The differential diagnosis of this disease includes gliomas, tuberculomas, and fungal infections^{2,13}. The diversity in the diagnoses makes the preoperative diagnostic techniques more important. CT and MRI approaches show these lesions as solid/semisolid lobulated masses; they may also be multifocal. Peripheral ring-like, heterogenous, nodular, and cauliflower-like enhancement patterns have been reported. Diffusion-weighted MRI is useful in distinguishing lesions from edema¹³.

Anthelmintic therapy for AE at the time of diagnosis can prevent the progression of the lesions. The transfer of *E. multilocularis* from wildlife to domestic or farm animals has facilitated human transmission^{4,14}. Humans are intermediate hosts¹⁵.

AE occurs in the form of a non-capsulated solid mass. Unlike cystic echinococcosis, there is no laminated membrane, which allows the parasite to invade the host tissue in an alveoli-like manner^{4,16}. The cerebral metastasis mechanism is not clear, and in both our study and previous works, the protoscolex and the germinative membrane were

not present in the resected specimens^{4,8}. Furthermore, there may not always be larval metastasis to the brain; in some of our cases, we had to resect lesions piece by piece to protect the eloquent areas and important fibers, and we did not observe any recurrence in any case through the end of the follow-up duration. Thus, surgical resection seems to be a challenging but safe procedure. We recommend performing MRI tractography before surgery and using intraoperative neuromonitoring to avoid eloquent areas. For safer resections, the craniotomy can be wider, especially when the lesion occurs with widespread edema.

Conclusions

AE of the brain is a rare but life-threatening parasitic disease. Regardless of the primary focus, surgery for cerebral involvement of AE is a challenging but safe treatment choice with appropriate surgical techniques and the help of radiological examinations.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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Informed Consent

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Ethics Approval

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Authors' Contribution

Mete Zeynal: Planning, designing, data collection, literature survey, interpretation of the results. Mehmet Emin Akyüz: Collecting data of the work and statistical analysis. Mehmet Hakan Şahin: Conception of the work. Mehmet Kürşat Karadağ: Collecting data of the work. Handan Alay: Collecting data of the work. Hakan Hadi Kadioğlu: Statistical analysis. Caner Fahrettin Kara: Conception of the work. Muhammet Elveren: English editing.

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