

# Cystic Echinococcosis of Lung and Heart Coupled with Repeated Echinococcosis of Brain – A Case Report

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## ABSTRACT

*Echinococcosis is rarely encountered as a cystic brain disease. In this article we are presenting a case of a young woman repeatedly operated due to echinococcosis of lung, heart and brain. Recurrent brain echinococcosis developed despite preoperative and postoperative albendazol therapy after first and combined therapy with albendazol and praziquantel after the second brain surgery. The mechanism of recurrence remains unclear (primary infestation, dissemination after spontaneous or intraoperative cyst rupture or new infestation).*

**Key words:** multiorgan echinococcosis, brain, heart, lung, brain surgery, albendazol, praziquantel

## Introduction

Human echinococcosis is caused by larval stage taenia of *Echinococcus* species<sup>1,2</sup>. There are six species of echinococcus, four of which are important in human medicine; *Echinococcus granulosus*, *Echinococcus multilocularis*, *Echinococcus vogeli* and *Echinococcus oligarthus*<sup>1</sup>. Recently *Echinococcus shiquicus* and *Echinococcus felidis* have been discovered with transmission path to humans yet being unknown. Cystic echinococcosis is a zoonosis caused by *Echinococcus granulosus* and is endemic in parts of Southern Europe, Mediterranean, South America, Africa, Turkey, Australia, New Zealand, India, Russia and China, most frequently in cattle raising areas<sup>1,3,4</sup>. In our surrounding it is most frequently encountered in Dalmatia and in nearby countries (Bosnia and Herzegovina, Montenegro, South Serbia) and in autonomy region of Vojvodina<sup>3,5</sup>. *E. granulosus* is a cestode whose definitive host is a dog and similar species (wolf, wild dog) in whose intestine this taenia lives. Taenia eggs can be found in feces, fur and snout of a dog. Temporary hosts, in whom it is present in a form of water bubble, are many domestic and wild animals (herbivores) and humans. Temporary hosts are infected with eggs of the dog taenia when they get into the nature by feces or during the contact with the infected dog. Humans can be in-

fectured during the consumption of vegetables which went through inadequate thermal treatment or by playing with dog (mostly children)<sup>5</sup>. 10 genetic types of *E. granulosus*<sup>1</sup> are recognised among the temporary hosts (human, sheep, horse, camel, pig, deer). When taenia eggs get into intestine of temporary host it releases larvae (oncospheres) which then penetrate intestine wall thus entering the circulation and disseminate by blood into the different organs<sup>1,4</sup>. Dissemination can occur after spontaneous or intraoperative cyst rupture after which daughter cysts are disseminated by blood into other organs, different localisations of the same organ or they can create new cysts in site of initial localisation during which cyst can lose its unilocular character (Figure 1)<sup>2,5,6</sup>.

Most common localisation of cystic echinococcosis is liver (50–70%) and lung (16–30%). On rare occasion it affects other organs like spleen, kidney, abdominal cavity (2–3%), bones, muscle (0.5–5.4%), skin, heart (1–2%) and brain (1–2%)<sup>1–4,6–11</sup>. Cerebral echinococcosis is more prevalent in childhood<sup>9,12</sup>. When considering CNS infestation, supratentorial localisation is typical in parietal lobe, with skull, cavernous sinus, eye, cerebellum and ventricles being less frequently involved. Primary infec-

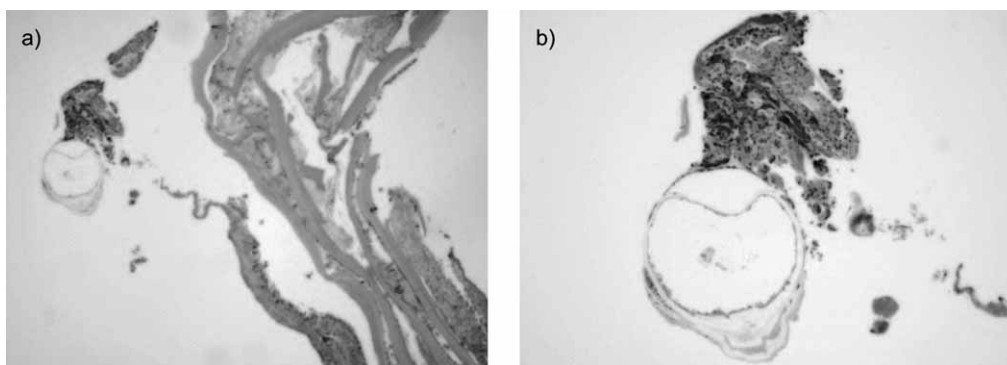


Fig. 1. a) *E. cyst outer layer and inner germinative layer with a daughter cyst; b) daughter cyst – higher magnification.*

tion usually consists of one cyst. More than one cyst is found in 30–40% of echinococcosis. Combination of echinococcus cysts of lung, heart and brain, as described in this article, is exceptionally rare<sup>3,6,14</sup>. Once the larva reaches the tissue, one hydatid cyst is developed with its outer acellular layer which covers inner germinative membrane. It is filled with bubbles containing protoscoleces<sup>1,2,4,5</sup>. By asexual divide of the inner capsule layer, numerous protoscoleces are formed. Due to internal division and daughter cyst development, the unilocular shape of a young echinococcus cyst is lost<sup>1,5</sup>.

Each cyst is surrounded by reactive host tissue<sup>1,5</sup>. The exact period of cystic echinococcus incubation is unknown, probably lasting many months or years, growing from 1 to 5 cm a year<sup>1,9,15</sup>. Slow growth of cerebral echinococcus cyst is well tolerated until it raises intracranial pressure or causes neurological symptoms by its size or localisation. Occasionally *E. cyst* can block the cerebrospinal fluid pathways, causing the stasis of cerebrospinal fluid and elevation of intracranial pressure by causing hydrocephalus<sup>5,6</sup>.

## Case Report

A 37 years old female housewife from Dalmatian out-back and from sheep, goat, cow and dog raising household is reported. She was presented to pulmonologist because of breathing difficulties, shortness of breath and suffocation feeling. Chest XR and CT scan revealed the cystic formation in the inferior part of her right lung. She was operated on November 11, 2006. The lower lobule of the right lung along with the cyst (dimensions 12 × 19 × 8 cm) was removed. Apparently there was no cyst rupture during surgery. A good recovery followed. Before and after surgery procedure, our patient did not receive antihelminthic therapy. During the may of 2008., she developed constant headache, vomiting, balance difficulties and weakness of the left limbs. During hospital admission in neurology department, the Echinococcus IHA was done (1:512 positive). CT and MRI of the head revealed 5 brain cysts of the right parietal lobe (3 large and 2 small) (Figure 2).

She was transferred to neurosurgery department of the same hospital. In preoperative period the albendazol was administered in daily dose of 10 mg/kg during 28 days. On the June 26, 2008. neurosurgery procedure was undertaken. A wide craniotomy was followed by atrophic brain tissue resection and cyst exposure. A silicon catheter was



Fig. 2. *Brain MRI revealing 3 large and 2 small echinococcus cysts.*



Fig. 3. *Intraoperative finding with visible cyst removed without rupture. Beneath the cyst the silicon catheter is also visible.*

used to instillate a warm saline between brain tissue and cyst wall which resulted in cyst removal without macroscopic rupture (Figure 3). Due to operative wound infection and osteomyelitis of the bone flap (Coagulasa negative Staphylococcus species) revision of the operative wound was done and bone flap has been removed. Postoperative CT scan showed no presence of brain cysts (Figure 4). During the postoperative period, our patient experienced sudden chest pain and breathing difficulties. Heart ultrasound revealed echinococcus cyst in the left ventricle (Figure 5), which has already been published (Fabijanić et al.).

After hospital dismissal our patient received 5 cycles (28 days of therapy each) of albendazol at a daily dose of 10 mg/kg, divided in two doses with 2 week pause between the cycles. During the therapy there were no serious side effects. Afterwards she was IHA negative.

On February 28, 2009 heart surgery was performed and echinococcus cyst (dimensions 28×17 mm) was removed and mitral valvuloplasty was done. Patohistology specimen showed echinococcus cyst without daughter cysts. Another 28 days cycle of albendazol followed. Postoperative recovery

was uneventful. She experienced no chest discomfort nor chest pain as well as no clinical signs of raised intracranial pressure. During her preoperative preparation for cranioplasty on the previous operation site, brain CT showed extremely rare localisation of echinococcus cyst in posterior cranial fossa. Brain MRI confirmed smaller cysts in parietal region on the previous operation site and a large cyst in the right cerebellar region (Figure 6). IHA testing was done on September 5 and 23, 2009, in two separate laboratories, the results came negative.

On the November 29, 2009, eighteen months after the first, the second brain surgery was done with complete removal of all intracranial cysts using the same technique as previously described. After that combined therapy of albendazol (20 mg/kg) and praziquantel (25 mg/kg) was administered during the 12 week period with regular laboratory controls every three weeks. No therapy side effects were noted. Three months after completion of the therapy, she complained of a headache and dizziness. New brain MRI demonstrated new cyst in the left occipital region (Figure 7).



Fig. 4. Postoperative brain CT scan with good result, no visible new cysts.

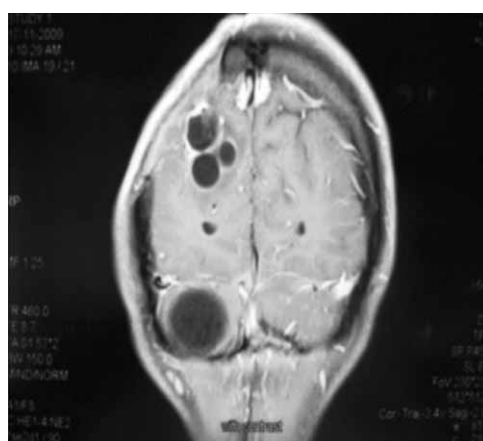


Fig. 6. Three small cysts in the right parietal and one larger in right cerebellar region.



Fig. 5. Echinococcus cyst is clearly demonstrated by heart ultrasound. Well demarcated formation on the front papillary muscle.

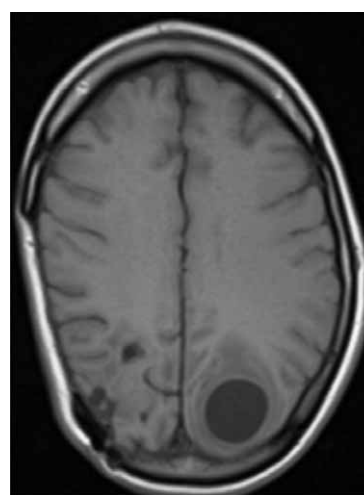


Fig. 7. Echinococcus cyst in the left occipital lobe.

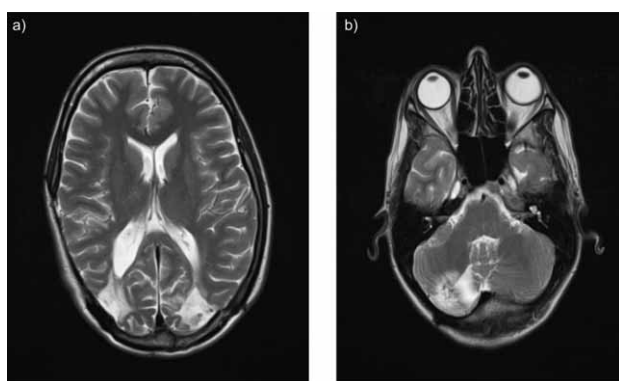


Fig. 8. a) Brain MRI with signs of gliosis in operative site; b) Gliosis in right cerebellar region, on both pictures there are no signs of new cysts.

Another 28 days cycle of albendazol (10 mg/kg) was administered preoperatively. Third brain surgery was done on May 6, 2011, the occipital cyst was removed without rupture. This cyst was very adherent to surrounding brain tissue and couldn't be removed using previously described technique. Microbiology and pathology results excluded the presence of daughter cysts. Subsequent MRI from October 4, 2011 did not show any cerebral cyst, only the signs of postoperative cerebral gliosis were present (Figure 8).

Starting with the 5. day after surgery, another cycle of albendazol was administered lasting 28 days. During therapy, elevated GGT (182 IU/L) was measured together with imbalance and vision difficulties. Therapy with albendazol was stopped (initially 3 cycles were planned).

Our patient is doing well now, with no subjective complaints other than gait imbalance and binocular vision inability. GGT is still elevated (77 IU/L) due to antiepileptic therapy. There are no signs of disease recurrence.

## Discussion

This article shows the case of multiorgan echinococcosis in a young woman from Dalmatian outback who was in contact with dogs. Whether echinococcosis developed because of the contact with dog or during the consumption of green salad (very common in Dalmatia) which was polluted by dog feces so it contained canine taenia eggs, it can't be determined.

It raises question about pathogenesis of heart and brain echinococcosis – whether or not it developed at the same time as the lung echinococcosis and it manifested later because of the slower growth of cysts in brain and heart; or it developed by dissemination after the surgery because of none antihelminthic prophylaxis; or else it developed during subsequent infestation, it can't be determined. It is known how echinococcus cyst which develops after hematogenic dissemination of larvae invasion through intestine has germinative layer, while cysts which appear after cyst rupture don't<sup>6</sup>. It is also well known that multiple cerebral cysts are often secondary, but also

after massive infestation many primary cerebral cysts can appear<sup>6,16,17</sup>. Multiple cerebral cysts are rarely described, but Cavusoglu 2009. presented multiple cerebral cyst case and gave examples of 17 cases from literature from which 9 of them were younger than 18 years<sup>6</sup>. Cyst which was removed during the last operation had no germinative layer so that would lead us to conclusion how it developed after microrupture and dissemination of daughter cysts, what was also described by others<sup>16–18</sup>.

Between second and last operation patient received numerous albendazol therapy cycles and still had many recurrences. Real question is if the therapy was inefficient due to cyst localisation and weak blood supply of tissue so medicaments couldn't reach target point within adequate concentration or it was the result of bad compliance. Appoint from that, patient was home medicated, so we can't be sure that she has taken a medicine on a regular basis. Third possibility is that it was a case of secondary cysts lacking the germinative layer making the therapy inefficient. In human echinococcosis, antihelminthic drugs are given prophylactically to prevent implantation of new daughter cysts during spontaneous or surgical rupture or therapeutically in cases of inoperable localisations. Literature data regarding the efficacy of albendazol and combination of albendazol and praziquantel in treating the parasitic brain cysts are contradictory<sup>19–22</sup>, same as in treatment of liver echinococcosis<sup>23</sup>, but it has been shown on a model of brain cysticercosis that the activity of the combination is time and dosage dependent<sup>24</sup>, while the earlier studies on a model of *E. granulosus* showed that the effect of the combination was time but not the dosage dependent<sup>25</sup>. It is established that the combination acts in additive manor but the exact mechanism is uncertain<sup>24</sup>. The study was conducted in vitro, in conclusion the authors suggest in vivo study of combination therapy *versus* monotherapy<sup>24</sup>.

IHA test is unreliable as a diagnostic parameter of echinococcosis, so the negative result after albendazol therapy does not exclude the presence of echinococcus cysts, it is most sensitive in liver and less sensitive in lung and brain echinococcosis which is understandable because cysts outside the liver are more often acellular and without germinative layer<sup>10,26,27</sup>. If the test was sufficiently specific and sensitive, which it is not, than it would be obvious that the recurrences were the consequence of the new infestations. Negative result of IHA in september of 2009. makes the possibility of new infestation less probable. Cyst growth rate in different organs<sup>10,26,27</sup> and also in different parts of the brain varies. In our case it seems that the cyst growth in cerebellum was faster than in parietal and occipital lobe.

Finally if it was the case of primary infestation with different speeds of cyst growth, than it is quite certain that combined therapy with albendazol and praziquantel has no advantage in comparison with only albendazol in therapy. In that case the patient compliance in terms of the right dosage and time of therapy is of utmost importance. If the microtrauma of the cyst wall happens during surgery and if protoscoleces enter the surrounding



tissue, it is important to have sufficient concentration of the drug in tissue to prevent implantation of daughter cysts and to start antihelminthic drug therapy as soon as possible after surgery.

It must also be underlined that the therapy is justified if it is a case of viable cysts with present germinative layer and daughter cysts and is not justified in prophylactic or therapeutic sense in the absence of germinative layer and daughter cysts so in secondary echinococcosis which are often outside the liver therapeutic and prophylactic usage of antihelmintics is questionable<sup>17</sup>.

Multiorgan echinococcosis incidence varies according to different studies<sup>28–30</sup> and surgical intervention may be done all at once or in sequence with the pauses between the surgeries<sup>28</sup>. In our case there were multiple surgical interventions because in the time of the first lung surgery and the first brain surgery we were unaware of the other localisations.

In this case report recurrent brain echinococcosis was described, but recurrence in other organs such as heart was described in the literature<sup>31</sup>.

The main method for distinguishing primary from secondary cysts is pathohistological examination of the cyst after surgery<sup>32</sup>.

The most efficient therapy in our case was the surgical therapy which is consistent with the other authors<sup>3,6,33</sup>.

In conclusion we can state that the first clinical symptoms in patients with cerebral echinococcosis, like with our patient, were headache, muscle weakness, vomiting and seizures in some. Serology tests were unreliable as with IHA in this case. The best diagnostic methods are brain CT and MRI. The best therapy is surgical removal of the cyst. Antihelminthic therapy and prophylaxis are often inefficient.

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## CISTIČNA EHINOKOKOZA PLUĆA I SRCA TE RECIDIVIRAJUĆA EHINOKOKOZA MOZGA – PRIKAZ SLUČAJA

### SAŽETAK

Ehinokoza se rijetko pojavljuje kao cistična bolest mozga. U ovom radu prikazujemo mladu ženu koja je operirana zbog ehinokokoze pluća i srca te u tri navrata ehinokokoze mozga. Recidivi ehinokokoze mozga su se pojavili usprkos preoperativne i postoperativne terapije s albendazolom nakon prve, i nakon kombinirane terapije albendazolom i praziquantelom nakon druge operacije mozga. Ostaje nejasno kako su recidivi nastali (primarna infestacija, diseminacija nakon spontane ili operativne ruptur ciste ili pak kao posljedica nove infestacije).