MODERN APPROACHES TO ECHINOCOCCOSIS DIAGNOSIS AND TREATMENT

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Abstract. The article presents the etiology of echinococcosis, the biology of the parasite, epidemiological data, the main methods for the diagnosis of echinococcosis in various localizations. They emphasized the importance of germicidal treatment with 87% glycerol solution. They substantiated the necessity of postoperative chemotherapy and the feasibility of organ-preserving operations, and the possibility of minimally invasive interventions. They discussed the surgical tactics for echinococcosis and the need for treatment in specialized surgical hospitals. They showed the experience of multi-stage surgical treatment of patients with echinococcosis.

Keywords: echinococcosis, diagnosis of echinococcosis, surgical treatment, minimally invasive treatment, liver echinococcosis, echinococcosis of lungs, echinococcosis of heart, echinococcosis of brain.

Introduction

Despite scientific and technological progress, the modern development of medicine remains relevant in the diagnosis and treatment of parasitic diseases.

In the last decade, there has been echinococcosis incidence increase and the disease geographical boundary expansion. In this regard, various errors are possible both in the diagnosis and treatment of patients in non-endemic regions due to the fact that some doctors do not take into account the possibility of this disease, especially since there are no pathognomonic symptoms in the clinical picture of uncomplicated echinococcosis, on the basis of which a reliable diagnosis could be made. At the same time, the patients with complicated echinococcosis are often provided with an erroneous diagnosis [1]. Interest in this disease does not run low today. Diagnostic and treatment techniques are being improved, views and approaches are changing. Many surgeons, including us, have been actively working on this issue for many years to the present.

Epidemiology

According to some estimates, more than 1 million people are affected by echinococcosis all over the world. Moreover, the incidence in some endemic and non-endemic regions varies by more than 200 times [2].

СОВРЕМЕННЫЕ ПОДХОДЫ К ДИАГНОСТИКЕ И ЛЕЧЕНИЮ Эхинококкоза

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Резюме. В статье представлена этиология эхинококкоза, биология паразита, эпидемиологические данные, основные методы диагностика эхинококкоза различных локализаций. Подчеркнуто значение методов гермицидной обработки 87% раствором глицерина. Обоснована необходимость послеоперационной химиотерапии и целесообразность органосохраняющих операций, возможности миниинвазивных вмешательств. Обсуждена хирургическая тактика при эхинококкозе и необходимость лечения в специализированных хирургических стационарах. Показан опыт многоэтапного хирургического лечения больных эхинококкозом.

Ключевые слова: эхинококкоз, диагностика эхинококкоза, хирургическое лечение, миниинвазивное лечение, эхинококкоз печени, эхинококкоз легких, эхинококкоз сердца, эхинококкоз мозга.

According to the WHO, the incidence rate of people with cystic echinococcosis in endemic areas can exceed 50 per 100,000 people a year, and in some parts of Argentina, Peru, East Africa, Central Asia and China, prevalence rates can reach 5–10%. According to the State Sanitary Inspection of Russia there has been a three-fold echinococcosis incidence increase among the population over the past 10 years; about 15% are the children under 14 years old. The total number of patients with echinococcosis in Russia can reach 50 thousand people. The average incidence of echinococcosis in Russia is 0.4 per 100 thousand people, but in some regions it is much higher (in Chukotka Autonomous Okrug — 9.1, Karachay-Cherkessia — 6.7, Orenburg Oblast — 4.2, Dagestan — 3.7) [3].

Parasite biology

Human echinoccosis is zoonosis (the disease transmitted to humans from animals) caused by tapeworms of the genus Echinococcus.

Cystic echinococcosis, also known as hydatid disease, or hydatidosis, causes the tapeworm Echinococcus granulosus [4].

In the medical literature, the disease caused by E. granulosus is traditionally called echinococcosis.

Adult Echinococcus is only few millimeters long (rarely more than 7 mm) and has no more than six segments, while

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other tapeworms can grow up to several meters in length and consist of several thousand segments (Fig. 1). An adult echinococcus has a specialized attachment organ in front, the scolex, which has four muscle suckers and two corolla of hooks. The body is segmented and consists of a number of reproductive units (proglottids), the number of which can vary from two to six. An adult worm is hermaphrodite. The last proglottid is half the length of the body and has a developed reproductive system [4].

E. granulosus requires two mammalian hosts to complete its life cycle. A number of herbivores and omnivores are intermediate hosts of Echinococcus. They become infected when the eggs of the parasite are absorbed along with contaminated food and water, and then the parasite goes through the larval stages of development in their internal organs. The final hosts of the parasite are carnivores: a sexually mature worm parasitizes in their intestines. Infection of these animals occurs when they eat the internal organs of the parasite intermediate hosts.

People are the so-called «random intermediate hosts». Infection of a person mainly occurs by contact with a dog or by eating contaminated vegetables. Echinococcosis mainly affects the population of rural areas with developed livestock and low socio-economic levels, however, there are the cases of the urban population infection (Fig. 2). Human infection with E. granulosus leads to the development of one or more hydatides, located mainly in the liver and lungs, and less commonly in bones, kidneys, spleen, muscles, and the central nervous system.

Echinococcus eggs (oncosphere) are coated with a membrane that dissolves under the action of gastric juice. The released parasites drill the intestinal mucosa and enter the liver through the portal vein system, where they develop into a mature cyst. Most parasites are delayed in the hepatic sinusoids; therefore, from 54 to 84% of echinococcal cysts are formed in the liver [6]. Individual eggs pass through the liver and, bypassing the heart, are retained in the pulmonary capillary bed, which leads to the formation of pulmonary cysts (15–20%). When a parasite enters a large circle of blood circulation, cysts (10–15%) are formed in the spleen, brain and bone marrow, heart, etc. Even the observations of isolated echinococcosis of the subcutaneous tissue of legs, uterus ligaments, eye, thyroid and pancreas are described as casuistic [6].

A maternal cyst, which is a bubble filled with fluid, slowly develops from the embryo of echinococcus. The wall of the echinococcal cyst consists of two membranes: the outer cuticular (chitinous) and the internal germinal. The cuticular membrane is the product of germinal membrane cell excretion and is similar to insect chitin in chemical nature. The membrane is impervious to microflora, host proteins, resistant to suppuration and performs the function of a semipermeable membrane, providing access to the parasite of low molecular weight nutrients and protecting the cells of the germinal membrane from the effects of adverse host factors. The germinal membrane, which carries out all the vital functions of the parasite, is divided into three zones: the parietal — cambial, the middle — the



Figure 1. Adult echinococcus (light microscopy, hematoxylin-eosin, 20-fold zoom).



Figure 2. Echinococcus development cycle. 1 — the final owners (dogs, jackals, wolves, foxes, martens and other predators); 2 — mature segments of the parasite containing eggs; 3 — egg (oncosphere); 4 — intermediate hosts (pigs, sheep, cattle, goats, deer, moose, camels and some other animals, as well as humans); 5 — echinococcal cyst (larva); 6 — the liver of an intermediate host with echinococcal cyst.

zone of calcareous bodies and the inner — the zone of brood capsules with developing protoscolexes and acephalocysts. Considering that the cuticular and germinative membranes are macroscopically represented by a single entity, they are often combined in the literature into the concept of «chitinous membrane». Outside, an echinococcal cyst is surrounded by a dense connective tissue fibrous capsule, which is formed as the result of protective reactions of the intermediate host against the products of the parasite metabolism and performs a peculiar skeletal and protective function, protecting the parasite from mechanical damage, and the ongoing invasion of the host «immune attack». After the maternal cyst rupture or perforation, the embryonic elements continue to develop with the formation of secondary echinococcal cysts in the lumen



Figure 3. Microscopy of the native drug: A - the contents of the dead cyst; B - living protoscolexes.

of the maternal or beyond (exogenous or endogenous echinococcal cysts). Exogenous cysts are very rare. The presence of daughter and grandchild cysts indicates a high fertility of the echinococcus larva.

Diagnostics

Diagnosis is often a difficult task, which is associated with the asymptomatic course of the disease in the early period of its development. Often the patients seek medical help when a parasitic cyst reaches a significant size up to adjacent organ compression or because of the cyst break in the pleural cavity, bronchi, etc. The most common instrumental diagnostic methods are ultrasound, x-ray of the chest and multispiral computed tomography.

The leading diagnostic method is ultrasound. The method allows you to diagnose echinococcosis at the stage when parasitic cysts are small, from 1.5–2 cm. The sensitivity of the ultrasound diagnostic method in echinococcosis detection makes 88–98%, and the specificity makes 95–100%. Echinococcal cyst has several characteristic ultrasound signs. This is a hypoechoic (anechoic) formation surrounded by a «chitinous membrane» — a hyperechoic structure, on the inner surface of which multiple hyperechoic inclusions, the so-called «hydatid sand», represented by germinal elements of echinococcus, are often determined. Uncomplicated echinococcal cyst with ultrasound is a spherical formation of the correct form with smooth walls and liquid contents.

A more important feature is the stratification of the cyst dense wall, the so-called double contour — morphologically this is the layer of the lymph between the chitinous membrane and the fibrous capsule. It is not characteristic of any other cystic lesions, and it always occurs in whatever organ the cyst is located in, except for the brain and bones, where the fibrous capsule does not form. Tape hyperechoic structures that do not change their position (exfoliated chitinous membrane) can be detected in the cyst lumen — the symptoms of a «frozen water lily» (described by Lagos-Garcia, 1924) and «snake» (described by Von Sinner, 1991), as well as daughter cysts (Fig. 4). There is a strong belief in the literature that a lot of partitions in the lumen should be considered the most characteristic for an echinococcal cyst. However, it is known that the parasite delimits itself from the host; otherwise the parasite may die. In the case of echinococcosis, either a dead maternal cyst with many daughter and grandchildren is detected, or it is a multiple echinococcosis, in which the cysts are located nearby and cause atrophy of the tissue caught between them during the growth process.

Echocardiography plays a central role in the diagnosis of cardiac echinococcosis, since the method allows to detect one / multi-chamber cysts, to identify the displacement of heart structures by a growing cyst, and to evaluate hemodynamic consequences.

An X-ray examination of the chest organs in the lung determines a homogeneous shadow of medium intensity, round or oval, with the correct clear contours (Fig. 5).

Echinococcal lung cysts of large sizes, filling the entire pleural cavity or a significant part of it, often cause the displacement of the mediastinal organs: the Vogano symptom, characterized by the presence of enlightenment areas in the costal-diaphragmatic sinuses, is visible both medially at the border and laterally.

The diagnosis of complicated pulmonary echinococcosis is often quite difficult and complicated after the break of an infected cyst in the bronchus. Many authors consider this symptom to be pathognomonic for an opened echinococcus — the symptom of a «floating membrane» or «collapsed membrane» (in the absence of fluid in the echinococcus cavity). For the first time this symptom was described by V.N. Stern in 1954.

In uncomplicated forms of pulmonary echinococcosis, chest x-ray is still a screening method.

Fibrobronchoscopy can provide some diagnostic (and, in some situations, therapeutic) help with pulmonary echinococcosis. When a cyst breaks into the bronchus, the fragments of the chitinous membrane can be detected in the lumen of the bronchus. At the same time, unlike other clinical, instrumental and laboratory methods, the diagnosis established by

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Figure 4. Echinococcal cyst of the right lobe of the liver (ultrasound image): A — with calcification of the wall along the entire perimeter; B — ribbon-like hyperechoic structure in the cyst cavity — exfoliated chitinous membrane.



Figure 5. Panoramic radiographs of the chest in direct projection, pulmonary echinococcosis. A — the cyst of the left lung with the diameter of 15 cm; B — the cyst of the right lung with the diameter of 12 cm, the left lung with the diameter of 8 cm.

bronchoscopy with cytological confirmation is in the nature of a conclusion, not an assumption.

For any complicated forms of the disease (a break in the bronchus or pleural cavity, suppuration, etc.), CT should be the method of choice. As compared to ultrasound, CT and MRI are characterized by higher sensitivity, panoramic image, and the accuracy of topical and differential diagnostics at certain locations. CT and MRI can detect cysts with the diameter of up to 0.5 cm, and differentiate small or dead «pseudosolid» forms of echinococcosis from tumors more effectively. According to the literature, the total accuracy of CT/MRI diagnostics for echinococcosis, exceeds 95%. The most important advantage of CT and MRI is that they make it possible to judge objectively the size of the cysts, their number and location, their relationship with the vessels, ducts of the bronchi, etc., assess the stage of the parasite development, and detect the damage of other organs by echinococcosis. These data are crucial to determine surgical access, operation type, its volume planning, and the assumption of possible intraoperative complications (Fig. 7).

The morphological research methods for echinococcosis reveal the characteristic structural elements of the parasite



Figure 6. Chest x-ray in the frontal projection. In both lungs, numerous rounded shadows are determined — echinococcal cysts.

larvae, which serves as an irrefutable confirmation of the diagnosis.

Reliable and basic methods of laboratory diagnostics are serological studies — EIA, IHT. In clinical practice, the data of serological studies are additional to the complex of clinical and instrumental examinations and serve in primary diagnostics, differential diagnosis, the assessment of complex treatment results (chemotherapy and surgical treatment), and for the detection of the disease relapse.

Treatment

An optimal and most common method for echinococcosis treatment is surgery.

There are three types of surgical intervention: traditional open, laparoscopic and minimally invasive.

The desire to minimize the morbidity of an operation also affected the traditional surgery of liver echinococcosis. It has been proven that a simple echinococcectomy, which consists in opening and antiparasitic treatment of a cyst (87% aqueous glycerol is currently an effective germicide), followed by removal of the membranes and, if necessary, by capitonnage of the residual cavity, gives equally satisfactory long-term results



Figure 7. A — CT: echinococcal cyst of the right lung; several daughter cysts, as well as a partially exfoliated chitin membrane are determined in the lumen of the maternal cyst, and at its periphery; B — MRI: multiple parasitic liver cysts; C — MRI: a dead liver cyst; a wrinkled exfoliated chitinous membrane is determined in the lumen; D — liver MRI: T1 mode; E — T2-mode: the double contour of the cyst shell is clearly differentiated, indicating its parasitic nature.

with respect to disease relapse, as well as total pericystectomy or liver resection, i.e. complete removal of the cyst even with the fibrous capsule.

The fascination with laparoscopic technology observed in the early years of liver echinococcosis treatment was somewhat extinguished. This trend has emerged both abroad and in Russia. And this is due to a rather high relapse rate after such operations. It turned out that various technical devices that prevent hydatid fluid from entering the abdominal cavity, as the cavity shrinks, no longer excludes the risk of seeding reliably. Intraoperative complications are also frequent, sometimes severe, up to a coma. The frequency of early relapse was significant (up to 30%) — six months or a year after the operation, which usually indicates an intervention defect. Laparoscopic interventions are advisable when it is technically possible to remove the cyst without opening it, i.e. with the possibility of performing the so-called ideal echinococcectomy. This situation develops with a regional, extraorgan arrangement of a cyst, which is quite rare.

Percutaneous echinococcectomy has been widely used in recent years. After accumulation of certain experience, the method is applicable almost always. The main contraindication to percutaneous echinococcectomy is the exit of germinal elements beyond the fibrous capsule — the so-called exogenous budding. The fact is that with this option of cyst development, it is not possible to act with a germicide on the budding fragment, and this almost always leads to the disease relapse.

The choice of surgical intervention method, in our opinion, depends on the size of echinococcal cysts, their localization and morphological features of the parasite development.

A huge impact on the results of treatment is provided by subsequent chemotherapy, or anthelmintic therapy. It is also necessary to influence the screenings of echinococcus of small sizes, not available to modern diagnostic methods. Echinococcus drugs damage the germinal layer of echinococcal cysts. The effect of treatment is evaluated by ultrasound — folds appear in the cyst.

- Albendazole 10–15 mg/kg per day for 3–6 months.
- Mebendazole 40–50 mg/kg per day for 3–6 months.

Clinical examples

Patient E., 45 years old, was undergoing treatment at the Oncology Center for cervical cancer T2N0M0, II A st. During a preoperative examination of the patient, according to abdominal MSCT, a multichamber parasitic cyst of 10×10 cm was revealed in the III-rd, IV-th, V-th, and VI-th segment of the liver. Oncologists recommended surgical and antiparasitic treatment of liver echinococcosis after the oncological disease treatment in a specialized hospital. They performed enhanced hysterectomy with appendages, three courses of induction PCT and combined pelvic radiation therapy according to a radical program. Against the background of cytostatic therapy, suppuration of the echinococcal liver cyst occurred, which required an emergency surgical intervention. An open echinococcectomy was performed. They also performed the resection of the echinococcal cyst walls of the liver right lobe,



Figure 8. Operative intervention scheme.

500 ml of pus were removed with a chitin parasite capsule. The cyst cavity was treated with glycerol solution (87%). The tamponade of the residual cavity by an omentum strand and drainage with polyvinyl chloride double-lumen drains was performed (Fig. 8). A month later, the course of antiparasitic therapy was carried out.

The patient K., 19-year-old, was admitted with a clinical picture of an incomplete external bile fistula, obstructive jaundice, purulent cholangitis, liver failure, and coagulopathy. Autopsy, rehabilitation and drainage of a parasitic liver cyst was performed in the hospital at the place of residence. During the postoperative period, an incomplete external bile fistula was formed. The patient was treated three times for recurrent bleeding from the area of the drained cyst. Examination by MRI revealed the stricture of the common bile duct. Given the nature of the pathology, in order to restore the patency of the biliary tract, the patient was hospitalized in the NMSC named after N.I. Pirogov. During examination according to fistulography, the contrast fills the residual cavity of irregular shape of 4.5×2.5 cm, with a partial filling of small intrahepatic ducts. According to ultrasound, fistulography and MRI in cholangiogenic mode, they revealed the signs of the common hepatic duct stenosis, moderately pronounced intrahepatic hypertension, the presence of a residual cavity of the echinoc-



Figure 9. Operation stages (intraoperative photo). A — the appearance of the residual cavity after the resection of the IV-th segment of the liver; B — bighepaticoyunoanastamosis on the loop turned off along the Ru.

occal cyst with the destruction of the intrahepatic biliary duct confluence. Taking into account the phenomena of obstructive jaundice, cholangitis and coagulopathy, the patient underwent complex conservative detoxification therapy and coagulopathy correction. The performance of endoscopic retrograde cholangiography, papillosphincterotomy, and percutaneous transhepatic cholangiostomy did not produce an effect; the phenomena of obstructive jaundice and cholangitis persisted. The patient was operated. They performed laparotomy, cholecystectomy, the resection of the IV-th segment of the liver, bighepaticoyunoanastamosis on the loop turned off along the Ru, and abdominal drainage. The postoperative course is smooth. During the follow-up examination, after the course of antiparasitic therapy, six months after the operation, there was no relapse data.

The patient Ch., 30 years old. Entered the hospital on June 2, 2010. She did not complain. The disease was detected during the physical examination at work. The condition is satisfactory. The vesicular breathing. Heart sounds are rhythmic, and clear. AP 120/80 mm of hc. Pulse: 78 beats per minute. General clinical blood and urine tests without features. Ultrasound revealed no cavities in the abdominal cavity. X-ray: a uniform shadow of medium size $(4 \times 5 \times 6 \text{ cm})$ is determined on the right in the lower pulmonary field; a bean-shaped shadow of $7 \times 6 \times 4.5$ cm is observed on the left in the lower pulmonary field. The patient was operated, a simultaneous echinococcectomy was performed from both lungs, and the capitonnage of the cyst bed by Delba. The postoperative course is smooth. Chemotherapy with albendazole was prescribed according to the scheme. The patient was examined after 12 months. Radiographically the lungs are straightened completely, there is no relapse data.

The patient R., 36 years old. He was admitted to the hospital on 10/17/02 with the complaints of general we-akness, coughing with blood streaks, sweating, shortness of breath, fever up to 390, and irregular heartbeats. He

considered himself sick since 1999, when pains behind the sternum and body temperature increse began to bother him from time to time. In June 2002, in one of the clinics in Moscow, he underwent the first operation: removal and rehabilitation of echinococcal cysts from the heart. During surgery: «... access - median sternotomy. There is a total adhesive process in the pericardial cavity. Only the front surface of the heart and the right sections were released among the adhesions, the remaining sections were strongly sealed, with many cysts of various sizes. The operation was performed without AC. Both pleural cavities were opened, the edges of the pericardium with several cysts were dissected, about 8 cysts were opened and sanitized, ranging from a pigeon egg to a chicken egg». A month later, the patient was discharged from the hospital. One month after discharge, a relapse was detected.

Multiple cysts were revealed in the posterior mediastinum, both lungs, in the heart and in the brain during examination according to x-ray, computed tomography, and echocardiography at the clinic of the Research Institute of Thoracic Surgery MMA named after I.M. Sechenov. Many cysts are multi-chamber. Large cysts in the projection of the right atrium make 78×60 mm, the left atrium — 37×24 mm, along the back surface of the left ventricle -32×23 mm. Cysts are squeezed and both atria are deformed, left atrium undergoes stronger deformation. The compression of the right pulmonary veins, the deformation and compression of the right branch of the pulmonary artery are determined. There is 29×28 mm cyst in the anterior sections of the interventricular septum. Computed tomography of the brain: two-chamber formation of 14×19 mm is determined in the projection of the upper parietal lobe on the right.

According to transthoracic echocardiography: left atrium — 4.4 cm, final diastolic volume of the left ventricle — 110 ml, end-systolic volume — 34 ml, enddiastolic size — 4.9 cm, end-systolic size — 2.9 cm, ejection

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Figure 10. X-ray examination of the patient Ch. A — radiograph in direct projection; B, C, D — computed tomograms before surgery.

fraction — 70%. Valve apparatus is without pathological changes. Cystic formations in the lower third of the interventricular septum make up to 1.5 cm. 2 cysts are determined behind the left atrium (Fig. 11).

The first stage of complex treatment on November 14, 02 — the patient underwent surgery: echinococcectomy from the right heart compartments, right lung, posterior mediastinum and pericardium. Access — right lateral thoracotomy. Partial pneumolysis. 8 echinococcal cysts from 2 to 6 cm were removed during the operation, including 4 along the right contour of the heart and behind the right atrium. All stages of cyst access and removal were carried out under the control of intraoperative oesophageal echocardiography (Fig. 12).

The second stage: the operation was performed on 12.12.02: an echinococcectomy from the left heart compartments, interventricular septum, pericardium, and posterior mediastinum. Access — left-side lateral thoracotomy. Severe adhesions in the left pleural cavity. Partial pneumolysis. The pericardial cavity is obliterated. The attempts to free the heart from adhesions led to bleeding from the myocardium, peric-

ardium, therefore, further attempts to isolate were refused. At this stage, it was difficult to differentiate highly sealed cysts, the structures of the heart and lungs using oesophageal Echocardiography. Subsequently, the cyst autopsy was performed under the control of intraoperative epicardial echocardiography through the pericardium. During the examination 2 large cysts were revealed in the posterior mediastinum. The cavity of the cysts is opened, the chitinous membrane is completely removed, the cavities are treated with glycerin. Under the control of echocardiography, the location of 2 cysts was determined which were opened in the thickness of the interventricular septum. The chitinous membrane was completely removed from the cysts, the cavities were treated with glycerin. 6 cysts were removed in total (Fig. 13).

The third stage on 01.03.03. The patient underwent craniotomy, the removal of echinococcal cysts from the brain (Fig. 14).

Subsequently, the patient experienced 4 courses of chemotherapy with albendazole at the dose of 15 mg/kg/day. The patient was discharged without complications.



Figure 11. The patient R., 36 years old. Diagnosis: echinococcosis with heart, lung, and brain damage. Transthoracic echocardiography. Echinococcal heart cysts (indicated by arrows), the position of the heart long axis, four-chamber position.



Figure 12. Intraoperative oesophageal Echocardiography: multiple echinococcal cysts of the heart (indicated by arrows).



Figure 13. The patient R., 36 years old. Closed echinococcectomy from the lower third of interventricular septum without AC.



Figure 14. The patient R., 36 years old. Diagnosis: echinococcosis with heart, lung, and brain damage. Operation stage: the dura mater was opened, hydatide in the right parietal lobe of the brain.

Summary

Reconsideration of approaches to the diagnosis and choice of treatment for the patients with echinococcosis remains a very important topic today. The patients with echinococcosis, regardless of the cyst size and location, should be sent to a surgical hospital with the experience in treating such category of patients. The choice of intervention method is based on the technical capabilities of a hospital and the cyst characteristics. Performance of an operation under the conditions of anti- and aparasitism, the use of germicides with proven effectiveness, and mandatory postoperative chemotherapy almost minimizes the development of relapse.

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