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ECHINOCOCCOSIS: DIAGNOSIS AND TREATMENT

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Abstract

Echinococcosis also remains a serious problem today. Highly informative diagnostic methods allow hepatic echinococcosis to be diagnosed at its early stage. This brings mini-invasive, saving operations under ultrasound, X-ray, TV, and endoscopic guidance up to a new level. The accumulated experience suggests that the current high-tech operations that are an alternative to traditional access surgery can be extensively used. However, only strict observance of a protocol for saving operations, their performance in specialized hospitals, and compulsory antiparasitic therapy with albendazole will be of benefit to mini-invasive surgery for hepatic echinococcosis.
Key words: ECHINOCOCCOSIS, mini-invasive surgery, intervention radiology, endosurgery

Introduction

Hippocrates wrote in his writings about "jecur aqua repletum"—a liver filled with water—and to treat this disease (most likely referring to echinococcosis), he suggested burning the abdominal wall with a hot iron to remove the fluid filling the liver [1]. It was only in 1801, when the mature form of Taenia echinococcus was isolated, that Rudolphi coined the term "echinococcus."

The most common are Echinococcus multilocularis and Echinococcus granulosus. In Western literature, the term "echinococcosis" is more commonly used, implying the genetic unity of the parasites that cause the disease. In Russia and the CIS countries, their original division into alveo- and echinococcosis is common. Alveococcosis is usually found only in humans, has an infiltrative growth similar to a cancerous process, and almost never leads to the development of cystic formations. Echinococcosis affects humans and farm animals, and it always goes through a cyst formation stage.

Diagnosis and treatment of patients with echinococcosis have undergone significant changes over the past 30 years. Many morphological features of the parasite have been identified, and strategies for surgically preserving echinococcosis have been defined.

Epidemiology

The geographical prevalence of the disease is evidenced by the fact that it has not been detected in the Arctic and Antarctic alone. Incidence is directly related to sanitary practices and peaks in regions with annual temperatures of approximately 10–20°C. In economically developed countries, the increase in incidence is primarily due to immigration and tourism. Physicians' lack of awareness of echinococcosis leads to late diagnosis, a lack of sanitary and preventive measures, and, consequently, inadequate treatment of patients with echinococcosis.

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Pathogenesis and Pathomorphology

Echinococcosis is one of the most severe parasitic diseases. It is caused by the tapeworm Echinococcus granulosus, which infects dogs. The parasite's intermediate hosts include humans and farm animals.

Dogs become infected by ingesting the entrails of animals with echinococcal cysts. The embryonic elements (protoscolices and acephalocysts) located within the cyst attach to the wall of the dog's small intestine and develop into sexually mature individuals. Mature segments containing 400-800 echinococcus eggs (oncospheres) detach from the abdomen. Infected dog feces contaminate their fur, grass, and soil; the eggs enter the intestines of sheep, pigs, camels, and other animals.

A person can become infected by petting a dog or eating contaminated vegetables. The role of meat products should be considered minimal, as both humans and farm animals are intermediate hosts, and heat-treating meat almost always kills the parasite. The possibility of infection through meat is only relevant for people involved in slaughtering livestock, cutting meat, and skinning. The widespread belief, even among medical professionals, that a healthy person can become infected from an infected person has not been proven.

The oncosphere is covered by a membrane that dissolves under the influence of gastric juice. Released parasites pierce the intestinal mucosa and enter the liver via the portal vein. After lingering in the hepatic sinusoids, they develop into mature cysts. Thus, 54 to 84% of echinococcal cysts form in the liver. Individual oncospheres cross the liver barrier and enter the pulmonary capillary bed through the right chambers of the heart, which in 15–20% of cases is accompanied by the formation of pulmonary cysts. In 10–15% of cases, after crossing the pulmonary barrier, the parasite enters the systemic circulation, attacking all human organs and tissues [2]. To date, there are no descriptions of cases of echinococcosis of the teeth, nails, and hair.

The echinococcal embryo slowly develops into a mother cyst, which resembles a fluid-filled sac. This fluid is a serum transudate and has antigenic properties. If it enters the patient's bloodstream, it can cause an eosinophilic reaction and/or anaphylactic shock.

The organ that hosts the oncosphere forms a fibrous capsule around the developing cyst, which consists of three cell layers. The inner (smooth) layer consists of spindle-shaped cells, the middle layer consists of oval connective tissue cells, and the outer layer consists of connective tissue fibrils [3]. Calcium salts often deposit within the fibrous capsule, and in some cases, the entire capsule calcifies.

The wall of an echinococcal cyst consists of two layers: the outer cuticular (chitinous) layer and the inner germinal (germinal) layer. The cuticular membrane is an excretory product of the germinal membrane cells, similar in chemical nature to insect chitin. The membrane is impermeable to microflora and host proteins and functions as a semipermeable membrane, providing the parasite with access to low-molecular-weight nutrients and protecting the germinal membrane cells from the effects of adverse host factors [4, 5].

The germinal membrane, which performs all vital functions of the parasite, is divided into three zones: the parietal cambium, the middle zone of calcareous bodies, and the inner zone of

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brood capsules containing developing embryonic elements (protoscolices and acephalocysts). After maturation of the brood capsule, it ruptures, and the embryonic elements settle to the bottom of the cyst under the influence of gravity, forming so-called echinococcal sand. Because the cuticular and germinal membranes externally form a single capsule, they are collectively referred to in the literature as the chitinous membrane.

Between the fibrous capsule and the cuticular membrane, a microscopic gap remains, filled with lymph, from which the parasite obtains nutrients. Thus, the two membranes of the echinococcus are closely adjacent to each other but do not fuse, leaving a potential slit-like space that has a certain diagnostic value [6].

A threat to the life of the maternal cyst triggers the self-preservation mechanisms of the genus; secondary echinococcal cysts develop from the embryonic elements, and the germinal membrane undergoes endogenous or exogenous budding.

Fins (echinococci)—unilocular vesicles—originate from the oncospheres. Within a month, they reach 1 mm in diameter. After a year, the size of individual echinococcal cysts varies from 2–3 to 20–30 mm and depends on the pliability of the affected organ and the condition of the parasite itself. The average growth rate of parasitic vesicles is 1–3 cm per year [7].

Hydatid cysts can be localized in any part of the liver. However, the right lobe is most often affected (50–80% of cases), due to its larger size and wider portal vein branch, through which the parasite embryo enters. Invasion of the left lobe of the liver is observed in approximately 30% of cases, and both the right and left lobe together in 20–30% [3]. Parasitic cysts are usually solitary; multiple hydatidomas occur in approximately one-third of cases [8].

Diagnosis

Early diagnosis of the disease is often difficult due to the lack of clear symptoms, especially in the early stages when the cyst is located deep within the organ.

Laboratory tests for echinococcosis are nonspecific and provide only auxiliary information for confirming the diagnosis. This primarily applies to eosinophilia, which occurs in 18–83% of cases; some authors note an increase in the white blood cell count and total plasma protein levels characteristic of patients with echinococcosis. The lymphocyte count is usually reduced, while the levels of all immunoglobulin classes are elevated. Interestingly, most patients have blood type III (B). Immunological methods are of great, if not decisive, importance in the diagnosis of echinococcosis. The Casoni reaction, one of the first immunological tests, which was widely used until recently, has lost its relevance due to its limited information content and the risk of anaphylactic reactions, which can be quite severe. In recent years, the latex agglutination test (LAT), indirect hemagglutination assay (IHA), and enzyme-linked immunosorbent assay (ELISA) have been considered the most informative. They have virtually no contraindications and are used to detect echinococcosis and relapses through repeated administration. When several immunoassays are used simultaneously, their diagnostic efficacy exceeds 80%. However, the presence of an echinococcal cyst should initially be suspected, and only then will the physician refer the patient for specific tests.

Patients often seek medical attention when the parasitic cyst has reached a significant size or complications have developed (suppuration, rupture into the bile ducts, abdominal or pleural cavity, etc.). In most cases, a routine ultrasound examination reveals a single-cavity anechoic

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or hypoechoic lesion with clear, smooth walls and a symptom of distal echo enhancement. However, such an ultrasound image is associated with a simple liver cyst, while a typical ultrasound image of an echinococcal cyst is associated with a multilocular fluid-filled lesion. In reality, a living echinococcal cyst is a single-chamber fluid-filled lesion, and the development of additional cysts indicates problems with the underlying cyst. For this reason, the detection of a fluid lesion during an initial ultrasound examination should raise alarm, and it's best to use this as a training aid.

In light of the above, visual diagnostic methods, primarily ultrasound, are particularly relevant. This method allows for the diagnosis of small parasitic cysts, allowing for more frequent, more cost-saving interventions. Modern ultrasound machines with high resolution, color Doppler mapping, and the ability to perform 3D reconstruction of the ultrasound image allow specialists to detect the cyst itself and evaluate its characteristic features.

An echinococcal cyst with a hypo- or anechoic structure is characterized by a multilayered wall. The chitinous membrane is defined as a hyperechoic structure, often with a hypoechoic layer between the germinal and cuticular layers. Multiple hyperechoic inclusions—echinococcal sand—are often visible on the inner surface of the chitinous membrane. The fibrous capsule appears as a hyperechoic rim on ultrasound. It is separated from the chitinous membrane by a hypoechoic layer, which represents the lymphatic cleft.

Duplex scanning does not detect blood flow in the capsule of the echinococcal cyst or in the walls of the daughter cysts. Three-dimensional reconstruction of the ultrasound image of the echinococcal cyst allows for more precise differentiation of its wall layers.

Detachment of the chitinous membrane is evidence of the death of the parent cyst. On ultrasound imaging, it is visualized as a band-like structure of increased density within the cyst lumen. The presence of additional cystic inclusions (daughter cysts) is characteristic only of echinococcal cysts. A diagnosis of echinococcosis is confirmed by a combination of three characteristics.

Ultrasound is one of the most promising diagnostic methods for liver echinococcosis (in combination with serological tests for echinococcosis), allowing for a diagnosis in most cases. However, false-negative serological test results, observed in more than 10-20% of patients, and difficulties in differential diagnosis of small cysts and their pseudotumor forms using ultrasound often lead to delayed diagnosis and unsatisfactory treatment results [9, 10].

To clarify the nature of the disease and differentiate between parasitic and non-parasitic cysts, computed tomography (CT) and magnetic resonance imaging (MRI) are advisable. In the presence of giant echinococcal cysts and multiple lesions, interpreting ultrasound results is difficult. In these cases, it is necessary to combine ultrasound with CT or MRI.

Densitometric values obtained during CT scanning of echinococcal cysts vary in large cysts, ranging from 10-25 units. H (for an echinococcal cyst and 0-15 H units for a non-parasitic cyst. This allows us to distinguish echinococcal cysts from non-parasitic ones and polycystic liver disease even in the absence of other differential diagnostic features.

The density of the contents of an echinococcal cyst increases significantly (20 H units) after the death of the parasite [11]. A double-contour wall is possible. CT allows us to determine the thickness of the fibrous capsule and the presence of calcification in it, to identify areas of capsule destruction, and sometimes the exit of daughter cysts beyond its limits (Fig. 3c). However, CT data cannot always accurately diagnose. Thus, E.S. Belyshev et al. note that in the pseudo-solid form of echinococcosis with perifocal inflammation, determining the

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echinococcal nature using CT is difficult. The CT image can be assessed as a liver tumor or abscess [10]. False-negative diagnostics are caused by the small size of the lesions or the isodense nature of the lesions and normal organ parenchyma [12].

With a diameter of 60 mm, the cyst wall is poorly defined (indicative of young age), which makes differential diagnosis extremely difficult. Our experience shows that MRI is highly informative in diagnosing echinococcal cysts, even at small sizes. One of the most important advantages of MRI is the absence of radiation exposure, which, along with ultrasound, makes the method indispensable for use in pediatric surgery.

By obtaining a clear image and a picture of the relationship with large vascular and ductal structures of the liver, surrounding organs and tissues, it is possible to plan the type of surgical intervention.

When performing MRI, echinococcal cysts are characterized by the presence of pronounced hypointensity (T1-weighted image - VI) and hyperintensity (T2-WI) signals. Septa in the cyst lumen, the walls of daughter and granddaughter Cysts have a hypointense signal. The chitinous cyst membrane is also characterized by the presence of a hypointense signal on T1- and T2-weighted images. The difference in hypointensity between the fibrous capsule and the parasite's chitinous membrane creates a two-layer image of the cyst wall on tomograms. Linear areas of decreased signal intensity in the lumen are characteristic of a dead cyst and represent exfoliated chitinous membrane. Calcifications in the cyst wall are defined as areas of absent MR signal, i.e., as dark areas in the walls with low or very low signal intensity. The separation of small cysts from the main lesion appears as a peripheral increase in signal on T2-weighted images and in the STIR sequence and reflects disease activity [10].

The use of MRI in various modes improves the effectiveness of differential diagnosis of parasitic diseases with a wide range of primary and secondary focal liver lesions. MRI is also highly helpful in determining the organ of origin of small cysts. It can reveal the double-contour structure of the membrane, divided into chitinous and fibrous layers, as well as the presence of daughter cysts.

Echinococcal cysts are always rounded, due to their active life, leading to increased pressure within the cyst cavity. This causes weak spots in the fibrous capsule surrounding the cyst. On MRI images, these appear as inlets protruding into the surrounding liver parenchyma. This feature contributes to the development of a number of complications associated with echinococcal cysts.

Increasing cyst size leads to atrophy of the surrounding parenchyma and an increased risk of bile duct defects. MRI cholangiopancreatography (MP) allows for the detection of a biliary fistula with a high degree of certainty (which is important for planning and implementing minimally invasive treatment methods).

Difficulties in differential diagnosis, especially with small cysts, require obtaining material for morphological confirmation of the diagnosis. However, percutaneous diagnostic punctures for suspected echinococcosis were considered contraindicated until recently due to the risk of seeding the puncture channel and abdominal cavity with parasite germs.

The development of a strategy, a technique for performing safe percutaneous interventions, and the creation of specialized instrumentation that prevents complications have facilitated the widespread adoption of surgically conservative treatment for echinococcosis in everyday practice. Currently, extensive experience (over 300 cases, according to some authors) in performing percutaneous interventions for the treatment of liver echinococcosis has been

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accumulated worldwide. The first percutaneous puncture-drainage interventions for echinococcosis of the liver in Russia were successfully performed in 1986 by A.N. Lotov at the clinic of the 1st Moscow Medical Institute named after I.M. Sechenov and, independently, by A.V. Gavrilin at the A.V. Vishnevsky Institute of Surgery of the Russian Academy of Medical Sciences.

However, despite the apparent simplicity of percutaneous interventions, their implementation in the absence of experience and specialized equipment is fraught with the risk of severe intra- and postoperative complications, including death during the procedure. Severe anaphylactic reactions and even several cases of death during puncture of echinococcosis cysts have been described in the medical literature. However, the authors acknowledge that the complications and fatalities were due to improper technique. Currently, the use of targeted percutaneous punctures of echinococcosis cysts for differential diagnosis in specialized medical institutions is recognized. Their safety has been proven when the procedure is performed professionally and with strict adherence to the procedure.

Treatment

Traditional surgical interventions are still considered the "gold standard" for treating echinococcosis. Most commonly used are various types of echinococcectomy (closed and semi-closed) with partial excision of the fibrous capsule. Pericystectomy (complete excision of the cyst with its fibrous capsule) is considered more traumatic. Many advocate organ resection or removal of the cyst and its contents, but the parasitic nature of the disease and the real risk of recurrence should be kept in mind. These surgeries are performed through a wide, often combined, surgical approach. They are associated with a high risk of intra- and postoperative complications and patient disability. In most cases, formalin and hypertonic sodium chloride solutions are used as germicides. However, despite improvements in surgical techniques, surgical flexibility, and the introduction of various chemical and physical methods of parasite control, the recurrence rate remains high, reaching 12–33%. Repeated surgical interventions in the event of a relapse are considered even more traumatic. Furthermore, echinococcal cysts are subsequently detected in almost every second patient. The high rate of relapses has necessitated further experimental studies to determine their causes.

There are two known types of germinal elements of echinococcal cysts: protoscolices and acephalocysts. Protoscolices were considered of primary importance in the recurrence of the disease: the effectiveness of germicides was determined by their effect on them. This is likely due to the fact that the germinal elements of the cyst are predominantly represented by protoscolices and are easily detected by microscopy. Acephalocysts in the cyst are usually single and often undetectable; their role has remained unclear until recently.

In the course of experimental studies by F.P. Kovalenko [13], it was established that echinococcal protoscolices die within almost one minute of exposure to chemical agents. Acephalocysts, whose presence had previously been overlooked, were extremely resistant. Furthermore, germicides widely used in echinococcosis surgery—formaldehyde and 10–20% sodium chloride solutions—proved ineffective, failing to kill acephalocysts even after exposure for 10–15 minutes. Extended exposure (especially to formalin) increases the toxic effect of the drug on the human body. Subsequent studies demonstrated that in most cases, acephalocysts are the cause of relapse after surgery.

Also, the mass formation of microscopic acephalocysts from germ cells of the protoscolex stalk was observed for the first time. This means that under certain conditions, the number of

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acephalocysts in the cyst increases, which is undesirable and even dangerous, as it makes the cyst quite aggressive and resistant to germicides, and also increases the risk of relapse after treatment.

Another extremely important feature of the parasite was identified for the first time in humans: exogenous budding of the echinococcus, a pattern characteristic of alveococcosis. This indicates that the parasite has the capacity for infiltrative growth, albeit less pronounced than that of the alveococcus.

Thus, the protoscolices are the most vulnerable element of the parasite and cannot serve as a criterion for selecting germicides. Intraoperative treatment of hydatid cysts requires highly effective germicides that specifically target the acephalocysts of echinococcus, the most stable component and the most important factor in the occurrence of postoperative relapses.

The effects of various chemical agents on the parasite's germ cells, particularly the acephalocysts of hydatid echinococcus, have been studied in vitro and in laboratory animals. The most reliable and suitable for practical use were 80–100% glycerin and 30% sodium chloride solution (see table). However, the use of 30% sodium chloride solution is associated with the risk of dilution with tissue fluid to an ineffective concentration. Glycerin is active even at significant dilutions, guaranteeing its greater reliability.

The results of pathological studies showed that glycerin affects not only the germinal elements contained in the cyst, but even exogenous cysts located 10–15 mm from the fibrous capsule of the cyst. This indicated the possibility of using glycerin for exogenous budding of the parasite and for surgical interventions that do not involve removal of the fibrous capsule of the cyst.

Until the late 1980s, traditional surgical interventions were predominantly used in the treatment of patients with echinococcosis. The surgeon was forced to resort to an unsafe and highly invasive procedure even in the presence of a small (30–40 mm) solitary echinococcosis cyst deep within the organ parenchyma. This necessitated the development of new, gentler surgical techniques for echinococcosis. Minimally invasive interventions top the list. Today, this should be the cornerstone of echinococcosis surgery. All the prerequisites for this have been created by history, the work of our great predecessors, and the many years of effective results achieved by Russian and foreign surgeons armed with high-tech diagnostic and treatment methods.

The main objectives addressed by specialists in developing minimally invasive surgical techniques were the hermetically sealed removal of fluid, preventing its entry into the abdominal cavity and seeding, and antiparasitic treatment of the cyst, ensuring the destruction of all germinal elements of the echinococcus. These issues can be addressed through meticulous adherence to cyst puncture techniques and the treatment of the cavity and its contents with glycerin.

It should be noted that the instrument should be inserted into the cyst cavity with strict adherence to ablastic procedures. After aspiration of the hydatid fluid, the cyst is treated with glycerin in a volume equivalent to the evacuated fluid. During the technique development stage, intraoperative microscopic monitoring was performed in each case, which showed that a 7-minute exposure to glycerin was sufficient in all cases to kill the germinal elements of the echinococcus, preventing seeding and allowing further procedures. To remove the cyst's chitinous membrane, the puncture channel is dilated using specialized instruments, and the parasite's chitinous membrane, exfoliated during antiparasitic treatment, is defragmented and removed. Complete removal of the chitinous membrane is verified radiographically. If

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incomplete removal of the chitinous membrane or the presence of a cystobiliary fistula is suspected, an endoscope is inserted through a special sleeve into the cyst cavity. Under direct guidance, the remaining chitinous membrane is removed and, if necessary, the fistula opening is treated. The surgery concludes by leaving a thin safety drain in the cyst for subsequent sclerotherapy of the residual cavity. Defragmentation of the membrane is performed using a guidewire and creating turbulent flow within the cyst by quickly injecting saline with a 20-gram syringe into the thin drain and simultaneously removing it through the thick drain along with fragments of the chitinous membrane.

Laparoscopic methods are used primarily for extraparenchymal cysts. It should be emphasized that single-stage laparoscopic echinococcectomy is highly dangerous. The use of various attachments and vacuum cups on the laparoscopic instrument does not ensure a complete seal during hydatid fluid aspiration. This can lead to parasite germ cells entering the abdominal cavity and carries a high risk of intraoperative complications and postoperative recurrence. Therefore, the operation should be performed only after obtaining objective evidence of complete destruction of the parasite germ cells, obtained during cyst puncture and antiparasitic fenestration of a nonparasitic liver cyst.

Surgical tactics for pulmonary echinococcal cysts differ, as the cysts often communicate with the bronchus. In this situation, it is advisable to perform surgery through a mini-thoracotomy approach, with video support if necessary, allowing for gentle (minimally invasive) interventions.

The use of minimally invasive techniques also improves treatment effectiveness in the most severe category of patients with combined echinococcosis. Surgery for the complicated cyst should be performed initially. Clinics have already accumulated experience treating patients with combined echinococcosis with extensive lesions of the lungs, liver, spleen, heart, and brain. A comprehensive approach using minimally invasive surgeries in this group of patients is even more justified, as it allows, in most cases, to avoid highly invasive combined surgeries.

Many authors recommend removing the chitinous cyst membrane when treating patients with echinococcosis. With open, laparoscopic, or thoracoscopic surgery, this presents no significant difficulties. With percutaneous procedures, removal of the chitinous membrane is associated with technical difficulties, especially for cysts measuring 40–50 mm. However, treatment with glycerin minimizes the risk of recurrence and, in addition to the destruction of the cyst's germinal elements, leads to the destruction of the germinal layer of the chitinous membrane. This is confirmed by the results of experimental and pathological studies, which have demonstrated that leaving the chitinous membrane in the cavity of a cyst pre-treated with a germicide is entirely acceptable. Therefore, with small cysts, there is no need to expand the scope of the procedure to remove the membrane. Experience has shown that it subsequently undergoes calcification. The use of germicides, adherence to ablastic procedures during surgery, and the use of sophisticated instrumentation do not completely eliminate the possibility of recurrence. Subsequent chemotherapy (CT) significantly affects treatment outcomes. It is also necessary to treat small echinococcal lesions that are inaccessible to modern diagnostic methods. Albendazole is the most effective drug against hydatid echinococcus. In recent years, this drug has become increasingly popular, as well as a standalone treatment for cysts <30 mm in size. Albendazole is particularly effective against pulmonary echinococcosis.

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Cumulative experience using minimally invasive surgical techniques for the treatment of echinococcosis in more than 350 patients significantly (more than 5-fold) reduced the incidence of complications; no fatal outcomes were recorded. Inpatient stays did not exceed 2 weeks. Postoperative chemotherapy is considered mandatory to prevent recurrence. The experience of most authors shows that chemotherapy virtually minimizes (<1% of cases) the risk of disease recurrence, provided all identified cysts are removed. The use of anti-relapse chemotherapy after surgery (regardless of the type of procedure) reduced the recurrence rate from 18.8% to 0.5%. Follow-up periods ranged from 3 to 32 years.

Conclusion

As is known, patients with echinococcosis are subject to dynamic observation after treatment. Before the introduction of chemotherapy, the observation period was 5 years. In recent years, due to the use of postoperative chemotherapy, the follow-up period may be reduced. The criterion for removing a patient from dispensary observation is a decrease in serological reaction titers to questionable levels or a negative test result. Typically, these periods do not exceed 1–1.5 years after surgical treatment, provided that full courses of chemotherapy have been administered.

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