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The authors declare that they have no conflicts of interest

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TREATMENT OF INOPERABLE LIVER ALVEOCOCCOSIS

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Abstract

A systematic review of the publication, on the topic of diagnosis and treatment of inoperable alveolar echinococcosis of the liver over the past 30 years, to study the effectiveness of various methods of treatment of inoperable alveococcosis of the liver.

We conducted a systematic search of literary data and selected sources from Google Scholar, PubMed, as well as research papers and online educational publications in English and Russian.

Our literature review included 120 papers in which, according to the authors with inoperable liver alveococcosis, 883 patients were described, out of 120 articles: 29 full articles, 23 literary reviews, 68 clinical cases described. The authors of the articles were from various countries, such as Turkey (26%), France (24%), Germany (20%), China (18%), England (6%), Japan (5%) and other countries in Europe and Asia.

Бауырдың ота жасауға келмейтін альвеококкозын емдеу

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Мүдделер қақтығысы:
Авторлар мүдделер қақтығысының жоқтығын мәлімдейді

Тұжырым

Соңғы 30 жылдағы бауырдың отаға жасауға келмейтін альвеолярлы эхинококкозын анықтау және емдеу тақырыбындағы басылымға жүйелі шолу, ота жасауға келмейтін бауыр альвеококкозын емдеудің әртүрлі әдістерінің тиімділігін зерттеу.

Біз әдебиет деректерді жүйелі түрде іздестірдік және Google Scholar, PubMed дереккөздерін, сондай-ақ ағылшын және орыс тілдеріндегі зерттеу жұмыстары мен онлайн оқу басылымдарын таңдадық.

Біздің әдебиет шолуымызға 120 жұмыс енгізілді, онда жұмыс істемейтін бауыр альвеококкозы бар авторлардың мәліметтері бойынша 883 пациент сипатталған, 120 мақаланың ішінен: толық мақалалар - 29, әдеби шолулар – 23, клиникалық жағдайларды сипаттау-68. Мақала авторлары Түркия (26%), Франция (24%), Германия (20%), Қытай (18%), Англия (6%), Жапония (5%) және Еуропа мен Азияның басқа елдерінен болды.

Түйінді сөздер:
альвеококкоз, бауырдың ота жасауға келмейтін альвеококкозы, альбендазол, бауыр трансплантациясы

Лечение неоперабельного альвеококкоза печени

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Аннотация

Систематический обзор публикации, по теме диагностики и лечения неоперабельного альвеолярного эхинококкоза печени за последние 30 лет, изучить эффективность различных методов лечения неоперабельного альвеококкоза печени.

Мы провели систематический поиск литературных данных и отобрали источники из Google Scholar, PubMed, а также исследовательские работы и учебные онлайн-издания на английском и русском языках.

В наш литературный обзор было включено 120 работ, в которых по данным авторов с неоперабельным альвеококкозом печени было описано 883 пациентов, из 120 статей: полных статей - 29, литературных обзоров - 23, описанние клинических случаев – 68. Авторы статецй были из различных стран, таких как: Турция (26%), Франция (24%), Германия (20%), Китай (18%), Англия (6%), Япония (5%) и другие страны Европы и Азии..

Конфликт интересов:
Авторы заявляют об отсутствии конфликта интересов

Ключевые слова:
альвеококкоз, неоперабельный альвеококкоз печени, альбендазол, трансплантация печени

Introduction

Alveococcosis - (Latin Alveococcosis; alveolar echinococcosis, multicameral echinococcosis) – helminthiasis from the group of cestodoses. The disease is common in Switzerland, Turkey, Japan, France, Russia, Central Asian countries, northwestern Canada and Alaska [1]. Alveococcosis of the liver is a parasitic liver cancer, due to its infiltrative growth, the ability to metastasize, as well as the high frequency of relapses after surgical treatment [2, 3]. Liver infection caused by E. multilocularis (alveococcosis) is a particularly difficult clinical problem, since their biology mimics that of slow-growing cancers [3].

In alveoacoccosis of the liver, due to direct spread, the diaphragm, peritoneum, hepatoduodenal ligament, pericardial sac, pleura, lungs, adrenal glands, kidneys, hepatic veins and inferior vena cava are most often affected. Distant metastases are usually localized in the lungs, brain, bones and spleen. Patients with alveococcosis of the liver may develop severe hepatobiliary complications, such as recurrent cholangitis, secondary biliary cirrhosis after prolonged cholestasis or Budd-Chiari syndrome [4-6].

Alveolar echinococcosis lesions are most often localized in the right lobe of the liver, and in advanced cases they germinate into large bile ducts and vascular structures (portal vein, hepatic veins and inferior vena cava), extensive liver surgery is often required with the risk of death as a result of uncontrolled bleeding or liver failure [7].

Due to infiltrating growth and the ability to metastasize, the course of the disease can be complicated by such complications as: the development of mechanical jaundice, portal hypertension, perforation of the decay cavity, germination into neighboring organs, ascites [2, 8-10]. Complications of the underlying disease, in turn, significantly limits the possibilities of treatment [11]. Extrahepatic localization of alveococcus is extremely rare, and damage to other organs in the presence of a focus in the liver is regarded as distant metastasis [12].

It should be noted that for the successful care of patients with alveococcosis in surgical hospitals, the following are important: a well-defined algorithm of diagnostic methods that determine the choice of surgical treatment tactics; classification that allows optimizing surgical treatment algorithms and routing of patients; a set of techniques for performing liver resections that make it possible to perform such operations in more patients and accordingly, reduce the proportion of patients requiring liver transplantation. Unfortunately, the diagnosis of alveococcosis is mainly established in the late stages of the disease with the manifestation of complications [3, 13, 15].

The epidemiological history includes the collection of information about the epidemiological environment, staying in endemic areas, food culture, and the profession of the patient. Most often, infection occurs when cutting carcasses, skins of infected animals, when non-compliance with the rules of personal hygiene and keeping animals (hunting dogs), when eating the liver of infected intermediate hosts [15-17].

Less often there are cases of infection when eating wild berries and herbs contaminated with animal feces. Also, risk factors include close contact with agricultural or domestic animals [15].

A group of WHO experts in 1996 proposed the classification of alveococcosis (PNM), which is currently used. It resembles the oncological classification (TNM) and allows a fairly objective assessment of the prevalence of a parasitic focus in the liver (P), taking into account the involvement of nearby organs (N) and the presence of distant metastases (M) [19, 20].

According to epidemiologic monitoring data from Europe and Asian countries, due to the asymptomatic course of the disease, at the time of diagnosis, more than 60-70% of patients are unresectable and it is impossible to perform radical surgery [21, 22].

Currently, WHO still recommends considering transplantation if all of the following signs are present: 1) severe hepatic insufficiency (secondary biliary cirrhosis or Budd-Chiari syndrome) or recurrent life-threatening cholangitis; 2) inability to perform radical liver resection; 3) absence of extrahepatic localization of alveococcosis. However, immunosuppression promotes the re-growth of larval remains and the formation or increase in the size of metastases [23]. Antiparasitic therapy should be administered orally at a dose of 10– l5 mg / kg / day, in 2 takes, with a fat-rich diet. In practice, adults are prescribed a daily dose of 800 mg divided into two takes for at least 2 years and follow these patients for at least 10 years [23].

According to various sources and authors, the

five-year survival rate after cytoreductive resection and liver transplantation was 40.0% and 66.7% [24, 25].

Continuous use of antiparasitic treatment in comparison with periodic administration of antiparasitic drugs according to the scheme can prevent the growth of metastases after liver transplantation, the survival rate after liver transplantation is 71% in 5 years, with a relapse-free survival rate of 58% [26]. Overall survival after liver transplantation is quite low: 85% after 1 year, 71% after 5 years and 49% after 10 years due to relapse of the disease [27].

A systematic review of the publication, on the topic of diagnosis and treatment of inoperable alveolar echinococcosis of the liver over the past 30 years, to study the effectiveness of various methods of treatment of inoperable alveococcosis of the liver.

We conducted a systematic search of literature data and selected sources from Google Scholar, PubMed, as well as research papers and online educational publications in English and Russian.

Inclusion criteria

We included sources that met our inclusion criteria: research papers in which studies were conducted in patients with inoperable liver alveococcosis. After reviewing a lot of literature reviews about Echinococcosismultilocularis, we can say that this topic is very relevant all over the world, but over the past 10 years there have been very few publications on inoperable liver alveococcosis, in connection with which we took sources for a period of more than 30 years.

We aspired to evaluate a sample from sources in which attention was paid to the treatment of this pathology in the late stages. We evaluated the articles in random order. Based on the key aspects. The data elements taken for this article included: study design, sampling method, number of patients and operations performed, determination of the result, randomized controlled trial.

Our literature review included 120 papers in which, according to the authors with inoperable liver alveococcosis, 883 patients were described, out of 120 articles: 29 full articles, 23 literary reviews, 68 clinical cases described. The authors of the articles were from various countries, such as Turkey (26%), France (24%), Germany (20%), China (18%), England (6%), Japan (5%) and other countries in Europe and Asia.

Classification

For the first time in 1996, a group of WHO experts proposed the classification of alveococcosis (PNM), which is currently used. It resembles the Oncological Classification (TNM). The PNM staging system for liver alveococcosis was proposed in 2006 by the European Network for Coordinated Surveillance of Liver Alveococcosis [20, 26].

According to this classification, surgical treatment is justified in the group of patients with peripheral or mono-lobar localization without involvement of the main vascular structures, P1N0M0 and P2N0M0, which indicate I-II stage of the disease, respectively. Patients with P3 and P4 with any N and M, who belong to the III and IV stages of the disease, due to the progression of the disease, radical surgery is not indicated (known as R0) [28].

According to the WHO classification, the following principles should be followed in the treatment of patients with liver alveococcosis (Table 1).

Table 1.
A stage-by-stage approach to the treatment of alveolar echinococcosis

WHO Classification	Operation (R0)	Pallia-tivecare	Drugth-erapy	Recommendations	
P1N0M0	++		+	Radical resection (R0) BMZ for 2 years PET / CT control	Maximum
				Radical resection (R0) BMZ for 3 months	Minimum
P2N0M0	++		+	Radical resection (R0) BMZ for 2 years	Maximum
				Radical resection (R0) BMZ for 3 months	Minimum
P3N0M0			+	BMZ continuously PET/CT/MRI initially and 2 years apart	Maximum
				BMZ continuously	Minimum
P3N1M0		++	+	BMZ continuously + PET/CT/MRI initially and 2 years apart	Maximum
				Surgical intervention ifindicated	Minimum
P4N0M0		++	+	BMZ continuously + PET/CT/MRI initially and at 2-year intervals	Maximum
				Surgical intervention ifindicated	Minimally
P4N1M1		++	+	BMZ continuously + PET / CT/MRI initially and at 2-year intervals	Maximum
				Surgical intervention ifindicated	minimally

Discussion

According to the above table, WHO recommends the management of patients with liver alveococcosis as follows:

1) Antiparasitic drugs are mandatory for all patients, temporarily after complete resection of lesions and for life in all other cases;

2) Minimally invasive treatments should be preferred over cytoreductive resection whenever possible;

3) Radical resection is the first choice in all cases where it is possible [22].

In our opinion, the above-mentioned WHO classification does not make it possible to determine the extent of liver damage, the presence of the prevalence of the process in the main vessels and bile ducts, an assessment of the state of the liver parenchyma, the volume of the presumed non-affected part of the liver, which affect the further tactics of treatment of patients.

Of course, this classification is not an alternative, but it is necessary to revise the classification in the future or possibly supplement it to determine the optimal tactics and routing of patients among medical institutions, which will certainly lead to an increase in the resectability and radicality of surgical interventions, and improve treatment results.

Drug treatment of inoperable liver alveococcosis

Long-term drug treatment with benzimidazolescan actually be considered as the basis for the complex treatment of human alveolar echinococcosis [29]. Mebendazole (MBZ), a benzimidazole derivative, was the first successfully used drug [30, 31].

Mebendazole (MBZ) is a highly effective broad-spectrum anthelmintic widely used for the treatment of nematode, cestode and even protozoal infections. After its use began in 1970, MBZ was the first drug in the BMZ group that was found to have a lethal effect on metacystodes in infected patients [32].

Mebendazole is insoluble in water, and therefore it is believed that the drug is not readily available for the treatment of liver alveococcosis in humans, since MBZ is absorbed at the intestinal level, reaching the liver there is very little active substance left. In this regard, it is believed that it is not inactive for the treatment of liver alveococcosis [33]. In patients with alveococcosis of the liver, MBZ should be prescribed for at least 2 years after radical surgery or permanently in inoperable cases, as well as in patients who have undergone incomplete resection or liver transplantation [29]. Long-term MBZ therapy is usually well tolerated, in some patients it has been used for more than 20 years [34].

However, from 5 to 40% of patients treated with MBZ with liver alveococcosis, adverse reactions were described [35-38]. In the treatment of patients, there were side effects such as gastrointestinal disorders, hair loss, neutropenia, anaphylactic reactions, glomerulonephritis, dizziness, headache, mental visibility, hematotoxic effects and abnormal serum transaminase levels, notably most of these reactions occurred during the first month of taking the drug [39, 40].

In recent years, few studies have been aimed at improving the chemotherapeutic activity of MBZ. This is largely due to the gradual replacement of MBZ with albendazole [47].

Albendazole (ABZ) is a derivative of BMZ with a wide spectrum of activity, including in helminthiasis and protozoal infections. First introduced for human use in 1982, ABZ has now replaced MBZ as the drug of choice for the treatment of E. multilocularis, mainly due to its improved bioavailability, superior efficacy, ease of administration and fewer undesirable effects [38, 44, 48, 49]. In addition, ABZ is 40% cheaper than MBZ [40].

Nevertheless, the availability and/or cost of ABZ continues to be a problem in many socio-economically disadvantaged countries and even in high-income countries [50].

Oral administration of ABZ is currently recommended at a dose of 10-15 mg per kg of body weight per day - in two takes for the treatment of E. multilocularis [29].

Brunetti E and his co-authors [29], at the consensus of WHO and the Informal Working Group on Echinococcosis, focused on the issue of continuous use of ABZ at a dose of 10-12 mg/kg/day. Serum levels of the drug should be measured at regular intervals. Toxic hepatitis, hematological diseases, alopecia may occur in a group of patients treated with ABZ, requiring regular further medical supervision [29]. ABZ should be prescribed for at least 2 years, and these patients should be monitored for at least 10 years for possible relapses [29].

Continuous antiparasitic treatment should not be interrupted because it can be dangerous due to the spread of the process and the frequency of relapses [48-50].

Since ABZ is currently considered a relatively safe drug, continuous therapy is preferable to schematic monthly receptions. Recent descriptive studies based on a series of cases have shown that the frequency of undesirable side effects associated with ABZ ranges from 3 to 5% [40,45,46], and some studies have not reported their absence [47]. The most frequently described adverse reactions were jaundice, severe headache, cough, hemoptysis, changes in serum transaminase levels, dizziness, hair loss and itching [40, 45, 46].

The healing effect of a patient with an inoperable lesion has not yet been established, but should include a negative PET/CT result, a calcified component of alveolar echinococcosis lesion of more than 50%, as well as the disappearance of specific antibodies [51, 52].

Also, in the treatment of liver alveococcosis, such drugs as broad-spectrum nitazoxanide [54, 55] and Thiazolides [53], or the antifungal drug amphotericin-B-deoxycholate [56, 57] were studied. Genistein and genistein derivatives are active

against metacestode in vitro [58].

The transition to clinical use was carried out only in relation to several drugs: conventional and liposomal amphotericin B was used as a life-saving treatment in several patients who did not tolerate ABZ [59]. Nitazoxanide, a broad-spectrum anti-infective drug, demonstrated remarkable efficacy in an experimental model [54], but could not demonstrate efficacy alone and in combination with ABZ or amphotericin B [60, 61].

The goal of treating inoperable liver alveococcosis with Albendazole is tumor regression, absence of disease progression, which is considered a success, since increasing formation can cause serious problems such as blockage or compression of the bile ducts, cholangitis, abscess, cirrhosis and portal hypertension [62].

Despite the successful long-term use of the drug, there are late complications, such as bleeding from varicose veins of the esophagus or cholestatic complications [31]. Hepatotoxicity and myelotoxicity are the most serious side effects of albendazole, discontinuation of treatment may be required in up to 4% of cases [29].

Long-term treatment with benzimidazole stabilizes the disease in 55-100% of patients [63]. A very important unique conclusion is that a noticeable regression of giant lesions (> 15 cm) is possible in 15-20% of patients with inoperable liver alveococcosis. Many clinical studies show that the correct treatment with albendazole is indicated in patients with inoperable liver alveococcosis, with the exception of patients with end-stage liver disease. For inoperable patients who are indicated for liver transplantation, some authors recommend taking antiparasitic therapy with benzimidazole before transplantation in 60-70% of cases [64, 65].

In conclusion, it should be noted that all patients with inoperable liver alveococcosis should be prescribed long-term treatment with albendazole. It may be reasonable to prepare a living donor for possible transplantation in the event of a severe complication, such as recurrent cholangitis, acute portal vein thrombosis or albendazole hepatotoxicity. Dilution may be a sign of a reaction to Albendazole. [66].

Some reports reported a 10-year survival rate of 80-90% of cases, which was achieved by improving conservative treatment with correction of complications during conservative treatment with minimally invasive methods [67, 68].

All inoperable patients with liver alveococcosis in the treatment of conservative therapy should be monitored by ultrasound, CT and/or MRI at intervals of 3-6months for the effectiveness or progression of the disease [29].

The availability of ABZ is hampered by limited distribution and increased cost not only in socially and economically disadvantaged areas, but also in a number of developed countries. In addition, this compound appears to have a parasitostatic rather than a parasitocidal effect, and there is no alternative drug for patients with E. multilocularis [70].

Minimally invasive methods of treatment of inoperable liver alveococcosis

Patients with inoperable liver alveococcosis and the presence of symptomatic complications: obstruction of the bile ducts, cholangitis and bacterial infection of the necrotic cavity, which develops in the foci of neglected lesions, symptomatic palliative treatment is used [71-73]. Non-surgical procedures, such as drainage of the biliary tract under ultrasound control or drainage of an abscess, were not performed until 1982 [74].With compression or germination of the formation into the bile ducts and the development of mechanical jaundice, with hepatic insufficiency, Percutaneous-transhepaticcholecystocholangiostomy or ERCP, EPST with endobiliary stenting is used to reduce biliary hypertension, hepatic insufficiency [76].

Percutaneous-transhepatic methods of decompression of the biliary tract

With compression of the biliary tract or the germination of liver alveococcosis, many complications develop for the patient, such as mechanical jaundice followed by liver failure, the development of cholangitis, which threaten the patient's life [76].

Percutaneous-transhepatic methods of decompression of the biliary tract are currently a mini-invasive first step in the treatment of patients with mechanical jaundice, cholangitis and liver failure. But there are also disadvantages of percutaneous-transhepatic methods of decompression of the biliary tract, as a rule, drainage is installed for a long time, and requires regular replacement to prevent obstruction. And also a big disadvantage of external drainage of the biliary tract is that it significantly contributed to the deterioration of the quality of life of patients [75].

Endoscopic methods

Endoscopic bile duct stenting currently almost completely replaces surgical palliative surgery and percutaneous drainage of the biliary tract for the treatment of biliary complications in patients with alveolar echinococcosis, as endoscopic dilation of bile duct strictures followed by the installation of several plastic stents provides internal drainage of bile into the patient's body [76].

A review of endoscopic procedures (ERCP) for the treatment of biliary complications of alveolar echinococcosis in several dozen clinical centers has shown that such procedures are currently used routinely and, as a rule, successfully alleviate symptoms and maintain long-term permeability of biliary strictures [75, 76].

Endoscopic bile duct stenting currently almost completely replaces surgical palliative surgery and percutaneous drainage of the biliary tract for the treatment of biliary complications in patients with alveolar echinococcosis. Although no specific studies have been conducted to assess the quality

of life of patients receiving such treatment, many authors suggest that this significantly contributed to improving the quality of life of patients with chronic biliary obstruction and multiple episodes of cholangitis [75].

Drainage of the decay cavity

Drainage of the decay cavity can be useful to reduce the risk of bacterial infection and relieve symptoms caused by large masses. A sharp regression with proper treatment with albendazole is possible in 15-20% of patients with inoperable liver tumors [74].Later, mini-invasive procedures were used to treat jaundice and abscess in patients with alveolar liver damage, and the average frequency of laparotomies per patient with cytoreductive surgery decreased from 2.8 to 1.4% [74].

After reviewing a lot of literature reviews, we did not find a lot of material about percutaneous drainage of the decay cavity for the treatment of patients with inoperable alveolar echinococcosis of the liver, perhaps in our opinion, when the decay cavity is drained and oxygen enters the alveococcus cavity, a possible death of the parasite metacystodes occurs. However, the evidence and conducted experiments on this fact are not described at the moment. We hope that in the near future, perhaps, some research will be carried out on this matter.

Cytoreductive liver resections in inoperable liver alveococcosis

Many authors describe that R1 resection led to a higher rate of disease progression than R0, and the frequency of complications associated with parasitism was similar to that observed only with benzimidazole therapy. Thus, surgery to remove R1 does not seem to offer any advantages over benzimidazole-only therapy in the treatment of alveolar echinococcosis, and it should be avoided [77].

At the time of diagnosis, the parasitic process in most cases passed into an incurable stage of the disease. On the one hand, it was recommended to perform resections, even if they are incomplete, in order to decompress bile ducts or remove the decay cavity [78]. The causes of incomplete resections were extensive liver damage, distant metastases or direct invasion into the vascular structures of the liver, vena cava and diaphragm or retroperitoneal space [79]. There are even cases of liver transplants that are considered cytoreductive due to non-radical removal of alveococcosis from the abdominal cavity or spread into the pleural cavity and lungs [80].

Many authors have reported a case of cytoreductive resection due to invasion of the vena cava and good long-term results in the early and late postoperative period [81]. With the appearance of a suppurated cavity and persistent septic status, not effective conservative treatment, the elimination of the parasitic focus is the principle of treatment, preferably by resection of R1 or even R2, if resection of R0 is impossible [82]. Thus, cytoreductive operations should be limited due to a variety of complications, such as: the risk of anesthetic benefits, the risk of uncontrolled bleeding, the risk of surgical infections and repeated operations and death [83].

Against this background, the value of cytoreductive operations in the data of many authors is considered doubtful [82]. In this connection, the frequency of cytoreductive resections began to decrease with the advent of mini-invasive and transplantation technologies [84].

In our opinion, during the surgical intervention, when the spread of the process into the surrounding tissues was detected and it was not possible to perform surgery in the amount of R0, cytoreductive resection was performed, or taking into account the development of various complications in the patient, the patient was prepared for cytoreductive resection to eliminate complications. Previously, cytoreductive surgery was considered the gold standard in the treatment of patients with inoperable liver alveococcosis. In our opinion, to date, mini-invasive methods with additional antiparasitic therapy have become the first link in the treatment of inoperable liver alveococcosis compared tocytoreductive surgery.

Transplantation methods

Liver transplantation, the most extensive liver resection, has been proposed as an alternative approach for unresectable alveolar echinococcal liver [85]. To date, various authors have reported about 100 liver transplants. [86-91]. Despite the negative picture of E. multilocularis infection, liver transplantation was associated with excellent long-term results, characterized by a 5-year survival rate of 85% [92].

Thus, the presented data seem to convincingly confirm liver transplantation as a surgical method of treating individual patients with unresectable alveolar echinococcosis of the liver. It is noteworthy that the results presented by other authors also confirm its effectiveness. A multicenter European-based study conducted by Koch and his co-authors reported a 5-year survival rate of 71% [93]. Similarly, in another transplant center, a corresponding 5-year survival rate of 77.8% was reported by Aydinli and his co-authors in a recent analysis of the results [94].

Autotransplantation

Due to the shortage of donor organs, an ex-vivo method was developed with subsequent autotransplantation of liver segments free of alveococcosis. This method, developed by Rudolf Pichlmayr and his team in Germany for the treatment of “inoperable” liver tumors in the 1990s, this method may represent itself as an alternative to liver allotransplantation in liver alveococcosis, especially interesting for such a chronic tumor-like infectious disease, extremely sensitive to immunosuppressive therapy [95, 96].

To date, liver allotransplantation is still used in advanced cases, especially when hepatic veins and vena cava are included in the parasitic lesion, when life-threatening complications occur, but a

shortage of donors and lifelong administration of immunosuppressants, accompanied by increased susceptibility to disease recurrence, prevented the use of this approach [97].

Allotransplantation

The high level of postoperative morbidity and mortality (30% during the first 6 months after transplantation), as well as the frequency of relapses (10% local and 20% with distant metastases) raise an ethical question, especially when the liver is obtained from living donors [98].

Liver allotransplantation, initiated for the treatment of liver alveococcosis in the mid-1980s, is associated with the risk of recurrence or progression of extrahepatic lesions of alveococcosis, especially brain metastases, due to suppression of immunity [99, 100].

In Europe, in addition to the recommendations of the Expert Consensus 2010, the shortage of donors, as well as the tendency to promote ABZ treatment in combination with minimally invasive methods of treatment in cases with advanced liver alveococcosis, contributed to a decrease in the number of patients-candidates for liver allotransplantation [101,102].

Contrary to this attitude, the beginning of the 21st century was marked by the publication of several clinical cases and a series of patients with liver alveococcosis who received liver allotransplantation, including transplantation from a living donor, from China, Turkey and the USA [103-114]. Carrying out liver transplantation against the international recommendation may be due to the clinical conditions of patients in these countries, due to late diagnosis in very advanced and complex cases, as was observed in Western Europe in the early 1980s. Earlier diagnosis, a reduction in the number of palliative surgeries, improved management of ABZ and non-surgical interventions and, possibly, resection ex vivo plus autotransplantation are likely to contribute to a reduction in the number of liver allotransplantations in alveococcosis in the future. The overall results suggest that liver transplantation should remain a "life-saving therapy" in very advanced cases.

Liver transplantation from a posthumous donor may benefit patients with progressive liver failure, with Budd-Chiari parasitic syndrome or when resection methods are exhausted, as well as patients with end-stage functional disorders caused by secondary biliary cirrhosis, secondary sclerosing cholangitis and postnecrotic cirrhosis [115-119].

Conclusion

The management of patients with inoperable liver alveococcosis requires an individual approach to each patient. Accurate diagnosis plays an important role in determining treatment tactics and affects the outcome of the disease. Various methods of basic (resection of the liver R0 and liver transplantation), mini-invasive (PTBD, ERCP, drainage of the decay cavity), drug (antiparasitic) treatment are used only for certain indications, with the right treatment tactics, good long-term results can be obtained. Liver transplantation is the last treatment option for patients with inoperable liver alveococcosis with severe hepatic cell insufficiency, portal hypertension with signs of bleeding from varicose veins of the stomach and esophagus, and intolerance to antiparasitic therapy.

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