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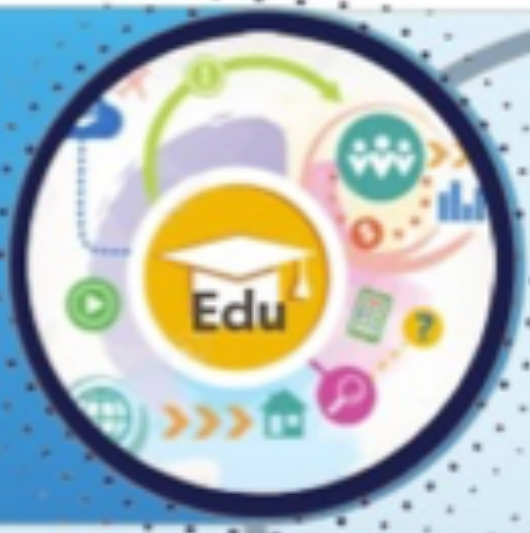

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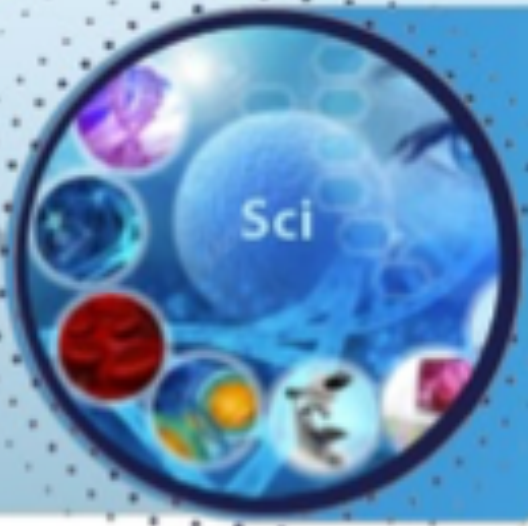

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Review Article

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Current State of the Problem of Studying the Clinical and Immunological Aspects of Hydatidosis Echinococcosis of the Liver

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ABSTRACT

Echinococcosis of the liver is still considered to be the predominant disease in developing countries, which, according to the World Health Organization, can affect up to 5% of the population, and up to 9.3% in highly endemic areas. The regions of Uzbekistan, especially the southern regions, such as Bukhara, Navoi, Kashkadarya and Surkhandarya, are among the regions in which statistical information on the prevalence of this disease is always in the leading positions. In recent years, information on the prevalence of echinococcosis of the liver has been increasingly found in European scientific publications. This circumstance is associated with a large flow of migrants from Asian regions. This, in turn, increases the urgency of the problem of diagnosing and treating hydatidosis echinococcosis of the liver by doctors in countries that were considered far from endemic areas affected by this disease. This paper presents in a review format the main literature data on the clinical and immunological aspects of hydatidosis echinococcosis of the liver

Keywords: hydatid echinococcosis of the liver, clinical manifestation, immunological changes

PART 1.

CLINICAL ASPECTS OF HYDATIDOSIS ECHINOCOCCOSIS OF THE LIVER

The clinical aspects and circumstances of detection vary greatly. The disease occurs mainly in the liver and lungs.

Although the disease is often benign, the mortality rate is not insignificant and the incidence is still high.

The initial stage of infection is always asymptomatic. Cysts can increase in size from 1 to 5 cm per year.

The liver is most often affected (50-70%). In 25% of cases, the lungs are affected in addition to the rest of the organs, including: the brain, kidneys, bones, heart, and pancreas.

The cyst is solitary in 65% of patients, double in 15-20%, and multiple in 10-35% of cases.

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There is either primary inoculation or secondary contamination due to cyst rupture and dissemination of daughter vesicles. [1]

Symptoms such as right upper quadrant pain, nausea, vomiting, or fever may occur depending on the size of the liver cyst and possible compression of adjacent organs.

The high incidence of asymptomatic hydatidosis echinococcosis of the liver indicates good tolerability of damage to this organ in parasitic infection.

The cyst is often not clinically manifested, it is latent for many years as it is quite well encapsulated.

When diagnosed, a liver cyst may be calcified (in 30-60% of cases).

Thin calcification can be found in active cysts, while complete calcification is a sign of parasitic death.

When developing, the cyst may compress the surrounding tissues without any clinical manifestation or with a progressive sensation of tightness or heaviness of the right upper quadrant, dyspepsia, fullness.

When the cyst is very large, palpation of the abdomen usually reveals hepatomegaly, a painless swelling that deforms the abdominal wall.

Complications occur in 20-40% of hospitalized patients with echinococcal liver cysts.

Three types of complications have been described: mechanical, systemic, and purulent-septic. [2, 3]

Mechanical complications can be categorized into adjacent compressions and ruptures. Compression of surrounding organs can lead to cholangitis or compression of the veins (hepatic, portal, vena cava), leading to portal hypertension and, in some cases, the rare Budd-Chiari syndrome.

A cyst can also lead to a rupture, which can be communicated or localized. A rupture can be localized when the endocyst breaks down without any fluid flow. In contrast, a rupture is reported when a fistula develops between the cyst and the biliary tract (leading to cholangitis), pancreatic ducts (leading to pancreatitis), adjacent veins, digestive lumen, or lungs.

Diagnosing a ruptured cyst is not easy because the symptoms are nonspecific and polymorphic. Abdominal pain seems to be constant (92-100%). In a series of 83 cases (13), hepatomegaly (75%), fever (34%), jaundice (8%), and pruritus (7%) predominate clinical manifestations. [4]

Biliary fistulas are the most common complications of echinococcal liver disease (40-60% of complications).

Liver cysts can rupture into the peritoneum (leading to secondary peritonitis) or into the pleural cavity (leading to pulmonary or pleural hydatidosis).

After intraperitoneal rupture of an echinococcal cyst of the liver, the mortality rate increases to 6%, and the incidence ranges from 20% to 35%. These rates are even higher in elderly patients with poor performance and comorbidities.

The estimated incidence of bronchial fistulas secondary to lung cysts ranges from 2 to 11%.

Cyst rupture can lead to mechanical complications as well as systemic reactions. These complications are rare (1%). The patient will complain of fever, chills, tachycardia, and shortness of breath due to anaphylaxis. This is due to the release of antigenic material and secondary immune reactions. It can appear both suddenly, against the background of a traumatic cyst rupture, and less often spontaneously. It can also occur more chronically when the fluid contents of the cyst slowly spill out into the bloodstream. [5, 6]

The clinical picture is more often benign and is associated with pruritus, urticaria, lymphedema, and bronchospasm.

These events can be severe, causing death within hours from anaphylactic shock as a result of the IgE-dependent hypersensitivity phenomenon type I. [7]

Liver abscesses can be caused by infection of the contents of the cyst. It is either secondary to the cyst fissure or secondary to the hematogenous infection. A recent study described the clinical and microbiological characteristics of superinfected echinococcal cysts. In this cohort, 7.3% of the 503 patients had a superinfected cyst.

Finally, 55.5% of super-infected cysts were of the CE2 type (according to the WHO classification). This result supports the theory that larval viability does not preclude cystic superinfection. [8]

There is no clear information on the viability of the parasitic cyst in bacterial superinfection. Manterola et al. found that fluid studies showed the nonviability of scolex in this type of cyst. [9]

Moreover, traditionally, this condition has been treated with simple drainage. But the same team also reports that cystostomy and drainage are usually associated with poor postoperative development with the formation of a residual cavity. This finding supports the theory that superinfection is not able to permanently kill the parasite.

Manterola et al. recommended a more aggressive procedure to achieve cure for super-infected cysts. [10]

The procedure consisted of surgical drainage, extirpation of the parasitic material, and resection of the peristal membrane with the surrounding healthy liver parenchyma.

Diagnostic tests are a combination of serology and imaging.

Routine laboratory examination may reveal eosinophilia and abnormal liver function tests. But all these laboratory abnormalities are non-specific for echinococcosis of the liver.

Imaging techniques are commonly used to detect cysts and characterize them in order to differentiate whether they are active or inactive in order to decide on the best therapeutic method.

Imaging is commonly used to visualize an echinococcal cyst and its components. These methods are precise and, when used together, often allow for a definitive diagnosis. They can also assess the presence and type of complication. [11]

Ultrasound is a first-line examination, as it has already been proven that with this imaging method, its sensitivity in detecting a cyst is 90-95%. [12]

The most common manifestation is a smooth, anechoic round cyst. When there are many membranes or daughter cysts, mixed signals or internal septa appear on ultrasound, which can be confused with an abscess or neoplasm.

To date, the most used classification is the Gharbi classification, which describes five stages of ultrasound examination. [13-15]

Ultrasound can be classified as active, transient, or inactive.

The presence of a cleft wall fluid accumulation (exfoliated laminated membrane) defines type II in the Gharbi classification and CE3a in the World Health Organization classification.

In addition, it divides CE3 into CE3a (detached endocyst) and CE3b (predominantly solid with daughter vesicles), which has influenced the choice of treatments. [16]

The appearance of the cyst on imaging depends on its stage of maturation.

X-rays of the abdominal organs are performed while standing. This examination can only detect the elevation of the diaphragm or the presence of calcification of the cyst.

In contrast, computed tomography has a higher sensitivity of up to 95%. It helps determine the size, number, and location of cysts. It shows extrahepatic cysts better than ultrasound. Computed tomography can also monitor the response to treatment and detect recurrences.

There is no doubt that computed tomography is much more effective than ultrasound, especially in detecting calcifications and complications such as rupture and peritonitis, and also provides a better study of anatomy. [17]

For these purposes, it is recommended to perform computed tomography using contrasts that are injected intravenously.

A typical image (Type I in the Garbi classification) shows a fluid density close to zero Hounsfield unit when it is homogeneous. On computed tomography, echinococcal cysts are hypodent compared to a normal liver. They are well bounded and are usually surrounded by a thick wall visible at different sites before and after injection. Thin calcifications are visible in 50% of cases.

Computed tomography also shows various stages (which are well described by ultrasound): abruption of the membrane, daughter vesicles, "rosettes", heterogeneous component. The membranes floating in the echinococcal fluid are pathognomonic.

In type 4 cysts (solid masses), hypervascularity of the internal component is never manifested, and if it is present, this sign excludes the diagnosis of echinococcosis of the liver.

Magnetic resonance imaging has no significant advantages over computed tomography, except for the examination of the intrahepatic and extrahepatic biliary tracts, inactive communications, and the examination of the vessels of the portal system.

The presence of bile in the internal component of the cyst can be detected by magnetic resonance cholangiography. [18, 19]

The latter is considered sensitive to the detection of such an anomaly, but unfortunately is not specific.

Monitoring the cyst using imaging techniques is considered an important aspect of assessing the course of the disease. [20]

Visualization of echinococcosis of the liver, in order to detect it, is one of the main components in the diagnosis of the disease. However, in recent years, due to the introduction of conservative treatment methods, these imaging methods have also shown their effectiveness in monitoring cysts.

The presence of a fluid-liquid level in a type II cyst (biliary reflux), dilation of the bile ducts, the presence of echinococcal material in the bile ducts, or cyst collapse are indicative of a biliary-cystic relationship. Under these conditions, the hyperintensity of the T1 cyst on magnetic resonance imaging is a clear sign of biliary communication. Such abnormalities can also be detected using magnetic resonance cholangiography.

The inactive form of the cyst can be judged by the collapse, disappearance of the innercept, calcification of the cystic wall, and detachment of the germ layer from the cyst wall.

Endocystic detachment from pericysta is likely due to decreased intracystic pressure, degeneration associated with host response, trauma, or response to therapy. [21, 22]

This sign can be used as a marker of cyst activity.

Many researchers often cite the importance of eosinophilia as the main laboratory diagnostic marker of echinococcosis of the liver. However, as the results of the researchers show, these arguments can be recognized as indirect.

Eosinophilia accompanies the invasive phase and disappears rapidly. Sometimes it persists (in 7-15% of cases) at a moderate level, and it may reappear when the cyst is damaged.

However, as direct arguments, it is possible to present information about other tests related to changes in the immunological response of the body.

Serological tests detect specific antibodies against E. granulosus. [23]

Qualitative immunodiagnostics are useful in making the initial diagnosis, while quantitative titers can be useful in verifying the effectiveness of treatment.

Detection of antibodies in blood serum is the method of choice. Serological testing should be performed systematically if the diagnosis is suspected, but its diagnostic accuracy is imperfect, with about 10% of false-negative and the same number of false-positive results in liver involvement. Liver cysts have a positive serological result in 85-95% of cases.

Tests that can be false positives have been found in other helminth infections, cancer, or immune disorders. [24]

False-negative tests have been found in children, pregnant women, and rarely due to humoral immunodeficiency. A negative serology does not rule out echinococcal infection. There is no correlation between the number and/or size of the cyst and the size (titer) of the serology. In contrast, if the cyst is calcified or inactive, serology is less likely to be positive.

A raw antigen, such as hydatidfluid or proctoscolex extracts, is used to perform tests based on the antigen/antibody interaction.

A distinction is made between qualitative and quantitative methods of serological diagnosis.

Immunoelectrophoresis and electrosyneresis are the most common qualitative methods for serological diagnosis of hepatic echinococcosis. These reactions aim to establish contact between the purified antigen and the patient's serum. In the immunoelectrophoresis method, antigens and antibodies create different precipitation arcs (from 1 to 15) when they meet. The arc-5 test has achieved higher accuracy for diagnosis: specificity is excellent (above 90%), but sensitivity is insufficient (less than 80%).

Quantitative methods typically include indirect hemagglutination, indirect immunofluorescence, and especially immunoassays (enzyme-linked immunosorbent assay) using purified antigen (fraction 5). [25]

These tests are based on reactions using gradually diluted serum to quantify the antibody titer. They have good specificity and excellent sensitivity. When combining the two methods, qualitative and quantitative, the sensitivity and specificity reached 90% and 95%, respectively. [26, 27]

Serological analysis allows you to monitor the effectiveness of conservative treatment. There is often an increase in antibody levels (even if they were initially negative) 6 weeks after surgical resection. After that, there is a slow decline until the negativity manifests itself between 1 and 5 years. This monitoring can also be used during conservative therapy. In secondary echinococcosis, there may be a rapid increase in the frequency of antibodies.

Aspiration of the cyst for the purpose of direct parasitological diagnosis is not usually performed in clinical practice. It is only indicated if serology and imaging are inconclusive. This method allows microscopic confirmation of the presence of proctoscolics, hooks or membranes. Active cysts will have watery fluids with increased pressure, while inactive cysts will have cloudy fluid with low pressure. The risk of spillage and anaphylaxis is minimized by prescribing benzimidazoles (mainly albendazole) before performing an ultrasound-guided procedure or computed tomography. [28]

Polymerase chain reaction techniques for fluid aspiration are increasingly accepted as an additional diagnostic tool for echinococcosis. It was designed to detect the nucleic acids of E. multilocularis and E. granulosus in biological samples. Polymerase chain reaction is most commonly applied to drainage material and biopsy specimens when serological methods are negative and/or contradictory. [29]

PART 2.

IMMUNOLOGICAL ASPECTS IN THE DEVELOPMENT OF ECHINOCOCCOSIS OF THE LIVER

As already indicated in the previous paragraph of the dissertation, oncospheres are the first that, appearing in human tissues, can cause a response of the body's immune system. Such changes

may be manifested by the onset of a non-specific inflammatory response in the form of lymphocytic infiltration. It covers the entire surface of the affected area, creating what is known as tissue inflammation around the cyst that forms. In this phase of the body's immunological response, eosinophils begin to actively manifest themselves, which begin to actively increase in number. Sometimes it is possible for the so-called giant cells to develop infiltration.

However, this immune response of the body only contributes to the formation of a mechanical obstacle, due to the activation of fibrin deposition and the subsequent formation of fibrosis in the area of the liver affected by echinococcosis.

Such a reaction of the body, first of all, is aimed at limiting the growth of the parasite in the liver, and secondly, with the correct structure of the chain reaction of the cell-humoral immune response, it can lead to the death of the parasite and the involution of the liver cyst. But, unfortunately, due to the presence of a low immune response state of the macroorganism, such a mechanism of the outcome of the disease does not happen so often.

Echinococcosis has also evolved to overcome the host's immune response. Taking into account that the host organism is more conducive only to limiting the process, the parasite is also actively engaged in the formation of its own protective layer, by thickening the cuticular membrane of the cyst. This process occurs due to the continuous reproduction of syncin cells.

In such a situation, the host body produces immunoglobulins that accumulate in the fibrous membrane of the liver cyst to enhance the immunological protective response. But the full cycle of the body's immune defense begins to manifest itself only after the parasitic oncosphere is strengthened in the stable zone of liver damage. The reaction of the host organism depends, of course, on the phase of development of the pathogen. The affected area is enveloped by an impressive layer of lymphocytes, macrophages and fibroblasts. As a response to the antigenic effect of the parasite, specific immunoglobulins are actively produced in the body. This reaction occurs throughout the entire period of the parasite's existence in the body. The host organism will comprehensively try both to limit the cystic formation of the parasite and to bring it to death [30].

According to P.R. Torgerson, such a response of the macroorganism occurs through the reaction of the immune system of the first line of defense. An important role in this is given to the recognition of antigens by means of the macrophage system and the HLA genetic key, which determine the functional state of the entire T-lymphocyte system [31].

Today, we no longer realize how important, from the point of view of fundamental questions of the body's immunological response, the methods of diagnosis for the assessment of the serological system have become. [32-34]

This mechanism of the host's response has made it possible to make a number of interesting assumptions, which today are one of the additional methods of diagnosis. This refers to the determination of freely circulating antibodies in the blood serum. This diagnostic method was one of the first to be based on the body's immunological response. [35, 36]

The theoretical basis of the host's immune response to parasitic infection is the presence of two mechanisms of reorganization. It has been proven that the main message in the body's response comes down to stimulating the immune response. This reaction is accompanied by the activation of cellular and humoral immunity and is aimed at suppressing the development of the parasite in the body. A similar mechanism of transformation of the body's protective properties has been described not only in echinococcosis but also in other helminths.

Another, second, scenario of the host organism's response is also possible, aimed at suppressing the immune system, which leads to the suppression of the entire defence system, both concerning its own antigens and foreign ones (homogeneous and heterogeneous immunosuppression).

Such a response mechanism is aimed primarily at the development of the manifestation of the disease, and the formation of its clinical picture. However, along with this, there are conditions for the survival of the parasite in the body, in the formation of hydatidosis with all the ensuing consequences of the disease.

In contrast to this variant of immunosuppression, in heterologous immunosuppression, there is a suppression of the body's protective properties in relation to other foreign agents (bacteria, viruses), which is accompanied by the manifestation of other inflammatory diseases, the duration of their course, and often the presence of bacterial carriage.

Under the influence of echinococcosis larvae, there is an imbalance in the system of lymphocyte subpopulations, which is expressed in the suppression of T-cells and in the stimulation of B-cells. Such a response mechanism of the host organism, although essentially manifested by the growth of protective blood cells, neverthe-

less does not lead to an adequate solution to the problem of destroying echinococcosis.

Thus, to date, the mechanisms of the immune response to parasitic infection, which can proceed along two opposite paths of development, have already been traced. Theories about possible variants of the development of an immune reaction in complicated forms of hydatidosis echinococcosis of the liver are still debatable and far from being resolved.

CONCLUSION

The available recommendations for the preparation of patients in the preoperative period are not completely clear. In particular, many works describe the requirements for mandatory immunotherapy as an option for the prevention of postoperative purulent-septic complications. At the same time, there is evidence of the importance of using such therapy only after surgical treatment.

The question related to the use of antiparasitic chemotherapy depending on the state of the body's immune system remains far from being answered. It is known that this method of preventing the recurrence of the disease and the development of residual cysts is very important, despite the presence of a number of side effects. Among such unfavorable effects of chemotherapy is its effect on the body's immune system. When and for what period it is recommended to use antiparasitic chemotherapy remains a debatable question.

Consequently, many questions related to the clinical and immunological aspects of prognosis and prevention of purulent-septic complications of echinococcosis of the liver still remain unanswered and far from being resolved. It is to these aspects of the problem under study that our next manuscripts will be devoted.

The author declares no conflict of interest

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JIGARNING GIDATIDOZ ECHINOKKOZNING KLINIK VA IMMUNOLOGIK OMILLARINI O'RGANISH MUAMMOSINING ZAMONAVIY HOLATI

Safarov S.S.
Buxoro davlat tibbiyot instituti

ABSTRAKT

Jigarning echinokokokkozi hali ham rivojlanayotgan mamlakatlarda asosiy kasallik sanaladi. Jahon sog'liqni saqlash tashkiloti ma'lumotlariga ko'ra, bu kasallik aholining 5% gacha, yuqori endemik hududlarda esa 9,3% gacha ta'sir ko'rsata oladi. O'zbekistonning ayniqsa Janubiy viloyatlari, xususan, Buxoro, Navoiy, Qashqadaryo va Surxondaryo viloyatlari ushbu kasallikning keng tarqalganligi to'g'risidagi statistik ma'lumotlar doimo yetakchi o'rinlarga ega bo'lgan hududlardan biri hisoblanadi. So'nggi yillarda Jigarning echinokkoz kasalligi tarqalishi to'g'risidagi ma'lumotlar Yevropa ilmiy nashrlarida tobora ko'proq uchramoqda. Ushbu holat Osiyo mintaqalaridan kelgan muhojirlarning katta oqimi bilan bog'liq. Bu esa, o'z navbatida, ushbu kasallikdan zararlangan endemik hududlardan uzoq hisoblangan mamlakatlarda shifokorlar tomonidan jigarning gidatidoz echinokkozini tashxislash va davolash muammosining dolzarbligini oshiradi. Ushbu maqolada jigarning gidatitoz echinokkozining klinik va immunologik jihatlari to'g'risidagi asosiy adabiyotlar ma'lumotlarini ko'rib chiqish formatida taqdim etiladi

Tayanch iboralar: jigarning gidatid echinokokkozi, klinik namoyon bo'lishi, immunologik o'zgarishlar

СОВРЕМЕННОЕ СОСТОЯНИЕ ПРОБЛЕМЫ ИЗУЧЕНИЯ КЛИНИКО-ИММУНОЛОГИЧЕСКИХ АСПЕКТОВ ГИДАТИДОЗНОГО ЭХИНОКОККОЗА ПЕЧЕНИ

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АБСТРАКТ

Преобладающим заболеванием развивающихся стран до сих пор считается эхинококкоз печени, который по данным Всемирной организации здравоохранения может поражать до 5% население, а в высоко эндемических районах – до 9,3%. Регионы Узбекистана, в особенности южные области, такие как Бухарская, Навоинская, Кашкадарьинская и Сурхандарьинская входят в число таких регионов, в которых статистические сведения о распространенности данного заболевания всегда находится в лидирующих позициях. За последние годы сведения относительно распространенности эхинококкоза печени все чаще встречаются и в Европейских научных изданиях. Данное обстоятельство связано с большим потоком мигрантов из азиатских регионов. Это в свою очередь, повышает актуальность проблемы диагностики и лечения гидатидозного эхинококкоза печени и врачами стран, которые считались далеко не эндемическими зонами поражения этим заболеванием. В данной работе представлены в обзорном формате основные литературные сведения относительно клинических и иммунологических аспектов гидатидозного эхинококкоза печени

Ключевые слова: гидатидозный эхинококкоз печени, клиническое проявление, иммунологические изменения