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DIAGNOSTIC AND TREATMENT APPROACHES FOR ECHINOCOCCOSIS OF THE LIVER

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The purpose of the study was to improve the results of surgical treatment for echinococcosis of the liver and the quality of life of operated patients due to the improvement of diagnostic and therapeutic approaches, prevention of postoperative complications and recurrence of the disease. 22 patients were treated for echinococcosis of the liver. The duration of the operation was 2 hours in case of echinococcectomy with atypical resection of the liver, in case of laparoscopic echinococcectomy – 1.2 hours, in case of puncture aspiration injection reaspiration technique – 40 minutes. No fatal cases were observed. Recurrence of the disease was found in 9.1 %. A radical and effective operation is atypical resection of a part of the liver with an echinococcal cyst. Laparoscopic echinococcectomy is an alternative to open atypical resection of a part of the liver with an echinococcal cyst. The main condition for performing puncture aspiration injection reaspiration under ultrasound and X – ray guidance is the absence of cystobiliary fistulae, since instillation of a cyst with a scolicial solution can be the cause of sclerosing cholangitis. The anti-relapse antiparasitic therapy with albendazole 10–15 mg/kg body weight twice a day or mebendazole 40–50 mg/kg body weight three times a day in three 28-day courses with a break of 14 days should be carried out for 3–6 months in the postoperative period.

Key words: treatment, diagnostic, echinococcosis, liver, approaches, echinococcectomy.

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ДІАГНОСТИЧНІ ТА ЛІКУВАЛЬНІ ПІДХОДИ ПРИ ЕХІНОКОКОЗІ ПЕЧІНКИ

Метою дослідження було покращити результати хірургічного лікування при ехінококозі печінки та якості життя оперованих хворих за рахунок вдосконалення діагностично-лікувальних підходів, профілактики післяопераційних ускладнень і рецидиву хвороби. На лікуванні з приводу ехінококозу печінки знаходилося 22 хворих. При ехінококектомії з атиповою резекцією печінки тривалість операції складала 2 години, при лапароскопічній ехінококектомії – 1,2 години, при методиці PAIR – 40 хв. Летальних випадків не спостерігали. Рецидив захворювання виявлено у 9,1 %. Радикальною і ефективною операцією є атипова резекція частини печінки з ехінококовою кістою. Лапароскопічна ехінококектомія є альтернативою відкритій атиповій резекції частини печінки з ехінококовою кістою. Головною умовою виконання puncture aspiration injection reaspiration під УЗ та рентген- навігацією є відсутність цистобіліарних норниць, так як інстиляція кісти сколіцидним розчином може бути причиною склерозуючого холангіту. У післяопераційному періоді на протязі 3–6 місяців слід проводити протирецидивну антипаразитарну терапію альбендазолом по 10–15 мг/кг ваги двічі на день або мебендазолом по 40–50 мг/кг ваги тричі на день трьома 28- денними курсами з перервою 14 днів.

Ключові слова: лікування, діагностика, ехінококоз, печінка, підходи, ехінококектомія.

The study is a fragment of the research project “Development and implementation of new methods of minimally invasive and endovascular interventions in metabolic syndrome, endocrine pathology, diseases of the lungs, esophagus, liver and extrahepatic ducts, stomach, pancreas, colon and rectum, blood vessels”, state registration no. 0119U003573.

Echinococcosis of the liver refers to chronic parasitic diseases, in which single or multiple cystic formations develop in the liver, the causative agent of which is the larval stage of *Echinococcus granulosus* [4, 7, 13]. The incidence rate of echinococcosis among people is 5.9 per 100,000 population, while the recurrence rate reaches 23.2 % in endemic regions [2, 9, 12]. The number of patients with echinococcosis ranges from 0.4 % to 7.3 % of all parasitic diseases in Ukraine. The Odesa region, especially the southern regions of the region, is endemic for echinococcosis among people [7].

The main route of infection with oncospheres is the gastrointestinal tract. An asymptomatic form of the disease and a period of clinical manifestations are distinguished in the course of echinococcosis of the liver [4, 5, 15].

The echinococcal cyst is single-vesicular in most cases, but daughter cysts grow in the mother cyst [4, 6, 14]. The ratio of the frequency of damage to the liver and lungs, as the most frequent targets of damage by echinococcus, is 2.5:1 [4, 6, 10]. The specific serological methods of indirect hemagglutination and latex agglutination reactions are used for laboratory diagnostics, the diagnostic sensitivity of which reaches up to 100 %, currently [2, 4, 7]. A general blood test, liver and kidney tests, and other biochemical studies allow determining the general reaction of the body to echinococcus infection [2, 4, 5]. The use of ultrasound examination, computer and magnetic resonance imaging allows to establish the presence of a cyst, its size, localization, relationship with other adjacent organs [2, 4, 7].

There are three methods of treatment of echinococcosis: drug, surgical with open access and surgical with laparoscopic access and puncture percutaneous under ultrasound or radiological control at

present [1, 8, 10]. The surgeon should have a differentiated approach to choosing a method of surgical treatment of liver echinococcus: how to remove the cyst, what to do with fibrous capsule, how to eliminate the residual cavity [3, 11, 15].

The optimal treatment option for echinococcosis is radical closed removal of the cyst, which is a reliable method of preventing recurrence [1, 3, 7]. Modern approaches to surgical treatment of echinococcosis of the liver are based on organ-preserving principles [1, 10, 11]. An alternative to open laparotomic echinococcectomy of the liver is laparoscopic echinococcectomy, mini-access echinococcectomy and the PAIR (puncture aspiration injection reaspiration) technique under ultrasound and X-ray guidance at present [7, 8, 11]. It is necessary to carefully process the walls of the fibrous capsule with the use of chemical and pharmacological drugs, or use the method of diathermocoagulation, cryodestruction in the case of echinococcectomy, which is accompanied by the opening of the chitinous membrane and its removal together with the daughter scolexes [4, 7, 9]. Germicidal drugs give unsatisfactory results at the stage of conservative treatment of echinococcosis of the liver [4, 7, 13]. Benzimidazole and its derivatives – mebendazole, albendazole are used to prevent recurrence of echinococcosis after surgery. They can also be used at the stage of surgical and puncture treatment of echinococcosis of the liver to prevent recurrence [4, 7, 9].

Thus, the problem of treatment of echinococcosis of the liver and its complications, prevention of recurrence of this disease remains relevant and requires further improvement.

The purpose of the study was to improve the results of surgical treatment for echinococcosis of the liver and the quality of life of operated patients due to the improvement of diagnostic and treatment approaches, prevention of postoperative complications and recurrence of the disease.

Materials and methods. 22 patients were treated for echinococcosis of the liver in the clinic of the Department of Surgery No. 1 of the Odesa National Medical University on the basis of the department of minimally invasive methods of surgical treatment of the Odesa Regional Clinical Hospital from 2017 to 2022 years. There were 7 women (31.8 %), men – 15 (68.1 %) aged 22 to 56 years. Middle age was 39 ± 1.95 years.

The diagnostic algorithm for echinococcosis of the liver was based on laboratory diagnostics, which determined the general reaction of the patient's body to echinococcus invasion. A general analysis of blood and urine, biochemical studies of liver and kidney samples, and hemostesiological parameters were studied. Examination of patients for the detection of IgG antibodies to Echinococcus granulosus by the method of solid-phase enzyme immunoassay of the indirect hemagglutination reaction was mandatory. The ultrasound examination, computer tomography with or without contrast enhancement, magnetic resonance imaging were performed from the methods of topical diagnostics.

We performed the following surgical interventions for echinococcosis of the liver: liver resection with a closed echinococcal cyst, liver resection with an echinococcal cyst with the opening of the latter (open), laparoscopic echinococcectomy, puncture aspiration injection reaspiration (PAIR) method of echinococcal cyst removal.

The anti-relapse antiparasitic therapy with albendazole at 10–15 mg/kg of body weight twice a day or with mebendazole at 40–50 mg/kg of body weight three times a day was carried out in the postoperative period for 3–6 months. Three 28-day courses of antiparasitic therapy with a break of 14 days were used as a rule. The criterion for withdrawal of chemotherapy drugs is a negative reaction of indirect hemagglutination to echinococcosis, absence of clinical signs of echinococcosis, and instrumental confirmation.

The study was carried out in accordance with the principles of the Declaration of Helsinki. The study protocol was approved by the Local Ethics Committee for all participants. Patients' informed consent was obtained for the study. The obtained results were processed using the StatSoft “Statistica 5.5” application program package with the calculation of the arithmetic mean of the studied indicator (M), the standard error of the mean (m), relative values (frequency, %) and the Student's parametric test. At the same time, differences at $p < 0.05$ were considered statistically significant.

Results of the study and their discussion. The main complaints of 16 (72.7 %) patients with echinococcosis of the liver were moderate pain and discomfort in the right hypochondrium, which increased after eating and during physical exertion, which was the main reason for consulting a doctor. When collecting epidanamnesis, no clear relationship with the region of residence was found. It should be emphasized about the contact of patients with domestic and farm animals. An objective physical examination revealed periodic unexplained subfibrillation. Skin rashes of a papular nature were observed in 4 (18.2 %) patients with echinococcosis of the liver, in 3 (13.6 %) – moderate jaundice with total bilirubin values up to 120 $\mu\text{mol/l}$, which was accompanied by a rash. The course of the disease was asymptomatic in 6 (27.3 %) patients.

Clinical-morphological characteristics of the contingent of patients are presented in eable 1.

Table 1

Clinical and morphological characteristics of patients (n=22)

Characteristics	Abs./ %
By origin:	
primary	17 (77.3 %)
recurrent	5 (22.7 %)
By the number of cysts :	
single	16 (72.7 %)
multiple	6 (27.3 %)
By localization :	
right lobe	11 (50.0 %)
left lobe	4 (18.2 %)
both lobes	6 (27.3 %)
According to the diameter of the cyst:	
small (up to 5 cm)	4 (18.2 %)
medium (6–10 cm)	16 (72.7 %)
large and giant (10 cm or more)	2 (9.1 %)
Complicated forms of echinococcosis:	
cyst suppuration	5 (22.7 %)
cyst rupture	2 (9.1 %)

The diagnosis of echinococcosis of the liver was established for the first time in 17 (77.3 %) patients, 5 (22.7 %) patients were hospitalized again due to echinococcosis of the liver (recurrence). Solitary echinococcal cysts were diagnosed in 16 (72.7 %) patients, polycystosis was found in 6 (27.3 %) cases. Damage to the right lobe of the liver was observed 2.7 times more often than the left. Both lobes were affected in 27.3 % of cases. Small cysts with a diameter of up to 5 cm were detected in 18.2 % of cases, medium (6–10 cm) – diagnosed in most patients (72.7 % of observations) large and giant (10 cm and more) were observed in 2 (9.1 %) cases. 5 (22.7 %) had suppuration of an echinococcal cyst, which was accompanied by hyperthermia with a hectic temperature curve and signs of cholangitis out of the total number of patients. 2 (9.1 %) patients were brought to the hospital for urgent indications with the acute abdomen clinic. These patients underwent emergency surgery for intraabdominal rupture of an echinococcal cyst.

Laboratory indicators in patients with echinococcosis are presented in Table 2.

Table 2

Laboratory indices in patients with echinococcosis, initial data (n=22)

Laboratory indices	Mean indices
Hemoglobin, g/l	102±5.5
Erythrocytes, 10^{12}	2.75±0.15
Platelets, 10^9	434±11.5
Leukocytes, G/l	22.4±0.25
Eosinophils, %	5.7±0.29
Segmented neutrophils, %	76±3.8
ESR, mm/h	42±1.9
C– reactive protein mg/l	5.2±0.26
Lymphocytes, %	27±1.05
Total protein, g/l	58.2±2.9
Globulins, %	46.4±2.3
Albumins, %	53.6±2.7
Prothrombin index, %	115±5.8
Total bilirubin, $\mu\text{mol/l}$	26.6±1.03
Direct bilirubin, $\mu\text{mol/l}$	5.6±0.3
ALT, Units/l	45±2.05
AsT, Units/l	39±1.9
Lactate dehydrogenase, Unit/l	230±11.5
Alkaline phosphatase, Unit/l	280±14.2
γ – glutamyltransferase, Unit/l	34±1.7
Urea mmol/l	8.3±0.42
Creatinine, $\mu\text{mol/l}$	114±5.6
Detection of Echinococcus granulosus IgG antibodies (coefficient >1.0 – positive)	20 (90.9 %)

The clinical signs of anemia were characteristic, which were confirmed in the laboratory by the results of determination of hemoglobin and erythrocytes in patients with echinococcosis of the liver. The presence of an inflammatory process and its expressiveness in patients with echinococcosis of the liver is evidenced by the presence of leukocytosis and elevated ESR. The attention should be paid to the increased content of eosinophils, segmented nuclear neutrophils and lymphocytes, the specific proportion of which was 6.7 ± 0.3 , respectively; 78 ± 7.9 ; 27 ± 1.05 %, respectively in patients with echinococcosis of the liver from a diagnostic and prognostic point of view. Increased content of C– reactive protein and signs of SIRS were diagnosed, which were manifested by the presence of two or more criteria: heart rate > 90 bpm; temperature $< 36^\circ \text{C}$ or $> 38^\circ \text{C}$; the level of leukocytes in the blood < 4000 or $> 12000/\text{mm}^3$; breathing $> 20/\text{min}$ or CO_2 partial pressure < 32 mm Hg. Art in 5 (22.7 %) patients with echinococcosis of the liver. Dysproteinemia in echinococcosis of the liver was characterized by a decrease in the level of total protein and albumin fraction and an increase in the content of globulins.

The signs of hypercoagulation were characteristic, which were confirmed by elevated levels of the prothrombin index, which was on average 115 ± 5.8 %, and the content of platelets ($434 \pm 11.5 \times 10^9$) for patients with echinococcosis of the liver. Echinococcosis of the liver in patients was accompanied by an increase in the content of both total bilirubin and its direct fraction. Manifestations of jaundice were noted in 3 (13.6 %) patients. Patients with echinococcosis of the liver are characterized by increased liver function tests and increased levels of lactate dehydrogenase, alkaline phosphatase, and γ – glutamyltransferase, which indicates the development of liver failure. Elevated levels of creatinine and urea were diagnosed in 4 (18.2 %) patients with echinococcosis of the liver who had asymptomatic bacteriuria and indicated the onset of organ failure – the development of acute renal failure. The detection of IgG antibodies to *Echinococcus granulosus* confirms the diagnosis of liver echinococcosis in patients and indicates the chronicity of the infectious process. The coefficient of detection of IgG *Echinococcus granulosus* antibodies was positive and was > 1.0 in 90.9 % of patients.

Laparoscopic cholecystectomy was performed after the localization of echinococcal cyst in II, III, IV, V, VI segments of the liver according to the standard technique using the OTV – SC endosurgical complex "Olympus". Analgesia – endotracheal anesthesia with carbon dioxide pressure in the abdominal cavity of 10–12 mm Hg. A puncture and evacuation of the cyst contents, instillation of a scolicial solution (Betadine 1 % solution), removal of the contents of the echinococcal chitinous membrane and daughter blisters through a suction device were performed after the installation of the ports with working instruments. The intervention zone of the liver area was isolated with teardrops soaked in betadine solution to prevent the dissemination of the parasite. The next stage – elimination of the remaining cavity was achieved by treating the fibrous lining of the cavity with a diathermocoagulator, elimination of bile fistulas, if any, tamponade of the cavity with a cut strand of the omentum, installation of at least two drainage tubes with an internal diameter of 0.3–0.5 cm, which were removed externally in the right or left hypochondrium. The subhepatic space, the subdiaphragmatic suprahepatic space, and the abdominal cavity were drained with separate drains if necessary. Excision of the fibrous capsule was not performed.

The local infiltration anesthesia with a 0.5 % novocaine solution of 40.0–60.0 ml was used in most cases when removing an echinococcal cyst by the PAIR method for CL, CE1 and CE2 cysts. The through a skin puncture of an echinococcal cyst was performed under navigation ultrasound. It is mandatory to puncture the cyst through the liver parenchyma – as one of the options for preventing the spread of the parasite in the abdominal cavity. The subsequent stages consisted in evacuating the contents of the cyst, installing the cyst with a scolicial solution of alcohol 96 ° for 1/4–1/5 of the volume of the cyst contents. A drainage tube with a diameter of 12 F was either immediately placed on the puncture needle, or inserted into the cyst cavity along the guide and fixed to the skin.

Operative intervention for echinococcosis of the liver, which consisted in atypical resection of a part of the liver with an echinococcal cyst without opening the latter, was performed by us in 3 (4.5 %) patients. We performed echinococcectomy with opening of the cyst lumen in the case when the size of the cyst was medium, large, or giant, or it was polycystic, damage to both lobes of the liver, suppuration, rupture of the cyst. There were 4 such cases (18.2 %). Differential operative approaches such as upper median laparotomy, oblique subcostal approaches according to Kocher or Fedorov were applied.

We performed laparoscopic echinococcectomy in 10 (45.5 %) patients as a less traumatic intervention. The PAIR technique was used in 5 (22.7 %) cases and had its indications for use. An important issue when performing echinococcectomy is the elimination of the residual cavity after removal of the chitinous membrane of the echinococcal cyst. Regarding the fibrous capsule, its partial excision was performed in those cases when it was expedient to reduce the intussusception substrate.

Complete liquidation of the cavity was performed by us in 3 (13.6 %) cases with atypical resection of a part of the liver with an echinococcal cyst without opening it. There was incomplete elimination of the cavity after removal of the chitinous membrane of the echinococcal blister or blisters in other cases, accordingly. We applied tamponade to fill the cavity strand of the omentum in 10 (45.5 %) cases after removal of the echinococcal cyst. The intussusception of the fibrous capsule was performed after its partial excision in 6 (27.3 %) patients. External drainage of the cyst cavity is mandatory.

Intraoperative blood loss ranges from 50.0 ml when using minimally invasive techniques to 200–300 ml during laparotomy echinococcectomy, atypical resection of the liver with an echinococcal cyst. The duration of the operation was 2 hours in case of echinococcectomy with atypical resection of the liver, in case of laparoscopic echinococcectomy – 1.2 hours, in case of the PAIR technique – 40 minutes. The stay in hospitalization was from 10 to 3 days depending on the type of surgical intervention. The patients were discharged from the hospital for outpatient treatment with clear recommendations, in particular regarding the care of drains. No fatal cases were observed. Recurrence of the disease was found in 2 (9.1 %).

Thus, the main complaints of patients with echinococcosis of the liver were moderate pain and discomfort in the right hypochondrium. No clear relationship with the region of residence was found. An objective physical examination revealed periodic, unexplained subfibrillation, papular skin rashes, moderate jaundice with a rash. According to the authors, such manifestations are characteristic of echinococcosis of the liver [4, 7]. Recurrent echinococcosis accounted for 22.7 % of cases. Medium cysts (6–10 cm) were diagnosed in 72.7 % of observations. The obtained results coincide with the literature data [2, 4, 6]. In patients with echinococcosis of the liver, characteristic clinical signs of anemia, leukocytosis, increased ESR, eosinophilia, increased C– reactive protein, dysproteinemia, hypercoagulation, increased bilirubin, elevated liver function tests, levels of lactate dehydrogenase, alkaline phosphatase, γ – glutamyltransferase, creatinine, and urea were found, which is confirmed by studies of other scientists [2, 4, 7]. The detection of *Echinococcus granulosus* IgG antibodies confirms the diagnosis of echinococcosis of the liver in patients and indicates the chronicity of the infectious process [7, 13, 15]. Treatment measures were based on modern medical and diagnostic approaches for echinococcosis [1, 8, 10]. Intraoperative blood loss ranged from 50.0 ml to 200–300 ml. No fatal cases were observed. Recurrence of the disease was detected in 2 (9.1 %) cases.

Conclusions

1. An atypical resection of a part of the liver with an echinococcal cyst is a radical and effective operation for complete recovery and recurrence of the disease.
2. Laparoscopic echinococcectomy is an alternative to open atypical resection of a part of the liver with an echinococcal cyst.
3. The main condition for performing PAIR (puncture aspiration injection reaspiration) under ultrasound and X-ray guidance is the absence of cystobiliary fistulae, since instillation of a cyst with a scolicidal solution can be the cause of sclerosing cholangitis.
4. Antirelapse antiparasitic therapy with albendazole at 10–15 mg/kg of body weight twice a day or with mebendazole at 40–50 mg/kg of body weight three times a day should be carried out in three 28–day courses with with a break of 14 days in the postoperative period for 3–6 months.

Prospects for further research are aimed at studying the peculiarities of treatment and diagnostic approaches for intestinal obstruction in the conditions of a general surgical department.

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FEATURES OF THE COURSE OF PUBERTY IN GIRLS WITH LOW BIRTH WEIGHT

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65 girls in the pubertal period, living in the conditions of the city of Baku and Nakhchivan, were examined. The average age of the girls was 16.35±0.06 years. All girls were born at term with low body weight. The average weight of a newborn was 2.245±25.98 (1900–2500 g). In girls born with low body weight, a delay in physical and sexual development. The study of hormones revealed statistically significantly low levels of follicle-stimulating hormone (3.0±0.21 mIU/ml), luteinizing hormone (2.3±0.12 mIU/ml), free triiodothyronine (2.56±0.08 pg/ml), free thyroxine (1.3±0.02 ng/ml), estradiol (30.0±0.9 pg/ml) and high levels of prolactin (17.9±0.22 ng/ml), thyroid-stimulating hormone (2.96±0.19 mIU/ml), dehydroepiandrosterone sulfate (4.28±0.19 pg/ml), total testosterone (1.21±0.11 ng/ml), which reflected the presence of clinical and diagnostic manifestations of hypogonadotropic hypogonadism in this contingent of girls which affects the reproductive health of girls in subsequent periods of life.

Key words: puberty, fetal hypotrophy, hirsutism, hypogonadotropic hypogonadism, physical and sexual development.

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ОСОБЛИВОСТІ ПЕРЕБІГУ ПУБЕРТАТНОГО ПЕРІОДУ У ДІВЧАТОК З НИЗЬКОЮ МАСОЮ ТІЛА ПРИ НАРОДЖЕННІ

Нами обстежено 65 дівчаток, які перебувають у пубертатному періоді та проживають в умовах міста Баку та Нахчівані. Вік дівчаток становив 16,35±0,06 років. Усі дівчатка були народжені від доношеної вагітності із низькою масою тіла. Середня маса новонародженого становила 2245±2598 (1900–2500 г). Встановлено, що у дівчаток, які народилися з низькою масою тіла, відзначається затримка фізичного та статевого розвитку та клініко-діагностичні прояви легкого гірсутизму (14,1±0,08). Дослідження гормонів виявило низькі показники фолікулостимулюючого гормону (3,0±0,21 мМЕ/мл), лютеїнізуючого гормону (мМЕ/мл), трийодтироніну (2,56±0,08 пг/мл), вільного тироксину (1,3±0,02 нг/мл), Естрадіолу (30,0±0,9 пг/мл) та високі показники пролактину (17,9±0,22 нг/мл), тиреостимулюючого гормону (2,96±0,19 мМЕ/мл), дегідроепіандростерон-сульфату (4,28±0,19 пг/мл), вільного тироксину (1,21±0,11 нг/мл), що відобразило наявність у даного контингенту дівчаток клініко-діагностичних проявів гіпогонадотропного гіпогонадизму, що відбивається на репродуктивному здоров'ї дівчаток у наступні періоди життя.

Ключові слова: пубертатний період, гіпотрофія плода, гірсутизм, гіпогонадотропний гіпогонадизм, затримка фізичного розвитку, затримка статевого розвитку.

An urgent problem of modern pediatric gynecology is the study of the peculiarities of the course of puberty of girls born with low body weight.

According to modern literature sources, the term “small for gestational age” (SGA) includes newborns born with a low body weight relative to the expected gestation period [3, 5, 7].

It should be noted that in different countries, the mass-growth indicators of girls are evaluated by different criteria. Infants with low body weight include newborns with mass-growth indicators below 3 percentiles relative to the gestation period. These also include children born at term with low body weight