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Original article

HUMAN CYSTIC ECHINOCOCCOSIS IN ENDEMIC REGIONS IN BULGARIA - ULTRASOUND SURVEILLANCE, TREATMENT AND FOLLOW-UP OF PATIENTS

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ABSTRACT:

Introduction: Cystic echinococcosis (CE) is a chronic disease in humans, usually asymptomatic, but in some cases could be very severe with fatal outcomes. This parasitosis is a health and economic problem in many areas of the world. The actual spread among people with CE in endemic regions is not known. The purpose of prophylactic ultrasound examinations of people in some areas was to clarify the real prevalence of CE and to detect undiagnosed asymptomatic cases and recurrences.

Materials and methods: An abdominal ultrasound survey in four endemic regions in Bulgaria with the highest rate of registered patients with CE in Bulgaria for the last five years was conducted. For every patient with CE an epidemiological and clinical history, abdominal ultrasound examination, blood tests and ELISA IgG test for CE were performed.

Results: From all 8602 people examined, in seventeen persons (0.2%), liver hydatid cysts were found for the first time. Ssixty five (0.8%) reported a history of previous surgical treatment for CE, of which 54 (83.1%) had passed surgery because of liver CE and 11 (16.9%) had extrahepatic CE (pulmonary, cardiac, bone, spleen). In three (5.6%) patients, who were operated years before for liver CE, recurrences were discovered. In 11 (64.7%) patients devitalized CE_4 cysts were observed without any data for previous treatment. Three of the discovered patients with CE were treated with surgery, one with puncture-aspiration-injection-reaspiration, four only with Albendazole. The patients were successfully treated and followed for a period of five years.

Conclusions: During the prophylactic ultrasound examinations, a higher percentage of people infected with liver cystic echinococcosis was found compared to the official information. It should be noted that these results are found in areas with the highest incidence of this disease in the country. US screenings give the opportunity for early detection, timely treatment of infected people and to prevent severe complications in patient with CE disease.

Keywords: cystic echinococcosis, abdominal ultrasonography survey, treatment, Albendazole,

INTRODUCTION

Cystic echinococcosis is a chronic disease in humans with prolonged recurrent course of illness. Some of the cases are asymptomatic, but in others, a repeated surgical treatments may needed and severe complications developed. The high incidence of CE reported in some Eastern European countries was the reason for conducting an international project in Bulgaria, Italy, Romania, Spain and Turkey (Human Cystic Echinococcosis ReseArch in Central and Eastern Societies). The present paper reports results with focus on clinical findings and the treatment results in patients with CE, found in highly endemic regions of Bulgaria.

The practice of mandatory registration and reporting of cases with CE to the Ministry of Health and the European Center for Disease Prevention and Control is the reason why Bulgaria ranks first in Europe [1]. Even though the real number of people infected is not completely known and is defined as "hidden morbidity". The purpose of prophylactic Ultrasound (US) examinations of a large number of individuals in endemic regions was to clarify the true prevalence of CE and to detect undiagnosed asymptomatic cases and recurrences. Timely treatment is important to prevent complications in patients.

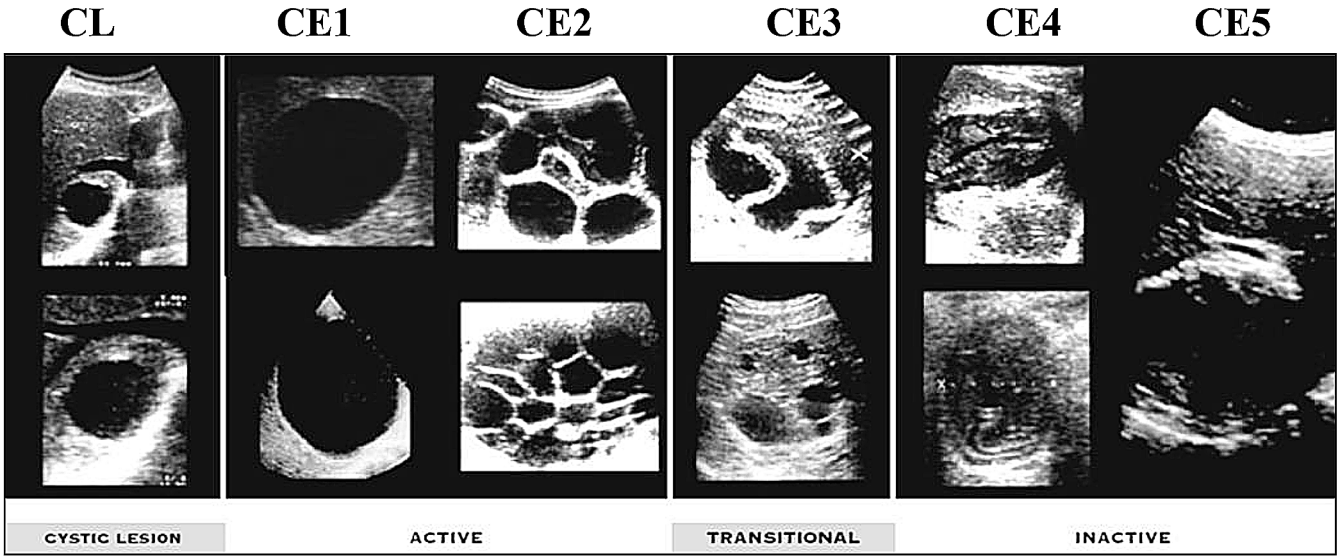
MATERIALS AND METHODS

Abdominal ultrasound research of 8602 people (3 to 85 years old) was performed over a period of two years (summer of 2014-2015). Confirmed CE patients were follow-up for five years in Specialized Hospital of Infectious and Parasitic diseases "Prof. I. Kirov" in Sofia. Four areas in Southeast, Northeast and Southwest Bulgaria with the highest rate of registered patients with CE in Bulgaria for the last five years were selected. WHO ultrasound classification (Fig. 1) for the typing of CE cysts was used [2]. The first clinical group starts with cyst types CE1 and CE2 and such cysts are active, usually fertile cysts containing viable protoscoleces. CE Type3 are cysts entering a transitional stage where the integrity of the cyst has been com-

promised either by the host or by chemotherapy and this transitional stage is assigned to the second clinical group. The third clinical group comprises CE Types4 and CE5 which are inactive cysts which have normally lost their fertility and are degenerative [2].

For every patient with CE an epidemiological and clinical history, abdominal US examination, chest X-ray for exclusion of pulmonary echinococcosis were performed. Patients with CE were examined and followed with laboratory tests (complete blood count, biochemical blood tests) and ELISA IgG test for CE (positive >1.1) after one, 6, 12 months and once a year for five years.

Fig. 1. Ultrasound Classification for typing of CE cysts (World Health Organization Informal Working Group on Echinococcosis standardized classification of echinococcal cysts. Acta Tropica 2003; 85: 253-261).



CL (Cystic lesion), CE (Cystic echinococcal) cyst

The patients detected during ultrasound screenings with active CE cysts were treated with surgery (three patients), one with puncture-aspiration-injection-reaspiration (PAIR) and four with Zentel (Albendazole) in a dose of 10 mg per kg, twice a day, without interruption, for six months.

RESULTS

Abdominal ultrasound data of people examined in endemic regions

Ultrasound screening campaigns were carried out in hospitals, health centers and primary schools. From all 8602 people examined in high endemic regions, 65 (0.8%) reported a history of previous surgical treatment for CE and 17 (0.2%) had new-found liver CE cysts.

History of previous surgical treatment for liver CE had 54 (83.1%) persons from all operated. From them 35 (64.8%) had a single operation, 13 (24.1%) had two operations, two (3.7%) had four surgical operations, two (3.7%) had both PAIR and surgery, one patient (1.9%) had two surgical interventions and PAIR treatment and one patient (1.9%) had all different types of therapy - surgery, PAIR, therapy with ABZ (5 months) and percutaneous drainage procedures under US control.

US characteristics show that six (11.1%) persons had calcifications in the liver after operation, 19 (35.2%) had liver post-surgical residual cavity without recurrence, five (9.3%) had devitalized cysts after treatment with ABZ, four (7.4%) had devitalized cysts after PAIR treatment and 20 (37%) did not have any specific significant US data concerning CE (no visible lesion).

Recurrences in liver CE were detected in three (5.6%) patients, from whom two patients were twice operated and one patient had one surgical operation with two months postoperative ABZ treatment.

During the US screenings, all types of liver CE cysts were found - CE_1, CE_2, CE_{3a} and CE_4. From 17 newly found cases, 11 (64.7%) devitalized CE_4 cysts were observed without any data for previous treatment and a "watch and wait" approach. In two newly found patients, giant CE_1 cysts (till 14 cm) in the liver were seen.

Eleven humans (16.9%) had passed surgery because of extrahepatic CE (pulmonary, cardiac, bone, spleen).

Treatment and US follow-up of patients with newly diagnosed CE

After establishing the diagnosis, three patients were treated by surgery, one patient with PAIR, four patients underwent therapy with ABZ. A thirteen-year-old boy with liver CE1, size 7/5 cm, discovered in the field (Fig.2a) with positive serology (ELISA IgG test 1.6) was treated with PAIR and two months prophylaxis against the recurrence the with ABZ. One year later, recurrence (daughter cysts inside) was observed (Fig.2b), and the ELISA IgG test elevated to 3.4). After three months ABZ treatment, the daughter cysts disappeared, the cyst content became heterogeneous (Fig. 2c), and the result of the ELISA IgG test decreased to 1.2.

Fig. 2a. Ultrasound of liver - active CE_1 cyst

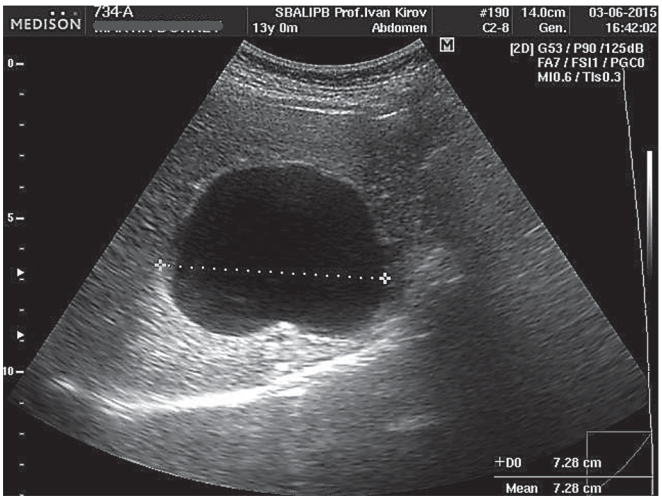


Fig. 2b. Recurrence after one year - CE_{3b} (daughter cysts)

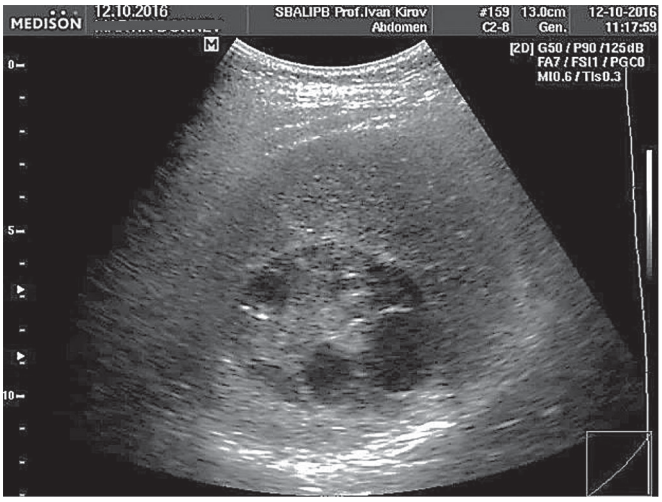


Fig. 2c. Three months after starting of ABZ therapy – inactive CE_4 cyst

Ultrasound data of recurrence in a 51-year-old patient one year after two surgeries and two months of ABZ therapy were discovered (Fig. 3a). Two CE_2 cysts in the liver with daughter cysts inside were seen. The ELISA IgG test was highly positive (6.1). The patient was treated with ABZ 10 mg/kg for 6 months without interruption. After therapy, daughter cysts disappeared, and ELISA titer increased (8.8). During the control examinations after 15 months, CE_4 (nonhomogeneous pseudo-solid content inside) (Fig. 3b) and a decrease in ELISA test (4.4) were found.

Fig. 3a. Two CE_2 cysts (8 cm and 11 cm) in liver

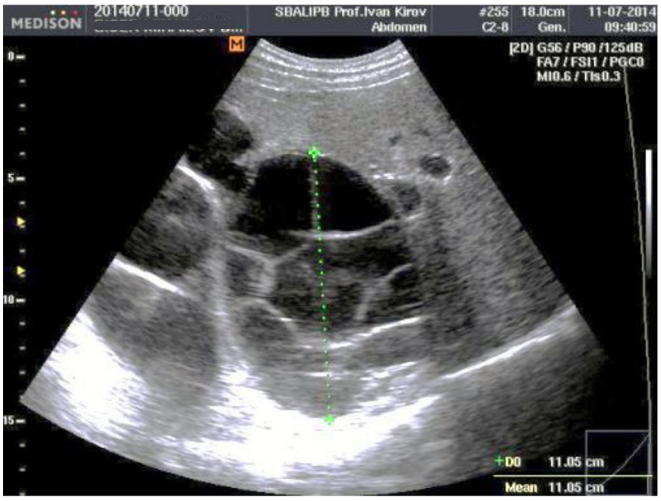
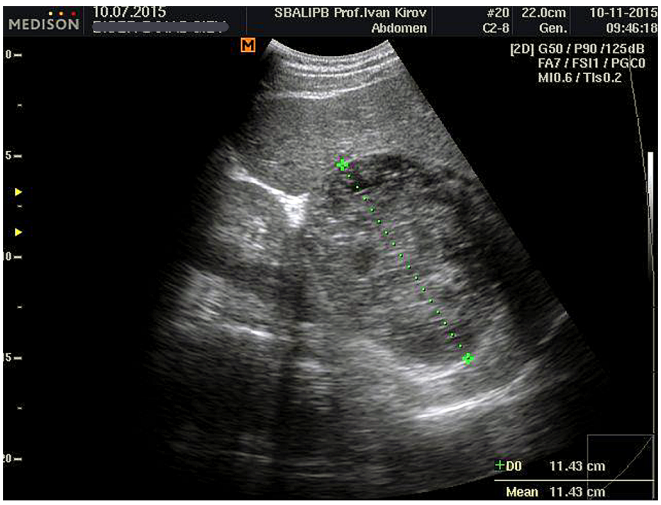


Fig. 3b. Devitalized CE_4 cyst after ABZ therapy



In all patients treated with ABZ, changes in CE cysts were observed. The US data of devitalization and successful treatment included a "water lily" sign showing detachment of the cyst membrane; gradual replacement of the liquid cyst content with hyperechoic, nonhomogeneous pseudo-solid one inside; disappearing of multiple septa and daughter cysts, reduction of the size of the cyst. These changes in CE cysts were accompanied by decreased titres of the ELISA test. No side effects or complications of ABZ therapy were registered.

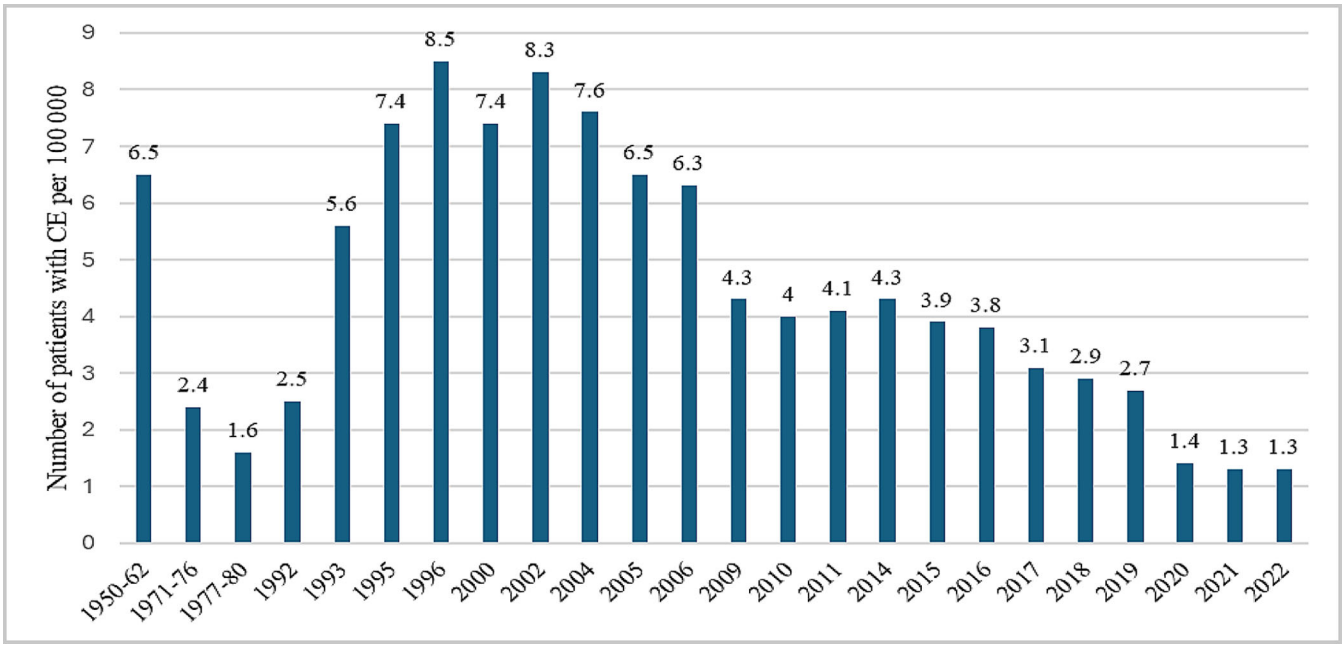
Ultrasound data for other pathology found except Cystic Echinococcosis

Among the people that had been screened, other various unknown pathologies until this moment were observed, such as: fatty liver, liver cirrhosis, liver haemangioma, cholelithiasis, calculus cholecystitis, choledocholithiasis, polyps and cholesterolosis of the gallbladder, nephrolithiasis, pyelonephritis, hydronephrosis, ureterolithiasis, splenomegaly and enlarged lymph nodes, even unknown situs inversus and pregnancy, and appropriate additional laboratory tests, image techniques, consultations and treatment were further recommended.

DISCUSSION

Human cystic echinococcosis is a high-endemic disease in some regions of Bulgaria. The data for registered patients with CE for 69 years (1950-2019) show that the annual number of cases in the country for the period of 1950-1962 is at high rates till 6.5 per 100 000 (%ooo) population [3]. After two decrees against rabies (in 1948 and 1960) and the measures taken in Bulgaria, the annual incidence of surgery for cystic echinococcosis decreased to the lowest value of 1.2 %ooo [4]. The number of cases again increased gradually to the highest value of 8.5%ooo in 1996 (Fig. 4). The registered cases with human CE gradually reduced and were twice lower in 2009 (4.3 %ooo) [5]. In the coming years, CE cases were under 4 %ooo, as from 2021 were 1,3%ooo) [6].

Fig. 4. Number of patients with cystic echinococcosis per 100 000 population for a period of 72 years



Unfortunately, CE is still diagnosed among children in the age group 0-18 years. For the period of 1996-2013, alarming data were published according to which CE was established in children aged 10 to 14 years at 9.4%ooo and in adolescents aged 15 to 19 at 9.3%ooo, while in adults for this period, it was 6.7%ooo [5, 7]. These data are higher than in the previous period between 1971–1995 when the annual incidence of surgery for CE in children under 14 years of age was 1.25 %ooo and in adolescents aged 15-19 years 2.03 %ooo [8]. This fact indicates the presence of transmission of the parasite from the main reservoir hosts to humans.

As a result of the first large abdominal ultrasound screening performed in four high endemic areas in Bulgaria, liver CE cysts in 17 humans were discovered. These data indicate a higher percentage of cases of CE (0.2%) compared to the official information for all country, but it should be noted that in most areas of Bulgaria, the number of CE cases are significantly lower or absent.

In terms of liver CE, there are four main possible types of therapeutic behavior - surgery, percutaneous puncture treatment (PAIR mini-invasive technique and drainage procedures), chemotherapy and "watch and wait". "Stage-specific" imaging approach based on the WHO ultrasound classification of CE seems to be the best available tool for rational therapeutic choice nowadays [9-10]. During ultrasound screening, we found recurrences in 5.6% of patients with CE after previous treatment. Prolonged follow-up of people with CE with abdominal US examinations and serological methods is needed because recurrences are observed after all types of treatments. According to other authors and our experience in the last 40 years, medical therapy is a successful method and an alternative for patients with all localizations of cysts [11-15].

CONCLUSIONS

Cystic echinococcosis is a benign and treatable disease in humans, but deaths are not uncommon after spontaneous rupture of a hydatid cyst followed by anaphylactic shock. Timely detection, appropriate treatment of this disease and long-term patient monitoring are important for human health. The spread of CE in the endemic regions of Bulgaria was one of the tasks of the international project HERACLES. The analysis of some results was presented [16-20]. With prophylactic ultrasound screenings, a greater frequency of cases of cystic echinococcosis was found, but it should be noted that these results refer to some regions with a high incidence of ñystic echinococcosis in Bulgaria. Prophylactic abdominal ultrasound examinations in endemic regions allowed timely detection and treatment of undiagnosed asymptomatic patients and recurrences.

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