New Options in the Management of Cystic Echinococcosis – A Single Centre Experience Using Minimally Invasive Techniques

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Rezumat

Opțiuni noi în managementul echinococozei chistice – experiența unui singur centru în utilizarea tehnicilor de abord minim invaziv

Obiectiv: Scopul acestui studiu este de a verifica dacă experiența pe 4 ani în utilizarea tehnicilor de abord minim invaziv în tratamentul echinococozei chistice (CE) se potrivește ca indicații și rezultate cu studiile importante pe această temă.

Metodă: În perioada 03.2014 – 03. 2018, 38 PAIR, 28 proceduri MoCaT (cateterizare modificată) și 7 drenaje percutanate au fost efectuate la 51 pacienți din 76 cazuri de chisturi hidatice hepatice (67,1%). Lotul a cuprins 26 bărbați și 25 de femei, iar vârsta a fost între 19 și 78 de ani. 7 pacienți au avut 2 sau mai multe chisturi hidatice și câte 2 proceduri au fost efectuate la 3 dintre aceștia; alți 11 pacienți au necesitat o a doua procedură pe parcursul supravegherii.

Rezultate: Evoluția pacienților a fost bună, iar supravegherea acestora a fost de minim 2 ani. Nu au existat efecte majore de natură chirurgicală. Am definit ca rezultat bun obținerea unei cicatrice sau a unei mici cavități cu pereți calcificați (hiperecogeni). Doar 2 (3,9%) pacienți au necesitat conversia la chirurgie deschisă. Complicațiile întâlnite au fost fistulele chisto-biliare în 15 cazuri (29,4%) și redeschiderea cavității în 11 cazuri (21,67%).

Concluzii: Metodele de tratament percutan pentru CE sunt sigure și eficiente, dacă se respectă utilizarea lor în funcție de tipul chistului. Tratamentul percutan este o alternativă mai ușoară la chirurgia

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deschisă și are rate mai scăzute de complicații și recăderi, precum și o spitalizare mai scurtă. Acum tratament de rutină, devine încet prima opțiune în abordul invaziv al CE. Rolul chirurgiei deschise este redus la CE cu complicații severe.

Cuvinte cheie: chist hidatic, tehnici minim invazive, PAIR, Mo-CAT, drenaj percutanat, cavitare reziduală

Abstract

Objective: The aim of this study is to verify if the experience on 4 years in using minimally invasive techniques in the treatment of CE could match regarding the indications and results with the major studies on topic.

Method: During 03.2014 – 03. 2018 period, 38 PAIR, 28 MoCaT procedures and 7 percutaneous drainages have been performed at 51 patients from 76 cases of hydatid hepatic cysts (67,1%). There were 26 men and 25 women, and the age ranged from 19 to 78. 7 patients have had 2 hydatid hepatic cysts or more and 2 procedures were performed at 3 of those patients; other 11 patients needed the second procedure during the surveillance.

Results: The evolution of the patients was favorable, and the surveillance was 2 years post-intervention at least. There were no major surgical adverse effects. We defined as an expected result obtaining a scar lesion or a small cavity with calcified walls (hyperechoic). Only 2 (3,9%) patients needed conversion to open surgery. The complications we have faced were represented by the cystic-biliary fistula in 15 cases (29,4%) and the re-opening of the cyst's cavity in 11 cases (21,67%).

Conclusions: The percutaneous treatment of CE is safe and effective, following the correct assignation according with the cysts' type. The percutaneous treatment of CE is an easier alternative to the open surgery and has lower rate of complications and relapses, and a shorter hospitalisation. Now routine, it becomes slightly the first option for invasive treatment of CE. The role of open surgery is restricted to CE with severe complications.

Key words: hydatid cyst, minimally invasive techniques, PAIR, Mo-CAT, percutaneous drainage, residual cavity

Background

Human echinococcosis is a severe zoonosis caused by *Echinococcus* (E.) tapeworms carried in the small intestine of carnivores, being larval forms (metacestodes). Among those species, two are often seen in the medical practice – *E. granulosus* and *E. multilocularis* – causing cystic echinococcosis (CE) and alveolar echinococcosis (AE), respectively.

Human CE is highly endemic in large regions of Mediterranean area, Eastern Europe, South America, the Near and Middle East, East Africa, Central Asia, Australia, New Zealand, China and Russia,. In Romania, over 1000 new cases of CE are found every year.

Almost any organ could be affected in CE by

metacestodes – the larval forms of the parasite. The main involved organs are the liver (75%) and the lungs (5-15%), followed by spleen, brain, heart, kidneys, muscles, bones (1).

CE Diagnosis

Clinical findings

After an undefined and variable incubation period, CE may become symptomatic if active cysts exert pressure on adjacent tissue or induce other pathologic events (1,2). The liver is the most common location for cysts to develop (69 -75%). The development of a cyst is slow and usually without specific clinical manifestations. However, mechanical, toxic or

septic effects can result in complications (21%). In general, clinical manifestations associated with liver cysts are divers, with patients presenting with abdominal pain, dyspepsia, fever or allergic manifestations, including a rash. Rupture to the biliary tree is a common occurrence (1,3,4), presenting with signs of cholangitis and/or bile duct obstruction (5).

Serology

Obviously, nor the intradermic reaction Cassoni is no longer used, neither complement reaction.

Sensitivity is variable: between 85 and 98% for liver cysts, 50–60% for lung cysts and 90–100% for multiple organ cysts with different locations, if serum antibody detection is the main method of serological diagnosis using indirect hemagglutination, ELISA, or latex agglutination, with hydatid cyst fluid antigens (6–9). Specificity of those tests is limited by cross-reactions due to other cestode infections (*Taenia solium*), some other helminth diseases, liver cirrhosis, malignancies, and presence of anti-P1 antibodies. In those dubious cases, confirmatory tests should be used (arc-5 test; Antigen B (AgB) 8 kDa/12 kDa subunits or EgAgB8/1 immunoblotting) (6–8). Immunoblotting is best for differential diagnosis and may be used as a first-line test (10). There is no significant diagnostic advantage using detection of parasite-specific IgE or IgG4. Eosinophil count, IgE and IgG4 are more elevated after rupture/leakage of cysts (6,11).

Imaging

US examination is the basic imagery technique in CE diagnosis for every abdominal locations, and could visualize cysts in other extraabdominal locations: smooth tissues, heart, even lung for peripheral cysts.

In 1995, the WHO-IWGE developed a standardised classification that should be applied, and allow a natural grouping of the cysts into three relevant groups: active (CE1 and 2), transitional (CE3) and inactive (CE4 and 5) (12). WHO-IWGE classification is the basis for the present guidelines; it differs from Gharbi's classification introduced in 1981 (13) by adding a “cystic lesion” (CL) stage (undifferentiated), and by reversing the order of CE Types 2 and 3. CE3 transitional cysts may be differentiated into CE3a (with detached endocyst) and CE3b (predominantly solid with daughter vesicles) (14). CE1 and CE3a are early stages and CE4 and CE5 late stages (*Fig. 1*).

Thoracic and bone involvement can be easily diagnosed using conventional X-ray exams.

Computed tomography (CT), and magnetic resonance (MR) imaging, with one T2-weighted imaging sequence are indicated in several particular presentations of CE: (1) subdiaphragmatic location, (2) disseminated disease, (3) extraabdominal location, (4) abscess and (5) pre-surgical evaluation. If possible cholangiopancreatography (MRCP) is needed in complicated cysts (abscess, cysto-biliary fistulae). MR imaging has better visualization of liquid

Figure 1. Ultrasonographic (US) appearance of CE according WHO-IWGE standardized classification

Figure 2. US, MRI and CT appearance of CE using WHO-IWGE Classification

areas within the matrix than CT (6,15) (*Fig. 2*). ERCP with or without sphincterotomy (ES) is a valuable technique especially for the cysts opened into the biliary tree.

Treatment Principles

Nobody can claim a “best” treatment option for CE. Furthermore, there is no clinical trial which analysed all the different treatment modalities, including “Watch and Wait.” Treatment indications are based on cyst characteristics (size, location, number, stage, complications), patient-related criteria (age, pregnancy, other pathologies, therapeutic risks, compliance of patients to long-term monitoring), available medical/surgical experience and equipment. Practically, it becomes a stage-specific approach, and could be complex (6).

Classically, albendazol 800 mg daily remains the basic treatment for CE, which is the start of every therapeutic approach, except the major emergency cases. The surgical treatment is preferred for large cysts (over 5 cm in diameter) or non-responsive cysts. After surgery, albendazole is carried on for at least 1 month (16,17).

The minimally invasive treatment for CE is one of the options of the WHO-International Working Group on CE (WHO-IWGE) state-of-the-art on Cystic Echinococcosis, becoming the first option of treatment since 2015. PAIR (Puncture, Aspiration, Injection, Re-Aspiration) is widely used now as treatment for hydatid hepatic cysts type CE1 and CE3a according WHO-IWGE classification, larger than 5 cm. It was proposed in 1986 by a tunisian team led by

Ben-Amor (18) and spread in 90 by Filice and Brunetti (19) in Italy. Placing a catheter at the end of the procedure (PAIR-D) is recommended for larger cysts. Akhan, in Turkey, has developed a new technique increasing the catheter's diameter and setting it under fluoroscopic control (MoCaT), using also a sustained lavage with NaCl 0,9%; after the complete evacuation of the cyst, verifying there is no biliary fistula, the cavity is washed for 7 min. with 96° alcohol; he recommends this method for type CE2 and CE3b cysts (20). Prophylaxis with ABZ 4 h before and 1 month after PAIR is mandatory (21).

The risks of these minimally invasive techniques are the same as the risks of every puncturing procedure (bleeding, infection, damage of the tissues), and those specific for CE:

- Anaphylactic shock or allergic reactions;
- Spillage of the cystic content;
- Too fast evacuation of the cyst may lead to open the biliary fistulae;
- Persistence of the daughter-vesiculae due to the incomplete evacuation or incorrect check-up of the procedure, which may lead to relapse;
- Sclerosing colangitis if the parasiticide compounds (96% alcohol) is used when the biliary fistula exist;
- Systemic toxicity of 96% alcohol or even NaCl 30% if the used amount is large (giant cysts) (22).

Material and Methods

The General Surgery Clinic of the „Colentina”

Teaching Hospital has implemented this minimally invasive techniques in treatment of CE in partnership with Hacettepe University from Ankara – Prof. Akhan O., as a part of the European Project FP7 HERACLES, dedicated to the hydatid disease.

The criteria to assign a patient for a minimally invasive treatment are:

- Cyst – related criteria:
 1. size: cysts over 5 cm in diameter;
 2. cyst staging: CL, CE1, CE3a cysts benefit by PAIR technique; CE2, CE3b, selected cases of CE3a and CE4 benefit by MoCaT technique;
 3. multiple cysts: they could benefit of those techniques;
 4. infected cysts, abscesses derived from CE: MoCaT;
- Patient – related criteria:
 1. pregnancy;
 2. non-responsive patients to the albendazol treatment;
 3. patients to whom the open surgical procedures could not be applied;
 4. post-operative relapses;
 5. patients who refuse open surgery, but need an invasive procedure.

Obviously, there are some contraindications as following:

- Non-cooperating patients;
- Cerebral, cardiac, medullar CE;
- Inactive / calcified cysts;
- Rupture of the cysts into peritoneal cavity, urinary tract, bronchiae;
- Cysts opened into the biliary tree (only for PAIR technique).

During 03.2014 – 03. 2018 period, 38 PAIR,

28 MoCaT procedures and 7 percutaneous drainages have been performed at 51 patients from 76 cases of hydatid hepatic cysts (67,1%). There were 26 men and 25 women, and the age ranged from 19 to 78.

7 patients have had 2 hydatid hepatic cysts or more and 2 procedures were performed at 3 of those patients; other 11 patients needed the second procedure during the surveillance. We performed 2 or more PAIR procedures on the same patient, if he had 2 or more CE1 cysts. If the cysts were in various stages (CE1 and 2, 3a, 3b), we performed PAIR and MoCaT in the same session. We didn't perform 2 MoCaT procedures at the same patient, nor in the same session, neither in seriated sessions.

Most of the cysts were found in the VIIth, Vth and IIIrd hepatic segments (14, 11 and 10 cysts respectively), followed IVB, VI and VIII segments. There was no preferred type of cysts according the location (*Graphic 1*).

According the stage of the cyst, we have found CE1 and CE3b type cysts mainly (29 and 20 cases respectively), followed by CE3a type cysts in a smaller number (7 cases). CE2, CE4 type cysts and CL were few in number (*Graphic 2*).

We used PAIR technique (Punction, Aspiration, Inactivation, Reaspiration) especially for CE1 type cysts, and very rare for CE3a type cysts (*Figs. 3-7*). We used CHIBA needles, 18G, 15 cm long. The cysts were punctured under ultrasound guidance, using regular ultrasound devices with 3,5 MHz convexe probes. Over 50% of the hydatid liquid is aspirated, then ultrasound compound is injected and the fluoroscopic control

Graphic 1. Cysts distribution after the evolution stage, following the location

Graphic 2. Cysts distribution into the segments according to the evolution stage

Figure 3. PAIR: puncturing the CE1 cyst

Figure 4. PAIR: the cyst is filled with NaCl 30%

Figure 5. PAIR: the cyst is re-aspirated

Figure 6. PAIR: after 3 months

Figure 7. PAIR: after 2 years

is performed (to be sure there is no biliary fistula), then this is aspirated too. The parasiticide compound (NaCl 30%) is injected and left in place for 9 min, then is aspirated and the needle is retracted.

For CE2, CE3b type cysts, even CE3a and CE4 type cysts in selected cases, we performed Modified Catheterisation using a 14 Ch pigtail catheter - Merit Medical locking drainage catheter 14F (*Figs. 8-15*). The first step is to

puncture the cyst, under ultrasound guidance. A small amount of hydatid liquid is extracted by aspiration (note the type of the cyst, which doesn't allow to aspire much more), then the fluoroscopic compound is injected and the fluoroscopic control is performed. The guide wire is inserted, and the path is dilated using the kit dilators. Then the 14 Ch pigtail catheter is inserted and an aggressive and effective lavage is performed, extracting the

Figure 8. The CE3b cyst is punctured

Figure 9. The guide wire is inserted

Figure 10. The 14Ch pigtail catheter

whole hydatid material within the cyst (magma, liquid, vesiculae). After ultrasound and fluoroscopic control which shows the complete evacuation, the catheter is left in place; if there is no biliary flow, a lavage of the

cavity using 96 alcohol for 9 min is performed. If biliary flow is seen, the catheter is kept in place till the biliary fistula would be closed, then the alcohol lavage is performed. Then the catheter is extracted.

Figure 11. Cyst's content is extracted: liquid, magma, membranes

Figure 12. CE3b cyst at the beginning of the procedure

Figure 13. At the end of MoCaT

Figure 14. Control image after 1 year

Figure 15. Control image after 1 year and 6 months

Graphic 3. The use of minimally invasive techniques according the cysts location

As parasiticide compound, 30% sterile saline solution (NaCl) or 96° alcohol were used, according the technique. Both types of minimally invasive procedures (PAIR and MoCaT) could be used no matter the location of the cysts. The single condition to choose a technique was the stage of the cyst (*Graphic 3*).

Results

The evolution of the patients was favorable, and the surveillance was 2 years post-intervention at least. There were no major

surgical adverse effects. Mortality was 0. We defined as an expected result obtaining a scar lesion or a small cavity with calcified walls (hyperechoic) (*Figs. 6-7, 12-15, 16-20*).

In 6 cases who underwent MoCaT procedure (21,43%), a persistent collection of the residual cavity has been developed, which has been drained percutaneously. The catheter was left in place for 2 to 7 days. The MoCaT drainage was used to treat 5 residual cavities after PAIR (13,16%), which didn't shrink after 1 year, due a biliary fistula. In those case, the dead proliferous membrana, which has been

Figure 16. CE3b cyst in the IIIrd segment

Figure 17. The cyst at the end of MoCaT procedure

Figure 18. The scar after 3 months

Figure 19. The scar after 6 months

Figure 20. The scar after 15 months

detached and fallen on the bottom of the cyst, could be evacuated, too. The results were also favorable.

Only 2 (3,9%) patients needed conversion to open surgery. One patient had a cyst which had a tough wall which could not be penetrated by the catheter's tip. The other patient suffered a severe anaphylactic shock during a PAIR procedure for a CE1 large cyst; the procedure was ceased, and the medical team decided after the remission of this complication to convert it to open surgery. In both cases, partial pericystectomy (de – roofing the cyst and removing the dome of the cyst as much as possible), cystectomy and drainage (Lagrot procedure) was performed.

The lenght of hospitalisation was 3-4 days for patients who underwent PAIR technique, and 6 - 22 days for those who underwent MoCaT technique.

The patients have been under our surveillance at least 2 years after the minimally invasive procedures.

The complications (*Table 1*) we have faced during the treatment of CE using the minimally invasive techniques were represented by the cystic-biliary fistula in 15 cases (29,4%) and the re-opening of the cyst's cavity in 11 cases (21,67%). The low debit fistulae, which were the most, closed under conservative treatment; those which had a debit over 500 ml/day needed endoscopic sphyncterotomy (3 cases). They are a complication which belongs to the cyst's stage (CE2, CE3a,b, CE4), not to a specific technique. Re-opening of the cyst cavity was due to the accumulation of lymph, bile and leucocytes, having no clinical sign (pain, fever,

jaundice, etc.). This was a complication linked directly to the our technique. All these patients needed percutaneous drainage which solved this complication. This drainage was left in place for 3-5 days, then it was removed after ultrasound control.

Discussion

For every invasive technique used in the treatment of CE, the rule is to associate albendazole 800 mg per day for at least 1 week before and 1 month after the procedure (22-24). The romanian experience (Crețu and al.) advocates 3 and even 6 months post-procedural (17). Applying this recomandation, the risk of relapse is highly reduced.

The question if the percutaneous treatment is safe and effective was debated in many articles at the late '90 and early 2000, especially for PAIR technique. Especially associated with albendazole, PAIR is a good option for CE1 and even CE3a cysts (23, 25-27). The rate of complications was comparable: 28.8% for Men et al. (25), who counted also the cyst-biliary fistulae. On the other hand, in a larger number of patients, Kahriman et al. counts only perihepatic hemorrhage, cavity infection, anaphylaxis and allergic reactions, thus he declares only 6,3% complications; the cyst-biliary fistulae are not described. If we consider the same categories, there were only 6 cases (anaphylaxis – 2, allergic reactions – 4), and our percent should be 11,8%.

As a newer procedure, Akhan's Modified Catheterisation (MoCaT) results were introduced in 2014 and 2017. On a cohort of 75 cysts, CE2 and CE3b type, Akhan et al. said that MoCaT is associated with a lower recurrence rate than other techniques, therefore it appears to be safe, reliable and efficient alternative" (20, 28). The indication to use minimally invasive techniques in treatment of CE has dramatically changed during the last 10 years. In 2008, in a state-of-art article on CE, Junghanss and al. recognised PAIR as a good and large used technique for CE1 and CE3a cysts, but defined the „non-PAIR percutaneous techniques" for CE2 and CE3b cysts as „rarely practiced”;

Table 1. Complications seen after using minimally invasive techniques for CE

Complication	Incidence
Refilling the cavity	11 (21,67%)
Biliary fistula / fistulae which needed SE	15 (29,4%) / 3
Anaphylactic shock	2
Conversion to open surgery	2
Bleeding	0
Intracavitary Abscess	0
Colangitis	0
Cutaneous Rush	4
Association of minor signs (rush, hTA, fever)	1

instead, they advocated surgery (14). In 2010 Brunetti and al. put both percutaneous treatment and surgery as options in treatment of CE for CE1,2,3a and 3b stages (6). In 2015, Menezes da Silva repeated those indications, but the percutaneous treatment is written first at every stage of CE (29).

We believe the minimally invasive techniques PAIR and MoCaT are indeed effective and safe methods of treatment, being performed quite easily. Their results are good and invite us to use them as the first choice; the role of the open surgery remains for those cases with severe complications. The problematic evolution of the remaining cavities could be solved with the minimally invasive techniques. It is very important to emphasise that minimally invasive techniques could approach any cyst, no matter the location. They are also the least aggressive techniques regarding the abdominal wall damage.

Conclusions

1. The percutaneous treatment of CE is safe and effective, following the correct assignation of CE1, CE2, CE3a and b and selected cases of CE4 type cysts.
2. The percutaneous treatment of CE is an easier alternative to the open surgery.
3. Percutaneous techniques have lower rate of complications and relapses, and a shorter hospitalisation.
4. Once experimental, now routine, they become slightly the first option for invasive treatment of CE.
5. The role of open surgery is restricted to CE with severe complications.

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Conflict of Interest

The authors declare no conflicts of interests.

Author's Contributions

All authors have equal contribution.

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