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Percutaneous Treatment of Giant Cystic Echinococcosis in Liver: Catheterization Technique in Patients with CE1 and CE3a

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Abstract
Purpose This study aimed to evaluate the efficacy, safety, and follow-up results of the percutaneous treatment of cystic echinococcosis (CE) patients with giant hepatic cysts (at least one diameter > 10 cm).
Methods Between January 2013 and 2018, 31 CE patients with 34 giant cysts classified as CE1 or CE3a (Gharbi type 1 or 2) according to the World Health Organization criteria and treated with the catheterization technique were analyzed retrospectively.
Results Thirty-four giant hepatic cysts were treated using the catheterization technique. Technical success was 100%. One procedure was sufficient for 27 of these cysts, while six patients underwent a second procedure due to recurrence, recollection or complications; one did not accept a repeat procedure and decided to refer to surgery due to pain. Ten (29%) major complications developed. The overall clinical success was 97%. The mean follow-up period was 20 months (5–61 months), and the total reduction in the cyst volume was 92%.
Conclusion The catheterization technique is effective in treating giant CE with acceptable complication rates.
Level of Evidence Level 4, Clinical Investigation.

Keywords Giant cystic echinococcosis · Giant hydatid cyst · Catheterization technique · Percutaneous techniques · Cystobiliary fistula · Abscess · Glue embolization · Coil embolization · Cavity infection · Fistula embolization

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Introduction

Although surgery is the traditional method for treating hepatic cystic echinococcosis (CE), medical, percutaneous, and "wait and watch" treatment alternatives have also emerged in the last four decades. Percutaneous techniques have been utilized safely with lower morbidity and shorter hospital stays [1–3].

CE can be classified according to the criteria of Gharbi or the World Health Organization (WHO). The WHO

classification was specifically developed to distinguish active and inactive types, which allows for clearly identifying the CE cases that need to be treated. In addition, cysts are classified depending on their diameter as "small CE" if smaller than 5 cm, "medium CE" if between 5 and 10 cm, and "giant CE" if larger than 10 cm [4]. Although the efficacy and safety of percutaneous techniques have been demonstrated in different patient groups and different types of cysts, few studies have confirmed techniques for treating large cysts [5–10].

The percutaneous techniques used in the treatment of CE are puncture, aspiration, injection and reaspiration (PAIR), catheterization [6], and modified catheterization (MoCaT) [11] techniques. PAIR and catheterization techniques are usually applied for the treatment of CE1 and CE3a. In contrast, MoCaT dedicated to the percutaneous treatment of CE2 and CE3b additionally involves the removal of the germinal layer and the laminated membrane (endocyst) [12].

The catheterization technique with hypertonic saline and alcohol, briefly described as the catheterization technique, was described by Akhan et al. [6] in an animal study and a series with long-term results [7]. This study aimed to evaluate the efficacy, safety, and follow-up results of percutaneous treatment involving the use of the catheterization technique in giant CE1 or CE3a according to the WHO classification.

Materials and Methods

Study Design and Patient Population

This study was approved by the local ethics committee, and informed consent was waived due to the retrospective nature of the study. Between January 2013 and 2018, 34 giant cysts (at least one diameter > 10 cm) belonging to 31 CE patients were treated. In addition to the giant cysts, six medium (5–10 cm) and three smaller (< 5 cm) cysts were detected in these patients. According to the WHO criteria, 26 of the 34 giant cysts were evaluated as CE1 (Gharbi type 1) and eight as CE3a (Gharbi type 2).

Fourteen of the patients were male, and 17 were female. The mean age was 49 years (range 19–85). Preoperative ultrasonography was performed on all patients. In addition, preoperative computed tomography images were available for 16 patients and magnetic resonance images for one.

Interventional Procedures

In all patients, albendazole was started at a total dose of 10–15 mg/kg at least 1 week before the procedure and 4 weeks after the procedure [7, 13]. All patients fasted for at least 8 h before the procedure and underwent complete blood count, coagulation parameters, and biochemical tests. The procedures were performed under sedo-analgesia. With the recommendation of the anesthesia department, premedication containing antihistaminic and steroid was administered to each patient to reduce the risk of anaphylaxis.

For small and medium cysts, either the PAIR or catheterization technique was employed [2]. To treat giant cysts, the catheterization technique was used, as described by Akhan et al. [6]. First, the cyst was punctured using the Seldinger technique with an 18-gauge needle and 20% of the calculated volume was aspirated, before 10% of contrast injection. Then, 80–90% of the calculated volume was aspirated by taking care not to remove the needle tip from the cyst, and 30% hypertonic saline was injected into the cavity. After waiting approximately 10 min and observing the separation of the endocyst from the adventitia (pericyst), an 8–12 Fr locked pigtail catheter with multiple side holes was inserted into the cavity using the modified Seldinger technique before aspirating the cyst content. After a possible cystobiliary fistula was excluded, 95% absolute ethanol equal to 30–50% of the initially estimated cyst volume, never exceeding 200 cm^3 per session, was introduced into the cyst [14, 15]. After 10 min, the catheter was left for gravity drainage. If the daily drainage was less than 10 cm^3, the cavitogram was repeated to confirm the lack of communication with the biliary system; ethanol sclerosis was undertaken as described above before catheter withdrawal. If the daily drainage was more than 10 cm^3, the catheter was kept in place for gravity drainage. Ethanol sclerosis at regular intervals was continued until the daily drainage was reduced below 10 cm^3, before the catheter was removed.

In cases in which a cystobiliary fistula (CBF) was detected during cystograms, the patient was followed up without hypertonic saline or ethanol application. If the amount of daily drainage was not reduced and CBF persisted, the patient was referred to endoscopic retrograde cholangiopancreatography (ERCP). If necessary, a biliary plastic stent with papillotomy was placed. If CBF was closed on the control cystograms, ethanol sclerosis under fluoroscopy was performed until the daily drainage was under 10 cc.

In patients with cavity infection during catheterization, antibiotic treatment was initiated according to the results of culture beside drainage.

Technical success was defined as successful catheter introduction into the CE. Clinical success was defined as cases with no mortality and no recurrence.

Follow-Up

Follow-up was performed 1, 3, 6, and 12 months post-procedure; then, continued annually. The size, volume, wall, fluid content, and ratio of the cyst and solid areas were evaluated by ultrasonography, and the patients' complaints were noted. During the follow-up, additional images, CT for 10 and MR for two patients, were also obtained. The term recollection is used for cysts with increased fluid component during follow-up but no signs of viability or infection. In contrast, the term recurrence refers to cysts with increased fluid components but with signs of viability.

Results

Thirty-four giant hepatic cysts of 31 CE patients were treated with the percutaneous catheterization technique. Presenting symptoms were abdominal pain in 12 (39%) patients and abdominal discomfort in 11 (35%). CE was found incidentally remaining of the patients. Twenty-eight patients had one giant cyst, and three had two giant cysts each. Two of these patients had pulmonary cysts and underwent surgical operation pre- and post-percutaneous procedure, respectively. The average cyst volume was 701 cm^3 (345–1787). Six patients (19%) required catheterization for one day. The mean and median catheterization times for all patients were 12 and 9.5 days, respectively (1–35). The mean sclerotherapy sessions required for sclerosis were 5.4 (1–14).

Catheters were inserted all the patients successfully; technical success was thus 100%. The separation of the endocyst from the adventitia (pericyst) was seen in all the CEs after the hypertonic solution injection. Twenty-seven of the 34 giant cysts were resolved with a single procedure, six required a second procedure due to recurrence, recollection or complications, and one patient did not approve the second procedure and requested surgical treatment.

The mean and median lengths of the hospital stay were 2.1 and 2 days, respectively, ranging 1–9 days. For the second procedure performed due to complications or recurrence, the mean and median duration of the hospital stay were 7.8 and 7 days, respectively, ranging 2–16 days.

Four of the 31 patients had a total of nine non-giant cysts, of which three were small (< 5 cm) and six were medium (5–10 cm). Three of these cyst lesions were treated with the catheterization technique and six with PAIR. In one patient treated by catheterization, recollection was detected during the follow-up and treated by recatheterization and sclerosis.

Complications (Fig. 1)

Major

Cavity abscess and CBF were observed in five (15%) and four (12%) giant cysts, respectively. In two giant cysts, abscess and CBF were seen together. In two cysts (6%), cavity abscess developed during catheterization as an early complication, and the treatment was continued with appropriate antibiotics. One of these two cysts required a total of 25 days of catheterization. In another patient in whom ERCP and plastic stent placement due to a persistent CBF were performed, abscess formation was treated by adding antibiotics to the drainage. The catheter was withdrawn on day 35. The remaining three patients (9.6%) had late complications and presented to the hospital with abscess formation after the catheter removal. One of these patients was admitted to the hospital four months post-procedure, and the second patient presented one month post-procedure with an abscess. For both patients, catheterization was applied for 18 days and complete recovery was achieved after treatment with appropriate antibiotics. In the last patient who revisited the hospital two months post-procedure due to abscess, the cavitogram revealed CBF despite the absence of a fistula in the first catheterization. ERCP was applied with the placement of a plastic stent. However, the fistula rate did not decrease. Therefore, the cyst was accessed through the existing catheter for the embolization of the CBF tract with coils and complete aspiration, and embolization of the cyst cavity was achieved successfully using the lumen glue (*N*-butyl cyanoacrylate [NBCA]) + lipiodol mixture on day 40 (Fig. 2).

The mean pre-procedural volume of four cysts with CBF (12%) was 886 cm^3 (461, 518, 1095, and 1468 cm^3). The mean catheterization time was 28 days (14–40). Fistulas were not detected on follow-up cystograms in two of these patients, and therefore, alcohol ablation was performed until the amount of drainage went below 10 cm^3, and the catheters were withdrawn on the 23rd and 14th days, respectively. The other two CBF coexisted with abscess formation, as explained above. There was no recurrence during the treatment follow-up of these patients with CBF.

Recollection was only observed in one cyst (3%). In this patient's first procedure, the CE volume was 879 cm^3 and decreased to 387 cm^3 at the four-month follow-up. Since the patient developed abdominal discomfort, ethanol (96%) was administered for sclerosis every other day after recatheterization. When below 10 cm^3 daily drainage, the catheter was removed. Recollection did not recur during follow-up.

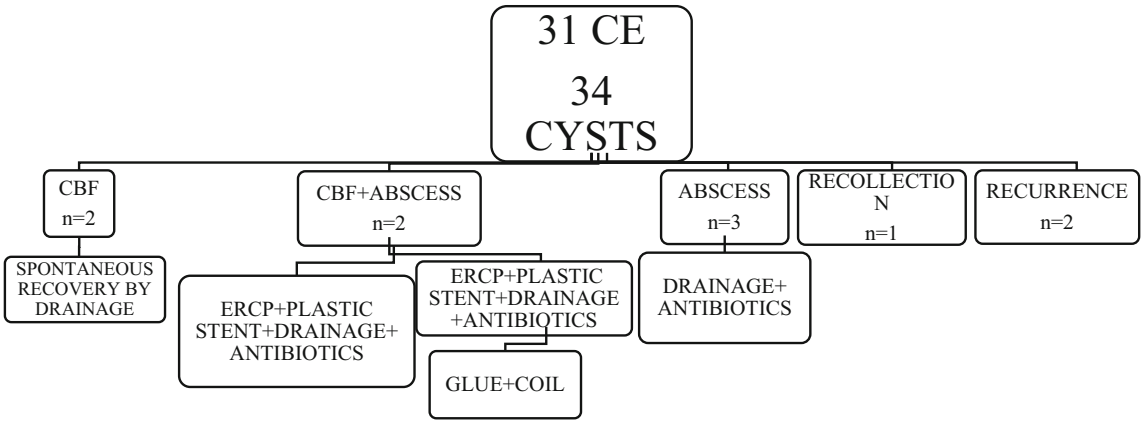

Fig. 1 Major complications and recurrence. CBF: Cystobiliary fistula

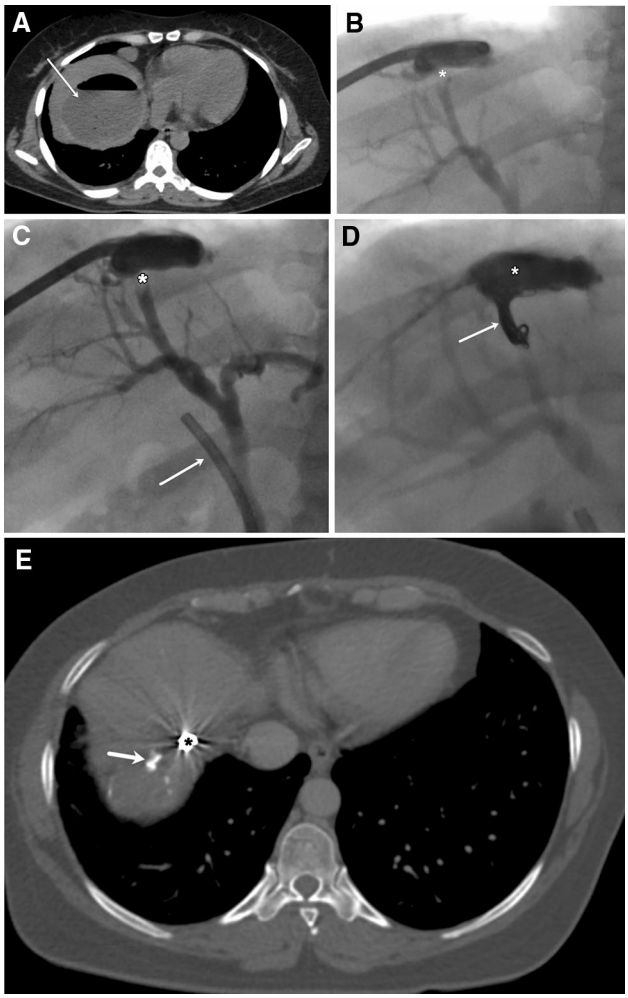

Fig. 2 A) A computed tomography (CT) scan obtained 2 months after intervention demonstrates a liver abscess (arrow). **B** Cavitography shows a thick cystobiliary fistula (CBF) (asterisk). **C** A plastic stent (arrow) for CBF (asterisk) is shown in fluoroscopic image. **D** CBF embolization with coil (arrow) and cavity embolization with glue and lipiodol mixture (asterisk). **E** At the second-year control, CT scan shows metallic coil artifact (asterisk) and glue + lipiodol cast (arrow)

Minor

As catheter dislocation occurred in one cyst (3%) on day 10, recatheterization was required. The total catheterization time was 25 days.

The pre-procedural volume (1036 cm^3) decreased to a pseudosolid appearance (167 cm^3) at the six-month follow-up. As the patient experienced pain, the patient preferred a surgical operation instead of reintervention. One patient (3.2%) developed urticaria during the procedure and was treated by antihistamines.

Recurrence

Recurrence was noted in two (6%) of the 34 giant cysts. The second procedure was undertaken in the fourth month for the first patient and eighth for the second patient. These patients were catheterized for 6 and 18 days, respectively, with gravity drainage and intermittent administration of a sclerosing agent. No recurrence was observed in the subsequent follow-ups.

Follow-Up

The clinical success rate at the end of the first procedure was 94% due to the recurrences. Following the second intervention, it increased to 97%. In this calculation, the single patient who requested surgery was evaluated as a failure of the procedure. The mean follow-up period was 20 months (5–61 months). The mean volume of cysts during follow-up was 54 cm^3, ranging from 5 to 167 cm^3. The total reduction in the cyst volume was 92%.

Discussion

Different options are available in the treatment of CE. Medical therapy with benzimidazole group drugs alone has often been found to be ineffective, but they provide benefits when combined with surgery or percutaneous treatment [16, 17]. Surgical treatment options consist of conservative, radical, and laparoscopic methods, as well as the management of the residual cavity using external tube drainage or omentoplasty, which is particularly important for conservative and laparoscopic surgery [18]. The morbidity of conservative surgical methods varies depending on the technique used to manage the residual cavity, but in most publications, it exceeds 30%. Recurrence rates are also reported to be above 10% [19, 20]. The morbidity rates of conservative surgical methods are significantly higher than radical and laparoscopic surgery [18]. Therefore, conservative surgical methods are not recommended, especially in combination with external drainage [18, 21, 22]. To minimize the complications and recurrence rates related to the residual cavity, radical surgical methods, such as pericystectomy and hepatic resection, are recommended, but the morbidity of these methods also increases as the size of the cyst increases and the cyst approaches the central area. Similarly, due to the risk of peritoneal dissemination and the higher surgical risk of the central and posterior areas, laparoscopic surgery does not present as an optimal treatment [18, 23]. Different publications suggest that the most important causes of increased surgical morbidity are the localization of the cyst, the presence of biliary communication, the size of the cyst, and cystobiliary fistulas, which may also be associated with large cysts [18, 23, 24]. In brief, surgery in giant CE is riskier than in small cysts.

In the current study, the catheterization technique was used in all giant CE1 and CE3a. The duration of the catheter depends on the cyst size and type, the presence of CBF, and infection of the cyst [5, 25]. In the literature, different catheterization times have been observed. For example, three different studies, in which 177 patients (most with CE1 and CE3a and non-giant cysts) were treated with the catheterization technique, reported that the catheterization time was one day (82%) for most patients and the mean value varied between 2 - 5 days [7, 8, 26]. In another study, Men et al. only treated giant CE1 cysts in 15 patients using the catheterization technique. The mean volume of the cysts was 2,400 cm^3 and the mean catheterization time was calculated as 32 days. In the current study, the mean and median catheterization times were 12 and 9.5 days (1–35), respectively.

CBF is one of the most important complications of percutaneous treatment since it significantly increases the catheterization time [10]. In addition, secondary procedures involving papillotomy and/or biliary stent placement via ERCP are often needed in the treatment of CBF. Although there is no common cutoff value for CBF formation in terms of size, many publications have suggested that the cyst size is an independent risk factor. This result was attributed to the rupture of the increased cyst pressure into peripheral bile structures as the cyst diameter increased [27, 28]. In studies investigating percutaneous treatment in non-giant cysts [7, 8, 26], cysts of various sizes with more heterogeneous groups [9, 29], and giant cysts [5], CBF rates have been reported of 3.2–6%, 0–6%, and 13%, respectively. In the current study, the rate of CBF was 12%, which is consistent with previous publications indicating the increased risk of CBF in larger cysts.

Men et al. found CBF at a late stage after treatment (24 months post-treatment) in a patient who had not initially presented with a fistula [8]. Similarly, in the current study, one of the patients discharged after the first procedure presented to the clinic at the second month due to abscess formation, and during the drainage and antibiotic treatment, CBF was detected. This patient had no indication of CBF in the first procedure. The detection of CBF only as a late complication post-treatment may be due to the inhibition of contrast distribution by the endocyst during cystography in the first procedure [25], or depending on the nature of the case, the difficulty of aspiration of the abscess with a negative pressure may have caused CBF [25, 30]. ERCP with stent placement was performed in the treatment of this patient, but since the drainage did not stop, the fistula opening was coiled and the cavity was aspirated and closed with glue using the technique previously described by Canyigit et al. [31].

Cavity infection or abscess formation is an important complication that prolongs the catheterization time, as in CBF [10]. In studies investigating percutaneous treatment in non-giant cysts [7, 8, 26], cysts of various sizes with more heterogeneous groups [9, 29], and giant cysts [5], the cavity infection rates have been reported in the range of 2.8–3.6%, 2.1–5.8%, and 26.6%, respectively. Longer catheterization time and application of ERCP during catheterization are listed among factors that increase the risk of cavity infection [10, 25]. In the present study, a total of five abscesses (15%) were observed throughout the study period. All these cysts were treated with catheter drainage and appropriate antibiotics.

Recurrence rates depend on the techniques used after percutaneous treatments and the type of the cyst; however, they generally range from 0–4% in the literature, especially for the percutaneous treatment of non-giant CE1 and CE3a cysts [7, 8, 26, 32, 33]. Men et al. reported no recurrence in the giant cysts in their 15-patient series [5]. In the current study, we calculated the recurrence rate as 6%, which is

slightly higher than the general rates reported in studies with non-giant hydatid cysts in the literature.

In giant cysts, the elimination of the mass effect and significant reduction of the residual volume post-treatment are more important than in non-giant cysts [5]. In percutaneous therapies, the volume reduction varies between 60 and 100% [3, 7, 26, 29, 33]. In their paper presenting the results of percutaneous treatment in CE patients with giant cysts, Men et al. reported an average volume reduction of 98.6%. In the current study, the mean volume reduction was 92%. However, in one of the patients, despite the 84% reduction in the cyst volume, this patient had persistent pain. As the volume of the cyst continues to be reduced for 2 years post-treatment [6, 7], we informed the patient that the volume reduction might continue. Although we could apply medical treatment or perform a second procedure, the patient preferred surgery.

The term recollection is used to refer to cysts that do not show any signs of viability after treatment but continue to collect fluid [10]. It is thought that recollection is caused by the transudate originating from the adventitia (pericyst) into a cyst in which the endocyst component has been destroyed [5, 34]. Recollection after percutaneous treatment is considered due to insufficient sclerosis [6, 35]. In this study, one recollection was observed (3.2%), and this patient was retreated with ethanol successfully. In their paper published in 2017, Akhan et al. reported recollection in two cysts (2.7%) among patients with CE type 2 and CE3b cysts. The recollection was not mentioned in the other papers, so the rates of this complication were not compared.

The hospital stay for CE patients' treatment varies according to the type of cyst, the treatment being applied, and the complications that develop [18]. Patients with non-giant CE1 and CE3a cysts stayed < 3 days, but this period is prolonged in the presence of CBF or abscess formation [5, 8, 26]. For giant cysts, Men et al. reported the hospital stay as 2–5 days, which increased to 8.7 days when complicated cysts were included in the calculation. In the current study, the mean duration of hospitalization was 2.1 days, ranging from 1 to 9 days. For the patients who required a second procedure due to complications or recurrence, the mean hospital stay was 7.8 days with a range of 2–16 days.

The primary limitation of this study is the small sample size and retrospective nature. In addition, since different treatment modalities were not used, it was not possible to compare the results according to the treatment option. Lastly, the follow-up duration was relatively short for CE.

Conclusion

The current study on the treatment of giant CE1 and CE3a showed that the percutaneous treatment of giant hepatic cysts (> 10 cm) using the catheterization technique is effective and reliable. The higher complication and recurrence rates with prolonged hospital stays are associated with cyst diameters larger than 10 cm.

As surgery is associated with higher complications in this group, a prospective randomized trial is needed to compare the results of percutaneous treatment and surgery for giant CE1 and CE3a.

Compliance with Ethical Standards

Conflict of interest None.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional ethics committee.

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