Treatment of Hydatid Disease of the Liver
Evaluation of a UK Experience

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Key Words
Hydatid cysts  •  Cyst biliary communications  •  Bile leak

Abstract
Background: Hydatid disease of the liver though endemic in many countries, is rare in the UK. We evaluated a 16-year experience of treating hydatidosis using a management protocol combining surgery with anti-scolicidals.

Patients and Methods: There were 30 patients. 14 (47%) males, median age 41 (range 25–72) years, of whom 21 (70%) were symptomatic. Diagnosis was by serological tests and imaging. All had disease confined to the liver and received peri-operative anti-scolicidal drug therapy.

Results: The initial 4 (13%) patients received praziquantel combined with albendazole for 2 weeks and the following 26 (87%) patients received two cycles of albendazole 400 mg twice daily for 28 days, with a 14-day break in between. However, 2 (7%) patients could not tolerate albendazole, one due to GI side effects and the other developed deranged liver functions. These 2 patients subsequently received praziquantel for 2 weeks. All patients underwent surgery. Subtotal cystectomy was carried out on 29 (96%) patients and 1 patient required a segmentectomy. Cystobiliary communications were identified in 15 (50%) of patients which were oversewn using fine absorbable sutures. Of these, 7 had the bile ducts decompressed using a T tube, with only 1 developing a post-operative bile leak. In comparison, 8 were not drained of which 6 leaked (p = 0.03). The median post-operative hospital stay was 8 days (range 5–24). Patients who developed post-operative bile leaks, however, needed prolonged abdominal drainage for a median of 21 days (range 18–24). Two (7%) patients developed histologically proven recurrent disease. The median follow-up was 56 months (range 3–87).

Conclusion: Surgery combined with anti-scolicidal therapy proved effective. Cystobiliary communications are common and, when identified, should result in the biliary system being drained, to avoid post-operative bile leaks.

Introduction

Hydatid disease is one of the commonest zoonoses. It is caused by the larval cysts of Echinococcus granulosus and results in the most severe form of cestodiases in man [1]. The disease is endemic to areas bordering the Mediterranean and Baltic seas, South America, Australia, New...
Zealand, and the Middle East [2, 3]. Though uncommon in the UK, the disease still occurs in England and Wales, especially in those who have been in close contact with dogs, in individuals who have traveled and worked in endemic areas, and in immigrants from high incidence areas [4].

There is no clear consensus on the most ideal form of treatment of the often complicated presentations of hydatid disease. In 1986, a multi-centre study conducted by the World Health Organization concluded that surgery should be the mainstay of treatment for hydatid disease and that medical treatment should be restricted to patients not fit for surgery, or be used to prevent post-operative complications [5]. Liver hydatidosis cannot be considered a ‘benign disease’, as it is progressive and often recurrent (10–15% of cases) [6, 7]. Mortality rates approach 10% in patients with recurrence [8]. For these reasons, surgery has remained the treatment of choice.

Surgical procedures performed for hydatid disease have varied from radical resections and total cystectomies to de-roofing of the cyst. Subtotal cystectomy has also proved effective and has been shown to have comparative operative morbidity and mortality [9]. Minimal access drainage procedures produce comparable ‘cure’ rates for liver hydatidoses [10–12]. This involves percutaneous aspiration of the cyst contents and infusion of scolicidal solutions into the cavity of the cyst. Selection of simple cysts for percutaneous drainage and the use of endoscopic retrograde cholangiography and drainage for cysts that rupture into the biliary system are gaining popularity in regions where the disease is endemic [13, 14]. The availability of scolicidal chemotherapeutic agents has resulted in combined medical and surgical treatment being carried out [15]. However, there still remains uncertainty with respect to what constitutes the ideal treatment for this disease, especially in a country where its incidence is low. We set out to retrospectively evaluate the management of hepatic hydatidoses at a tertiary referral centre in the United Kingdom.

**Patients and Methods**

All patients admitted to our unit with hydatid disease from 1986 to 2002 were studied. Inpatient and outpatient notes were reviewed along with clinical, laboratory, radiological, operative, and post-operative records.

The diagnosis of hydatid disease was made on the basis of positive serology, radiological appearance and histology. All patients had serological tests with an enzyme-linked immunosorbent assay (ELISA) and complement fixation (CF) test for *Echinococcus*. ELISA was positive in 29 (96%) of cases and CF was positive in 24 (80%).

<table>
<thead>
<tr>
<th>Presenting symptom/sign</th>
<th>Number (%) of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic</td>
<td>9 (30)</td>
</tr>
<tr>
<td>Symptomatic</td>
<td></td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>21 (70)</td>
</tr>
<tr>
<td>Abdominal mass</td>
<td>18 (60)</td>
</tr>
<tr>
<td>Jaundice</td>
<td>4 (13)</td>
</tr>
<tr>
<td>Fever</td>
<td>5 (17)</td>
</tr>
<tr>
<td>Recurrent pancreatitis</td>
<td>2 (7)</td>
</tr>
<tr>
<td>Breathlessness due to raised R/hemidiaphragm</td>
<td>1 (4)</td>
</tr>
</tbody>
</table>

1 Some patients had more than one symptom.

Eosinophilia, defined as more than 500 eosinophils per cubic millimeter, was noted in 10 (33%) patients. All patients had ultrasonography followed up by CT scan of the abdomen. One patient who presented with recurrent pancreatitis due to migration of daughter cysts into the bile duct had dilated intrahepatic bile ducts. A magnetic resonance cholangiopancreatography (MRCP) was performed which showed a complex hydatid cyst with multiple opacities in the intrahepatic bile duct. This patient, however, did not have a dilated common bile duct and hence did not require preoperative endoscopic retrograde cholangiopancreatography and decompression [14]. None of the other patients had pre-operative evaluation of the biliary tree.

**Statistical Analysis**

The Fisher’s exact and χ² tests were used for analysis of data where appropriate on SPSS version 10 for Windows (SPSS, Chicago, Ill., USA). p ≤ 0.05 was considered statistically significant.

**Results**

There were 30 patients admitted with hydatid disease during this period. Of these patients, 14 (47%) were male and 16 (53%) were female. The median age at presentation was 41 (range 25–74) years. Twenty-one (70%) patients presented with symptoms. Nine (30%) patients were asymptomatic at the time of presentation with the diagnosis being made incidentally during treatment for unrelated complaints (table 1). Seventeen patients (57%) were life-long UK residents, of which 4 (13%) gave a history of a relative having had the disease. The remaining 12 (43%) patients had either emigrated to the UK from countries where the disease was endemic or had visited endemic areas for long-term stays.

All patients had lesions confined to the liver. Twenty-one (70%) patients had lesions only in the right lobe of the liver, 5 (17%) patients had lesions in the left lobe only,
while 4 (13%) had lesions in both lobes of the liver. Of the cysts in the liver, 21 (70%) patients had solitary lesions while 9 (30%) had multiple cysts. One (4%) patient with multiple cysts had a liver abscess complicating a lesion while another presented with cholangitis. Migration of daughter cysts into the common bile duct resulting in recurrent pancreatitis was the presentation of 1 (4%) patient and has been reported previously [16].

Eleven (37%) of patients had had chemotherapy for *Echinococcus* initiated elsewhere with only 4 (13%) having had a previous surgical procedure carried out prior to admission to our unit (table 2).

**Drug Treatment**

The initial 4 (13%) patients had albendazole used in combination with praziquantel for pre- and peri-operative chemotherapy over a 2-week duration. In accordance with emerging evidence on the efficacy of monotherapy, 400 mg of albendazole alone as a twice daily dose (10 mg/kg per day), was subsequently used in the following 26 (87%) patients. The duration of treatment was limited to cycles of 28 days with a 14-days treatment-free period between cycles [15]. Liver biochemistry was assessed following the first cycle. The operative procedure was carried out mid-way during the second cycle. Two patients had three cycles. This was when the surgery was not carried out during the second cycle. In one this was due to an operative procedure for another indication during the second cycle, and the other had already received two cycles from elsewhere. One (4%) patient developed features of hepatotoxicity to albendazole in the form of deranged liver functions 2 weeks into treatment, which settled once the drug was stopped. Another patient had the drug stopped due to severe gastrointestinal side effects. These patients received praziquantel at a dose of 50 mg per kilogram per day for 2 weeks, to cover the surgical procedure.

**Surgery**

All 30 patients underwent surgery via a bilateral subcostal approach. Following mobilization of the liver, gauze towels soaked in 5% aqueous solution of povidone iodine were used to isolate the lesion and safeguard against the risk of spillage of cyst contents into the peritoneal cavity in 28 (93%) patients (silver nitrate soaks were used in the first two cases). The cysts were first partially decompressed using a wide-bore cannula followed by injection of scolicidal agents. 10% povidone iodine was used in 13 (43%) and hypertonic saline was used in 17 (57%) patients. Since 1995, a transparent disposable 10-mm laparoscopy port has been routinely inserted into the cyst, to enable drainage of the thick particulate matter and daughter cysts from within the cavity. There were no cases of anaphylaxis or allergic reactions during this procedure. The cysts were then opened and any remaining debris was scooped out along with the fibrotic pericyst wall lining the base of the cavity, followed by subtotal excision of the cyst wall. One patient (4%) required a segmentectomy due to the size and proximity of the lesion to major segmental blood vessels. None of the cysts were closely related to the vena cava. All patients also underwent a cholecystectomy.

A careful scrutiny of the remaining cyst cavity was then carried out for cystobiliary communications. It is uncertain if these communications when present were spontaneous or iatrogenic. Since 1996, methylene blue was injected into the biliary tree to identify communications with the cyst cavity. Intra-operative cholangiography was performed if clinical factors or operative findings suggested cystobiliary communications (table 3). These were oversewn with fine absorbable sutures (3/0 PDS). A transcystic biliary drain tube (10 Fr) was used to decompress the system in order to aid healing of the repaired cystobiliary communications. Obliteration if the remaining cavity with omentum was required in three cases. All patients had a 32-Fr passive drain inserted into the peritoneal cavity at the end of the operation.

Cystobiliary communications were identified in 15 (50%) patients. Of these, 8 of the initial patients studied had no biliary drainage. Six (75%) of the patients with no biliary drainage developed post-operative bile leaks. Due to this, the subsequent 7 patients with cystobiliary com-

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**Table 2. Treatment prior to admission to the Liver Unit, Queen Elizabeth Hospital, Birmingham, UK**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug therapy</td>
<td>11 (37)</td>
</tr>
<tr>
<td>Albendazole</td>
<td>8 (27)</td>
</tr>
<tr>
<td>Albendazole + praziquantel</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Mebendazole</td>
<td>2 (7)</td>
</tr>
<tr>
<td>No drug therapy</td>
<td>19 (63)</td>
</tr>
<tr>
<td>No previous operative procedure</td>
<td>26 (87)</td>
</tr>
<tr>
<td>Previous operative procedure</td>
<td>4 (13)</td>
</tr>
<tr>
<td>Percutaneous drainage</td>
<td>2 (7)</td>
</tr>
<tr>
<td>Laparotomy and biopsy</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Laparotomy and drainage of cyst</td>
<td>1 (4)</td>
</tr>
</tbody>
</table>

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Hydatid Disease of the Liver
### Table 3. Operative procedure and outcome

<table>
<thead>
<tr>
<th>Operative procedure</th>
<th>Finding of cystobiliary communication</th>
<th>Operative cholangiography</th>
<th>Post-operative complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>subtotal cystectomy (de-roofing)</td>
<td>None</td>
<td>Done</td>
<td>Persistent bile leak</td>
</tr>
<tr>
<td>segmentectomy</td>
<td>major duct communication</td>
<td>not done</td>
<td>pulmonary complications</td>
</tr>
<tr>
<td></td>
<td>minor duct communication</td>
<td></td>
<td>wound infection</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>none</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>15 (50%)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>1 (4%)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>9 (30%)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>6 (20%)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>13 (46%)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>17 (57%)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>7 (25%)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>3 (11%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1 (4%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>17 (60%)</td>
</tr>
</tbody>
</table>

Communications were drained via a T tube drain, and in comparison one (14%) developed a post-operative persistent bile leak \( p = 0.03 \). Nine (60%) of the cystobiliary communications occurred from major ducts. Five of these patients subsequently developed bile leaks. In six patients, cystobiliary communications were related to minor segmental ducts, and only 2 patients went on to develop post-operative bile leaks \( p = 0.4 \), NS.

Eleven (37%) patients developed post-operative complications. Seven (23%) patients developed post-operative bile leaks which required prolonged drainage. Three (10%) of these patients required ERCP and stenting in order to control the leak. Three (10%) patients developed chest infections and 1 (4%) developed a wound infection. The median post-operative stay was 8 days (range 5–24).

There was no statistically significant difference between the length of hospital stays of the patients who developed a post-operative bile leak and those who did not. However, the 7 patients who developed bile leaks were discharged from the ward with an abdominal drain in situ, which was removed at the out-patients’ clinic, once the bile leak had dried up. These patients had their abdominal drains removed following a median duration of 21 days (range 18–24). All 30 patients were followed up for a median period of 56 months (range 3–86) with clinical assessment, liver tests and abdominal ultrasound scans.

Histology was used to assess viability of the germinal membrane of the cysts and protoscolices. Viable protoscolices were found only in 4 (13%) patients. Two of these were in patients treated with a praziquantel-albendazole combination for 2 weeks. Viable protoscolices were also found in the patient treated with praziquantel following side effects of deranged liver functions for albendazole therapy. One patient, however, had had two cycles of albendazole.

Recent disease, identified as a cyst increasing in size on successive ultrasound examinations, was found in 2 (7%) patients. One of these patients had had praziquantel covering the first operative procedure following severe gastrointestinal side effects to albendazole. This patient developed recurrent disease on the opposite lobe 3 years into follow-up. This recurrence was treated with ultrasound guided aspiration of the cyst under praziquantel cover. The other patient had a recurrent cyst in the same lobe as the previous lesion one year after the first episode. This patient had two further 28-day cycles of albendazole and operative treatment as described above. Both patients have been well since.

### Discussion

The management of hydatid disease is challenging in a country like the UK where its incidence is low. Mortality rates following surgical treatment of the disease is reportedly less than 2% [9, 17]. With repeated surgery for hepatic hydatidoses, complication rates are higher with mortality rates of 10% [2, 8, 18]. Though not supported by controlled studies, it would be logical to manage these rare cases in tertiary referral hepatobiliary centers with standardized management protocols (fig. 1).

The hydatid cyst is a fluid-filled cavity, having an external dense host fibrous reaction (pericyst) and two internal parasite-derived layers (endocyst), which has an outer laminated and inner germinal layer. The germinal membrane is a single layer of cells which gives rise to brood capsules. These contain scoleces, and daughter cysts which float freely in the clear cyst fluid [19, 20]. The hydatid cyst enlarges slowly and remains asymptomatic for many years [9]. In our series, 9 (30%) patients were asymptomatic at the time of diagnosis. Symptoms arise due to pressure effects on adjacent organs or when a complication occurs. Infection and intra-biliary rupture are the most common reported complications [21]. Infection, however, occurred in only 2 (7%) of our patients and intra-biliary rupture in one (4%). This differs to most other series where up to 40% present with complications [21].

Sensitive serological tests of ELISA and CF [22] routinely used to aid diagnosis. ELISA and CF tests, however, rarely become negative even after 10 years, demonstrating the problems of using these tests to establish cure.
Fig. 1. Algorithm for the management of hydatid disease of the liver.

[23], hence these tests were not used for follow-up surveillance in our patients. Eosinophilia was seen in 10 (33%) patients which is less than the 58% seen in another series [9]. This however highlights the fact that eosinophilia may not be a reliable factor in the diagnostic work up of a patient with hydatidoses.

Hydatid disease effects the right lobe more commonly [9], which was the finding in 21 (70%) of our patients. The cysts are more commonly solitary as was the case in 21 (70%) of our patients.

Mebendazole, a benzimidazole, was the first compound tried in the treatment of human hydatid disease [24]. It was found to interfere with the mechanisms of glucose absorption that takes place in the wall of the hydatid parasite, subsequently causing cell autolysis [11]. Mebendazole, however, has a very poor absorption rate and does not reach high concentration levels in the cyst wall [25]. Albendazole, another benzimidazole has been found to have much better absorption achieving higher blood, cyst wall and cyst fluid concentrations [1]. Although albendazole sulphoxide, the active metabolite reaches predictable levels in the serum after an oral dose, cyst fluid levels are slow to reach therapeutic levels and are less predictable [26], thus requiring prolonged duration of treatment. The drug treatment protocol we used was based on previous studies [15]. Albendazole has been found to be effective in up to 80% of cases [15]. In our series we found that this treatment regimen proved to be effective in 86% of cases, with no evidence of viable parasites being found at histological analysis of cyst material post operation. Praziquantel is another agent used in the treatment of hydatid disease. However, at doses that can be used in humans, it does not produce levels adequate to kill the germinal membrane nor does it enhance the effect of albendazole on the germinal membrane [27]. For these reasons the use of praziquantel has been limited to patients who devel-
oped adverse reactions to albendazole. Unfortunately, albendazole is not available in the UK market at present. Albendazole was prescribed to our patients following special order to the manufacturers by the Hospital Trust.

Operative treatment for hydatid disease of the liver has been the treatment of choice [2, 5, 9, 18, 21, 28]. Drug therapy alone does not address the cyst which contains foreign parasitic material which will still remain after drug treatment is complete, and will always be at risk of infection, especially if a cystobiliary communication is present [5]. A review of the available surgical literature however, highlights the fact that there exists some disagreement over the preferred surgical technique for treatment of the disease. Recently, less-invasive techniques have been explored. Studies of laparoscopic techniques have shown good results [28], as has percutaneous drainage under ultrasound guidance [10–14]. However, there have been no controlled clinical trials comparing the efficacy of the less invasive techniques with open surgery. This issue could best be addressed in countries where the incidence of hydatid disease is high. Percutaneous drainage should not be attempted with cysts that have hyperechoic solid patterns without back wall echoes; that are infected or have cystobiliary communications which need to be closed off. It should not be attempted in cysts that have ruptured into the biliary tree, pleural or peritoneal cavity [29]. If percutaneous drainage is attempted in cysts having cystobiliary communications, re-accumulation of fluid or a prolonged bile leak could occur [29]. There also is a risk of infection and anaphylaxis due to spillage of cyst fluid with this method. Scolicidal agents like hypertonic saline [29] and alcohol [12] are used following percutaneous drainage of cysts and are left in the cyst cavity for periods of up to 20 min. The use of such scolicidal agents for such prolonged periods could also result in a caustic sclerosing cholangitis [30]. For these reasons this method of treatment is not favoured at our centre. Percutaneous drainage however is indicated over open surgery in patients who are high surgical risks due to systemic illness [29]. It also has a place in disease recurrence following surgery [29], as was the case in one of our patients.

With open surgery, the choice between a radical excision of the cyst or a partial excision of the cyst wall in the form of subtotal cystectomy has been another topic of debate. Proponents of the radical procedure argue that the less radical approach may leave behind disease. An exogenous daughter cyst may develop from the germinal layer and protrude beyond the deep surface of the cyst and be overlooked during the de-roofing procedure, thus resulting in a local recurrence of the disease [9]. Advances in imaging techniques and the use of operative ultrasonography largely reduce the risk of missing such an exogenous daughter cyst. Results with subtotal cystectomy have been shown to be similar to those of radical excision [9] and hence cystectomy is the preferred technique at our centre.

Post-operative bile leak occurred in 7 (23%) of our patients. This compares to the reported 13–30% incidence of bile leaks in other series as a consequence of small, undetected communications between the cyst and bile ducts [9]. If clinical factors or operative findings suggested a cystobiliary communication, an on-table cholecystography was carried out to check for leakage. Although this study was not a controlled trial, we found that there was a higher incidence of a post-operative bile leak if the biliary system was not temporarily drained in these patients. This higher incidence of persistent bile leak is largely due to the thick fibrous pericystic layer preventing closure of communications in the presence of normal intrabiliary pressure and absence of a decompressing stent [9]. Drainage and decompression of the biliary system permits faster healing of the communications after suture, thus reducing the risk of a bile leak and is recommended.

In conclusion, our experience suggests that albendazole given as described together with surgery is effective in treating patients with hepatic hydatidosis. If open surgery is undertaken, all attempts should be made to identify the presence of cystobiliary communications at operation, which, if present, should be oversewn and the biliary system drained to aid healing and prevent the complication of a bile leak.
Hydatid Disease of the Liver

Invited Commentary

Thomas W. Kraus
Surgical Department, University of Heidelberg, Heidelberg, Germany

The article describes the therapy of 30 patients who underwent surgical treatment for hydatidosis in the UK over a 16-year period in a single center. The approach is presented in a very educative fashion, but scientific innovations in the paper are rather scarce. The authors concluded that the patients should undergo surgery and a therapeutic algorithm is provided. All patients underwent surgery in combination with praziquantel and albendazole with good results. Taking into account the long time span analyzed, it has to be stated that during this time period diagnostic and imaging methods have markedly changed significantly, thus all data will probably be really comparable.

Furthermore, it has to be stressed in further intensity that alternative techniques to surgery have evolved in many parts of the world, particularly where hydatidosis is highly endemic. An alternative to surgery meanwhile is the PAIR method (i.e. puncture the cyst, aspirate fluid, introduce a protoscolicidal agent, then aspirate), which requires ultrasonographic guidance. Extreme care is essential to prevent spilling hydatid fluid into a body cavity because this may lead to anaphylactic shock. Albendazole

References


Hydatid Disease of the Liver
therapy may be combined with PAIR from 10 days before
to 30 days after the procedure.
PAIR is indeed a very promising and little invasive
and potentially very cost-effective technique, although
large-scale clinical trials have not yet been conducted.
Until then, most conservative surgeons in the West will
probably still accept that surgery is the treatment of
choice for most cases of cystic echinococcosis and usually
it also is successful. But it can be expected that the PAIR
method will rapidly gain growing importance in future
and it is also fostered by the WHO in many publications
and internet tutorials. This option should have been dis-
cussed in further detail.

The most interesting aspect of the current study is that
cystobiliary communications were identified in 50% of
patients. This is a very important issue to remember, even
if this is also a well- and long-known fact in the literature.
It is uncertain, according to the authors, if these commu-
nications when present were spontaneous or iatrogenic.
Since 1996, methylene blue was therefore injected into
the biliary tree, as communicated during the review pro-
cess to identify communications with the cyst cavity.
Interestingly, there was a higher incidence of postoper-
ative biliary complications in patients without biliary
drainage at the time of surgery and the authors give us
clear advice to take it seriously. The frequent existence of
these biliary communications is also a major argument
against the instillation of proctoscolicidal solutions,
which may cause severe chemical cholangitis. But even
this does not completely rule out interventional percuta-
neous therapy, as some centers perform endoscopic trans-
papillar drainage to manage potential cholangitis before
starting the percutaneous approach.