Cystic echinococcosis (CE) is endemic in the Mediterranean region, Central Asia, the Middle East, East Africa, Australia, New Zealand, and the southern part of South America.\(^1\)\(^-\)\(^3\) Human CE infections occur by accidental ingestion of eggs excreted with feces of infected carnivores. Oncospheres hatch in the duodenum, penetrate the intestine, and are transported via the bloodstream to various organs. The liver is the most commonly involved organ (52%-77%) because the liver filters oncospheres (if any) from the blood that flows from the portal vein, which drains the intestinal veins.\(^4\) If oncospheres escape this filtering process, they are introduced into the systemic circulation and settle in the lungs (10%-40%) or, rarely, in other organs (10%). Extrahepatic and extrapulmonary locations of the disease are described as "unusual" in previous articles.\(^4\)\(^,\)\(^5\) Because the symptoms vary according to the organ localization and the rate of parasite growth, the clinical diagnosis of CE is not easy. Medical radiological findings such as ultrasonography (US) is the first choice in the diagnosis of intra-abdominal cysts because US is easy to use and effective, and it is considered to be the "gold standard" in community-based surveys. Serology gives useful and complementa-
ry information on the nature of the cyst and concerning the issue of surgical intervention. Early diagnosis and subsequent treatment can reduce mortality. The risk of postsurgical relapses is one of the problems that can be faced after treating CE patients.

In this article, we described the results of 134 patients in respect of sites of involvement, clinical presentations, radiological findings, serological diagnostic evaluations, and outcomes of infected CE patients.

PATIENTS AND METHODS

A retrospective analysis of surgically treated CE was conducted between January 1993 and January 2014 in the General Surgery, Pediatric Surgery, Urology, Cardiovascular Surgery, Neurosurgery, and Orthopedics departments of University of Cukurova, Faculty of Medicine, Balcalı Hospital. Among the 661 patients managed for CE, 134 had unusual sites of involvement, and these patients constituted the population of this retrospective study.

To diagnose and determine the extent of the disease, US, computed tomography (CT), magnetic resonance imaging (MRI), conventional x-ray, intravenous urography, and transesophageal echocardiography (TEE) or transthoracic echocardiography (TTE) were used, and the modality chosen depended on the site of involvement. Generally, US and/or CT were the methods of choice in cases of abdominal involvement, while chest x-ray (CXR) and/or CT were used in cases of thoracic involvement. CT, MRI, and/or TEE were used in the case of cardiac disease. In cases of central nervous system (CNS) and spinal involvement, evaluators used CT and/or MRI; in cases where bones were involved, x-ray and/or MRI were preferred.

For the serological evaluation, the indirect hemagglutination (IHA) test was performed in all cases; however, a Western blot (WB) was performed in the 54 cases that occurred since the year 2000. Anti-Echinococcus granulosus antibodies were determined using IHA (Fumouze Diagnostics, France) and IgG WB (Euroimmun, Germany) techniques, each according to the manufacturer’s instructions. The diagnostic value for IHA was accepted as ≥1:320 titration; for WB, the presence of a p7 band was accepted as diagnostic.

Radiological methods and serological tests were used in the postsurgical follow-up of all patients.

RESULTS

There were 58 men and 76 women, with ages ranging from 6–67 years (average 45 years). Approximately 20.3% (134/661) of patients had cysts in an uncommon location. The results of uncommon locations of CE in the southern part of Turkey are given in Table 1. Among the 134 patients who had an unusual site of involvement, 41 cases (30.6%) also had liver (32 cases), lung (7 cases), or concomitant liver and lung (2 cases) involvement. In 93 cases (69.4%), unusual organ involvement was isolated without any liver or lung involvement.

Peritoneal cavity

The 24 patients with peritoneal CE underwent surgery. Among the 16 patients with isolated peritoneal disease.

| Site               | Number | %    | IHA ( +/-) | WB ( +/-) | X-ray | US EKO | CT | MR | Liver | Lung | Recurrence |
|--------------------|--------|------|------------|----------|-------|--------|----|-----|-------|------|------------|
| Peritoneal cavity  | 24     | 3.6  | 19/24      | 2/2      | -     | 21     | 24 | -   | 6     | 2    | -          |
| Retroperitoneum    | 12     | 1.8  | 9/12       | 5/5      | -     | 12     | 12 | -   | 3     | 1    | 1          |
| Kidney             | 18     | 2.7  | 11/18      | 7/7      | -     | 18     | 18 | 5   | 2     | -    | -          |
| Spleen             | 16     | 2.4  | 13/16      | 7/7      | -     | 12     | 16 | -   | 5     | 1    | -          |
| CNS                | 16     | 2.4  | 14/16      | 6/6      | -     | -      | 16 | 4   | 5     | 3    | -          |
| Muscle             | 14     | 2.1  | 10/14      | 5/5      | 9     | 9      | 12 | 11  | 3     | -    | -          |
| Bone               | 14     | 2.1  | 12/14      | 6/6      | 14    | 14     | 14 | 10  | 4     | 2    | -          |
| Heart              | 13     | 1.9  | 11/13      | 6/6      | 13    | 12     | 12 | 10  | 4     | 2    | -          |
| Pancreas           | 3      | 0.5  | 2/3        | 1/1      | -     | 3      | 3  | 3   | -     | -    | -          |
| Ovary              | 2      | 0.3  | 2/2        | 2/2      | -     | 2      | 2  | -   | -     | -    | -          |
| Thyroid            | 1      | 0.2  | 1/1        | -        | -     | 1      | 1  | -   | -     | -    | -          |
| Breast             | 1      | 0.2  | 1/1        | -        | -     | 1      | -  | -   | -     | -    | -          |
5 had a history of a liver or a lung surgery for hydatidosis, though at the time of the peritoneal disease, they were free of lung or liver disease. The IHA test was positive in 19 of 24 (79.2%) cases. The WB serological test was positive in 10 cases. Among the 5 IHA-negative cases, the WB test was positive in 2. During the follow-up of 19 cases (median follow-up: 60 months), no recurrence was detected.

**Retroperitoneum**

Twelve patients had retroperitoneal disease involvement. The most frequent presenting symptoms were abdominal pain and discomfort. Three patients had undergone previous surgeries for hepatic CE. CT demonstrated all of the lesions in all patients, whereas US did not detect any lesions in 2 of the patients (Figure 1). The IHA test was positive in 9 (75%) cases. The WB test was performed in 5 cases, and all 5 were positive, though one of these was IHA negative. During follow-up, 1 patient who had previously undergone drainage of multiple lesions had a recurrence in 1 lesion in the third postsurgical year. The recurrent lesion was treated percutaneously with the PAIR (puncture, aspiration, injection, and re-aspiration) technique, and no recurrence was detected during the 5-year follow-up period.

**Central nervous system**

Sixteen patients presented with neurological symptoms caused by CE of the CNS. Ten the patients were children (63%) (median age 8 years) and 4 were adults (37%). The most frequent presenting clinical symptoms and signs were headache (83%), papilledema (64%), and focal neurological deficits (33%). None of the patients had a history of surgery for CE. In 15 patients, lesions were located in the brain (Figure 2A), while 1 patient had a lesion located in the spinal canal (Figure 2B). The IHA tests were positive in 14 patients (87.5%). The WB test was performed in 6 cases, and positive results were obtained in all of them. During the follow-up period (median follow-up: 60 months), no recurrence was detected.

**Spleen**

Patients with CE of the spleen presented with non-specific symptoms such as left upper abdominal pain (80%) and splenomegaly (60%). However, in 1 case, repeated gastric variceal bleeding due to segmental portal hypertension was the first symptom. The spleen was infected with CE in 16 patients (Figure 3). Four of these patients had undergone previous surgeries for hepatic (3 patients) or pulmonary (1 patient) CE. Involvement was isolated in the spleen in 10 (63%) cases, and concomitant liver lesions were detected in 6 (37%) cases. The IHA test was positive in 13 cases (81%). The WB test was performed in 7 cases; positive results were obtained in all cases, though IHA results were negative in 2 cases.
Kidney
Eighteen patients with renal CE underwent surgery. In 17 cases (94%), CE lesions were isolated in the kidney, while in 1 case, concomitant liver lesions were detected. Among the 17 cases of isolated renal disease, 1 case had a history of a liver surgery for CE. Lesions were located in the right kidney (Figure 4) in 11 cases and in the left kidney in 7 cases. The IHA test was positive in 11 of 18 (61%) cases, while the WB test was positive in 7 of 7 cases, although 3 of these were IHA negative. During the follow-up period (median follow-up: 60 months), no evidence of recurrence was detected.

Muscle and subcutaneous tissue (soft tissue)
Fourteen patients with soft tissue CE underwent surgical treatment (Figure 5). The IHA test was diagnostic in 10 of 14 (71.4%) cases. Though WB test yielded positive results in 5 cases, the IHA test results were negative in 2 cases.

Heart
Thirteen patients with cardiac CE underwent surgical treatment. The first seven cases have been previously reported.1 The most frequent symptoms were dyspnea (60%) and precordial pain (30%). In all cases except 1, echocardiography was performed as the first examination. After detecting CE lesions on echocardiography, radiological examinations (CXR, CT, and/or MRI) (Figure 5) and laboratory tests (IHA, WB) were performed in 12 of 13 patients. The IHA test results were positive in 11 of 13 (84.6%) cases. The WB test was performed in 6 cases, and positive results were obtained in all.

Bone
Fourteen patients with osseous CE underwent surgery in the Orthopedics and Neurosurgery clinics (Figure 6). The most common presentation was pain and swelling of the involved region. A pathologic fracture was detected in 2 patients. IHA tests were performed in 14 cases, and positive results were obtained in 12 cases. WB tests were performed in 6 cases, and a positive result was obtained in all cases. A CXR, an abdominal US, and/or a CT scan were performed in all cases to locate the systemic disease. In 2 cases, hepatic CE was established. In 10 cases, the disease was isolated in the bone. In the postsurgical period, recurrence was detected in the 18th month and in the 21st month in 2 patients in whom excision and curettage were performed. Hence, these patients had to undergo a second surgery. Unfortunately, the other 2 patients with long bone involvement, in whom reconstruction was performed...
during the same surgery, experienced postsurgical infection and required a second surgery.

Pancreas
Three patients with pancreatic CE were treated surgically. In 2 cases, a preoperative diagnosis was successfully obtained by radiological examination, but in 1 case a laparotomy was required. The IHA test results were positive in both of these 2 cases. The WB test was performed only in 1 case, and a positive result was obtained. The third case was a 17-year-old male patient who was admitted with abdominal pain and jaundice. A US examination showed a pure CE lesion (5-cm mass) at the pancreatic head. CT and MR tests demonstrated a 5-cm-diameter CE mass around the head of the pancreas, and the encasement of both the choledochal and the pancreatic ducts indicated the possibility of a type I choledochal cyst. Magnetic resonance cholangiopancreatography showed that the cyst did not originate from the choledochal duct but displaced the choledochal duct laterally (Figure 7). Percutaneous transhepatic cholangiography showed lateral displacement of the choledochal duct, and the CE lesion did not fill with the contrast material. The serological test results (IHA) and the test for tumor markers were both negative. Histopathologic examination confirmed the diagnosis of a CE. No other organ involvement was detected on radiological examination.

Ovary
Two patients with ovarian CE were treated surgically. One was located on the right ovary and the other was located on the left ovary (Figure 8). The IHA and WB tests were positive in these 2 patients. One patient also had omentum involvement, which was misdiagnosed in another clinic as an ovarian malignancy. No evidence of recurrence was detected during the follow-up period (60 months).

Thyroid
One female patient had CE of the thyroid gland. She presented with a mass in the anterior aspect of the cervical area. A US examination revealed a 5 × 5 cm² cystic mass with characteristic features of CE in the right thyroid gland (Figure 9). A CT scan demonstrated an encapsulated cystic mass. An ultrasonographic examination of the liver and a chest x-ray were both normal. The IHA test results were positive. A CE lesion was completely removed with a right lobectomy.

Breast
A female patient with CE of the breast presented with a
painful mass on her right breast. On physical examination, a 5 × 5 cm² mobile mass with no auxiliary lymphadenopathy was detected. A US of the breast revealed a 5 × 4.5 cm² cystic lesion with daughter cysts circumscribed by means of a well-defined wall (Figure 10). An IHA test was performed for further work-up, and the result was positive.

DISCUSSION
CE with unusual localizations may cause serious problems of diagnostic confusion. The combination of clinical history, radiological findings, and serological test results (especially the WB) are valuable in diagnosing extrahepatic CE. Immunodiagnosis can play an important complementary role. It is valuable not only for primary diagnosis but also for follow-up of patients after surgical treatment.8-10,14 There are considerable differences in the specificity and sensitivity of the various tests. Ideally, a test should be specific with high sensitivity.15 Detecting circulating E. granulosus antigens in sera is less sensitive than detecting antibodies, which remains the method of choice. An IHA test has rather good sensitivity (between 60% and 100%) but poor specificity. WB allows molecular weight analysis of the antigens detected from the patient’s serum with specific results.15-17 WB serology is 80% to 100% sensitive and 88% to 96% specific for liver CE but less sensitive for lung (50%-56%) disease or other organ involvement (25%-26%).15 Thirty-one (23.1%) of 134 extrahepatic CE cases were evaluated as negative with indirect hemagglutination (IHA). However, positive results were obtained in all 54 cases evaluated with a WB test including the 10 IHA-negative cases. It is suggested that this contrast with the published studies may be because of the decreased number of WB tests performed in extrahepatic and extrapulmonary cases in the previous published studies, or because 41 of our cases had a history of accompanying liver and/or lung lesions.

Diagnosis is easily established with US, CT, or MRI scans of patients who have characteristic findings such as calcification of the cyst wall, presence of daughter cysts, and detachment of the germinative membrane. However, CE with unusual sites of infection may cause serious problems in the differential diagnosis.8-10,14,18,19 US is a noninvasive, accessible, inexpensive, highly sensitive (93%-98%), and specific (90%) imaging technique.8,14,20,21 The advantages of US for the diagnosis and follow-up of subcutaneous and soft tissue CE are well recognized. Sonography reveals echo-free cysts, floating membranes, and daughter cysts. The radiological findings of CE involving skeletal muscles are similar to those involving parenchymal organs such as the liver, kidney, and spleen.22 A multivesicular lesion is the characteristic of CE on US examination. The presence of small, dense, mobile echoes in the cyst is due to hydatid sand. The presence of small, dense mobile echoes in a cyst is specific or even pathognomonic of CE.8,20,23 However, imaging methods are insufficient in the differential diagnosis of a simple type I CE cyst. Echocardiography is a valuable diagnostic method for cardiac CE.3,24,25 In all but 1 case, the preoperative diagnosis was established by echocardiography during investigations for other suspected causes. The retrocardiac area or the posterior aspect of the heart can be better evaluated with TEE.3,8 A CT and an MRI are further diagnostic evaluations.3,8,26 A CT scan and/or an MRI should be performed in all suspected cases of CE or to elucidate the relationship of the cysts with adjacent organs and tissue for deciding the most appropriate surgical strategy. Further, these imaging techniques are essential for the preoperative evaluation of cases such as intracranial, spinal, or osseous CE.8,19,26-31

The peritoneal cavity and retroperitoneal CE accounted for 6% to 16% of cases in the published studies. The brain is also an uncommon site for CE. CNS involvement occurs in 2% to 3% of patients, and in endemic areas these CE lesions account for 2% of all intracranial space-occupying lesions.8,27,32-37 Children are more frequently affected when compared with adults. It has been suggested that ductus arteriosus patency dur-
ing the neonatal period may be a cause of the increased vulnerability of children because it allows the passage of parasites from the periphery to the brain.37-39 All CE were supratentorial and solitary, but no multiplicity was detected. Consistent with our series, cerebral CE reported in the published studies is usually supratentorial and solitary.8,37-42

Although it is rarely contaminated by Echinococcus (0.9%-8%), the spleen was one of the most frequently involved organ reported in the published studies.9,10,38 In our study, spleen involvement was determined in 2.4% of all CE cases. Primary spleen involvement occurred in 10 (62.5%) cases. It is believed that the oncosphere may migrate to this location from the portal vein during bouts of increased abdominal pain.10,12,19,41,44 CE of the urinary tract is uncommon, and the kidneys are the most frequently involved organs of the urinary tract. CE of the kidney occurs usually as isolated disease.9,10,45-47 In our series, 94.4% of all renal CE occurred as isolated disease.

The involvement of the muscle and the soft tissue occurred in 2.1% of all CE cases and was observed in 10.5% of unusual CE cases. Echinococcosis of the musculoskeletal system is found in 0.5% to 4% of the patients suffering from CE ductus arteriosus. The involvement of muscle alone is much rarer. There are few reports of primary muscular CE, perhaps because the parasites have to cross the hepatic and pulmonary barriers to reach the muscles. Further, the presence of lactic acid in the muscles provides an inhospitable environment.30,49 In contrast to the published studies, 9 isolated cases were found in our series.

The rate of cardiac involvement was 1.9% in our study and 0.2% to 2% in the published studies.8,10,24 The myocardium of the left ventricle was reported to be the most frequently (75%) involved site.10 In our study, 5 of 10 myocardium-localized cases and 1 pericardium-localized case were the result of secondary CE. Prousalidis and colleagues reported that the CE of the myocardium is considered a primary disease and that hydatid cysts of the pericardium are considered a secondary disease.10 In fact, primary pericardial CE lesions are extremely rare.24,26,50-53

CE affects the bones in 1% of reported cases, and the pelvis or spine in 57% to 65% of cases.22,54 While the pelvis and the spine were the most involved bones reported in the published studies, the rate of pelvic and spinal infection was 33% in our series. We believe that the most important factor in the variation of rates compared to the published studies is the increased presence of intracranial intraosseous (parietal) CE in our series—these have been reported very rarely in the published studies. Usually, the diagnosis is established intraoperatively by an experienced surgeon. Although there have been advances in imaging techniques and improvements in surgical treatment combined with the use of antihelminthic administration, the published studies report a local recurrence and/or infectious complication rate of 50% in patients with CE of the bone.22,54-57 In our series, recurrence occurred in 2 cases of cyst excision with curettage. Additionally, infection developed after simultaneous reconstruction of 2 other cases of long bone resected. Based on our experience, we recommend that prosthesis replacement should be performed in another sequence.

Pancreatic involvement has been reported in 0.25% to 0.75% of adult cases of CE, and the mode of infection is presumed to be hematogenous. However, local spread via the pancreatic or bile ducts has been suggested; peripancreatic lymphatic invasion has also been observed as a mode of infection.9,10 Three cases of CE located in the pancreatic corpus or head (0.5%) were reported. The pre-operative diagnosis of CE of the pancreas may be difficult because it may be confused with a pseudocyst, choledochal cyst, simple cyst of the pancreas, cystic pancreatic neoplasm (such as cystadenocarcinoma), true congenital cyst, or post-traumatic pancreatic cyst. Radiological investigations and serological tests are valuable for the differential diagnosis; however, a diagnostic laparotomy could be necessary in some patients.9,10,58,59 Radiological and serological tests were insufficient to diagnose CE in 1 case of our study, and diagnostic laparotomy was required.

The incidence of thyroid gland involvement was 0.15% in our series. CE presents as a solitary cystic lesion in the thyroid gland. The management of thyroid CE is surgical; complete excision should be the procedure of choice.9,60-62 The breast is a rare primary site accounting for only 0.27% of all cases.8,58 Although rare, CE should always be suspected in patients with palpable breast lumps, especially in endemic regions. The appearance of a mammary CE on US evaluation varies in all patients, and a variety of sonographic patterns have been previously described.8,63-67 The presence of a CE lesion with a well-defined wall having racemose interior containing daughter cysts is a slowly growing breast mass is suggestive of a CE.8,64,65 CE should be suspected while conducting the differential diagnosis of pelvic cystic masses.8,66 As in our cases, primary ovarian CE may be confused with ovarian cystic tumors.

The recurrence rates of CE exhibited a large range based on the site of the disease (0%-50%).17,22 In our study, recurrence occurred in 2 cases in which only
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Drainage was performed, and rupture occurred intra-operatively and involved the bone. In addition to these cases, recurrence occurred in retroperitoneum, which was treated with PAIR.

In conclusion, CE with unusual localizations may cause serious diagnostic confusion. The combination of the clinical history, radiological findings, and serological test results (especially the WB) are valuable for diagnosis. CE may develop in every organ of the human body and should be considered in the differential diagnosis of cystic masses, especially, in patients in regions where CE is endemic.

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