

Evaluation of non-surgical methods in treatment of pediatric liver cyst hydatid

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Abstract

Aim: Hydatid cyst is a zoonotic infestation caused by helminthes of the *Echinococcus* genus and humans are intermediate hosts infected with the contaminated fresh food or water. The cases in Turkey are confined to Eastern Anatolia region. Evaluating the prevalence, symptoms and signs of hydatid cysts along with the treatment procedures and response in pediatric cases are vital for better diagnostic and treatment approaches in children.

Material and Methods: The study was conducted retrospectively with a total of 27 children diagnosed with hydatid cyst admitted to Research and Education Hospital of Kafkas University Medical School, Turkey in 2016 and 2019.

Results: The mean age of 27 cases reported here was 11.59±4.95. Liver involvement was observed in all of patients reported here and all patients were seropositive. Ten patients underwent Puncture Aspiration Injection Re-aspiration procedure and 17 patients did not undergo. After the Puncture Aspiration Injection Re-aspiration treatment, there was an improvement in all patients for the marker levels.

Conclusion: We think that Puncture Aspiration Injection Re-aspiration is superior to non-surgical medical treatment in pediatric patients.

Keywords: Eastern anatolia; liver cyst hydatid; non-surgical method; PAIR method; pediatric disease

INTRODUCTION

Hydatid cyst is a zoonotic infestation caused by helminthes of the *Echinococcus* genus (1). *Echinococcus granulosus* is a parasite consisting of two to 11 rings with a length of 2.8 mm and a width of 0.6 mm. The adult form is hermaphrodite (2). *Echinococcus* life cycle requires two hosts, one definitive and one intermediate host. Human are intermediate hosts and are infected by receiving eggs and rings filled with feces belonging to the main host or from the contact with the contaminated fresh food or water. The parasite is transported through the small intestine and the venous route to the liver. It can subsequently settle in various organs including lung, kidney, spleen, muscle, brain, and bone tissue (1,3).

Hydatid disease is endemic in Central Asia, Middle East, East Africa, Austria, South America, New Zealand and Mediterranean countries (2,4). The cases in Turkey are confined to Eastern Anatolia region (5). The course of the disease can be asymptomatic. However, owing to the widespread use of modern imaging methods, the detection

of the incidents without symptoms has increased. The most common symptoms are abdominal pain, nausea, vomiting, respiratory distress, cough, headache, and impaired hearing and vision. While liver involvement is more common in adults, lung involvement is more common in childhood (6-8). In the patients with hepatic involvement, abdominal pain is the most common clinical symptom when the length and diameter of the cyst is 5 cm or more (9). In the hydatid cyst of the lung, hemoptysis and chest pain are the common symptoms (10).

The routine clinical diagnosis of the disease is made by serology and radiological imaging methods in the presence of symptoms and signs (11). Diagnosis is made serologically by showing specific hydatid cyst antibodies in serum. Although puncture is not used directly in the diagnosis of hydatid cyst because of the risk of anaphylaxis and spread, puncture is used as part of Puncture Aspiration Injection Re-aspiration (PAIR) treatment method (12-14). PAIR is performed as catheter drainage treatment or modified catheter treatment. PAIR can be applied in cysts smaller than 5-6 cm. If the

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diameter of the cyst is above 5-6 cm, catheter treatment can be applied. In children, the upper limit for PAIR can be up to 8 cm (15). Benzimidazole derivatives are used as medical treatment in PAIR (16-19). In addition, serological or pathological diagnosis can be made in this aspirated fluid (20). USG provides information about the presence, size and location of the cyst, but also shows pathological findings indicating that the lesion is hydatid cyst according to the classification of Gharbi et al. (21).

Surgical and percutaneous methods are routinely applied in the treatment of the disease. Nonetheless, evaluating the prevalence, symptoms and signs of hydatid cysts along with the treatment procedures and response in pediatric cases are vital for better diagnostic and treatment approaches in children. In the current work, we report the clinical and paraclinical information of children admitted with hydatid cyst.

MATERIAL and METHODS

Prior to the study, approval from the local ethical committee of Medical Sciences of Kafkas University was obtained. The study was conducted retrospectively with a total of 27 children diagnosed with liver cyst hydatid admitted to Research and Education Hospital of Kafkas University Medical School, Turkey in 2016-2019.

A set of complete epidemiologic, clinical, and therapeutic data gathered from all the 27 cases that were 3–18 years old obtained from the Hospital Information System. The patients over 18 years of age were not considered.

The data including gender, age, demographic data, history of contact with animals, hydatid cyst features, Gharbi classification, application of PAIR method, complications, and clinical features were obtained and used for further analyses. Furthermore, blood alanine aminotransferase

(ALT), aspartate aminotransferase (AST), Hemoglobin (HB), and platelet count levels (PLT) during the presentation to clinic was obtained and employed in the analyses.

In the PAIR procedure, 95% absolute alcohol or 25% sterile hypertonic saline was used as a scolical agent. PAIR was then performed as percutaneous puncture of the cyst followed by aspiration of the maximum quantity of the cystic content. The injection of a scolical agent and reaspiration of the agent after 15 minutes were performed in all the pediatric cases.

The data were analyzed with statistical analyses program R. Student's t-test was used to assess the difference between means of the two groups and Chi-square test or Fisher Exact test was used to infer frequency distributions among groups. A p-value of <0.05 was used to determine the significance throughout the analyses.

RESULTS

We first evaluated the demographic variables. The mean age of 27 cases reported here was 11.59±4.95. We also grouped cases based on being above and below 6 years old. We age grouping along with gender and living place. Among a total of 11 cases that were living in urban areas, three male cases were above 6 years old whereas the other three were below the 6 years of age. All of the five female cases that were living in urban cities were all above the 6 years of age. When we look at the cases coming from rural lifestyle, all the 11 male cases were above 6 years of age. The two of the 5 female cases coming from the rural areas were younger than 6 years of age whereas the other three cases were older than 6 (Table 1). Liver involvement was observed in all of patients reported here and all patients were seropositive.

Table 1. Frequency distribution (percentages) of age groups, gender and living place of 27 cases analyzed

	Urban			Rural		
	6 years old	>6 years old	Total	6 years old	>6 years old	Total
Gender						
Female	0 (0%)	5 (18.5%)	5 (18.5%)	2 (7.4%)	3 (11.1%)	5 (18.5%)
Male	3 (11.1%)	3 (11.1%)	6 (22.2%)	0 (0%)	11 (40.74%)	11(40.74%)
Total	3 (11.1%)	8 (29.6%)	11 (40.74%)	2 (7.4%)	14 (40.74%)	16 (59.26%)

Table 2. ANOVA analyses for the effect of continuous biochemical variables on the lesion stage among 27 cases analyzed

Source	DF	Sum of Squares	Mean Square	F Value	P-value
ALT	4	111.7	27.9	0.63	0.65
AST	4	1288.3	322.1	3.81	0.02
HB	4	19.2	4.8	5.07	0.005
PLT	4	30607.1	7651.8	0.83	0.52

As determining the level of cystic cases based on the easily obtained blood parameter would be an invaluable tool, we conducted an ANOVA analyses for each of the blood parameter for lesion stage. We detected that the change in the AST and HB levels changed among the lesion stages detected whereas the change in the ALT and PLT values were not corresponding to the changes in the lesion levels (Table 2). When we investigated the nature of significance, we found that the Gharbi 3 mean was significantly different from all other levels in both AST and HB.

Ten patients underwent PAIR and PAIR was not performed (non-PAIR) in the other 17 cases. We subsequently tested if PAIR method was more effective to eliminate the lesion scores. We compare the frequency of the changes in lesion stages (from Gharbi 1 to Gharbi 5) between PAIR applied patients and non-PAIR applied group using Fisher Exact Test. According to the Gharbi classification, 81.5%

of our patients were assigned to Garbi-1 and Garbi-2. At the initial reporting, only 11.1% of the patients were found to be at the Garbi-5. After the treatment, there was an improvement in all patients for the marker levels. About 13 out 17 patients had a seronegativity marker whereas all other 14 cases indicated seropositivity with a decrease in the score. The Fisher Exact Test results revealed that the sum of the probabilities of "unusual" tables was $p = 0.354$ whereas the probability of the estimated 5x2 contingency table was $p=0.009$. The result indicated a significant difference in terms of the improvement in the course of liver cyst between PAIR applied patients and non-PAIR applied patients (Table 3). We also performed a Fisher Exact test to discern the pattern of change in the level of improvement in the serological marker in respect to the PAIR application in an analogous manner. The results in the serological marker level did not indicate a significance pattern (Table 3).

Table 3. Frequency distribution of the response to PAIR and non-PAIR treatment for lesion stages and serological marker levels along with the Fisher Exact test for significance levels among hydatid cyst cases analyzed

Change in the Gharbi levels	PAIR applied cases	Non-PAIR applied cases	Change in the Marker level	PAIR applied cases	Non-PAIR applied cases
4	6	6	4	0	1
3	2	1	3	7	8
2	2	6	2	2	7
1	0	1	1	1	1
0	0	3			
Total	10	17	Total	10	17
Table p-value		0.009			0.055
Threshold p-value		0.354			0.612

DISCUSSION

Hydatid cysts are common in underdeveloped and developing countries where uncontrolled animal slaughtering is performed, stray street animals are abundant, and infected animal waste is dumped into the public areas. It is a common disease in regions where livestock is the main source of livelihood and thus it is a public health problem endemic to the regions of Turkey where animal husbandry is intensive (1,7,22,23). Presence of relatively common cases of hydatid cyst in Eastern Anatolia, Southeast Anatolia, and Central Anatolia regions were reported earlier. Our study was conducted in Kars province of Eastern Anatolia region where animal husbandry is the main source of livelihood (24). The 27 cases reported here are gathered in four years. However, an earlier retrospective study in Iran reported 37 pediatric cyst hydatids cases from the liver in a period of 12 years (25). The number of cases reported here indicates an elevated occurrence of the disease in the Eastern Anatolia.

When gender of children in our study is considered, 63% were found to boys and 37% were girls. Based on the number reported here, we found a clear deviation from a random distribution. Previous studies from Turkey has either reported a balanced distribution (26,27) or a higher frequency among females (28,29). We think that the higher proportion among boys could be attributes to the fact that boys are shepherds or involved in the animal care more often than girls due to the domestic division of labor which in turn elevates the prevalence of the cyst hydatid.

Increasing the independent clinical predictors for the presence of cyst would be invaluable for easy and accurate detection of cyst hydatid along with Gharbi level (21). We tested the blood parameters of ALT, AST, HB, and PLT against the liver cyst hydatid and found that the AST and HB levels changed significantly among different lesion stages. However, there was not a linear relationship where a cut-off value could be assigned to each group in either of the significant parameters. The only elevated level in both of the significant parameters was in Gharbi 3 where there

was only one case. The case was a Hepatitis B carrier that caused an unexpected elevation in the parameters.

In a study performed by Chai et al., 46.2% of the patients were given medical treatment for 6 months and 85.3% for those treated for 12 months had success in curing cyst hydatid (30). The rate of seronegativity after the PAIR was found to be 70% whereas the rate of seronegativity was 41% among patients who received solely medical treatment (non-PAIR) in six months in our study. The results indicated that PAIR method in 6 months period was as effective as a 12 months period of non-PAIR treatment. The underlying cause of the success in the PAIR method could be attributed to the fact that oral ingestion of the medicine reduces the effectiveness compare to the direct injection to the cyst. In fact, absorption of medicine from the gastrointestinal system is reported to be only about 5-10% (31).

CONCLUSION

Pediatric liver cyst hydatids are more common among males than females in Eastern Turkey. Prevalence of liver cysts is also higher among children living in rural areas. Since 70% seronegativity is detected in 6 months in PAIR applied patients, we think that PAIR is superior to medical treatment in pediatric patients in terms of curing length.

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