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Ten-year follow-up of children with hydatid cysts

Kist hidatikli çocuk olguların on yıllık izlemi

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Abstract

Aim: Hydatid cystic disease is an endemic parasitic disease that is common in the world. We aimed to review the demographic, clinical and laboratory findings, and treatments and outcomes of children with hydatid cyst disease, and to determine the factors affecting treatment response in two pediatric pulmonology centers in the central region of Turkey.

Material and Methods: The clinical records of patients aged below 18 years who were followed up between January 2006 and December 2016 because of hydatid cyst disease were reviewed retrospectively. The patients' ages at the time of diagnosis, sexes, living areas (rural / urban), dog contact history, presence of hydatid cyst in other family members, symptoms, organs involved, dimensions of cysts, laboratory results, treatments and post treatment responses, follow-up, and outcomes were noted.

Results: In a period of 10 years, 50 pediatric patients were followed up with a diagnosis of hydatid cyst. The mean age was 9.3±0.5 years and 33 (66%) of the patients were male. Fifteen patients were living in a rural area and 35 were living in an urban area. Fifteen patients had a history of contact with a dog and 10% had a positive family history. Thirty-six patients had lung involvement, 25 had liver involvement, 14 (28%) had both lung and liver involvement, and six patients had organ involvement other than lung and liver. The indirect hemagglutination test for hydatid cyst was positive in 24 of 40 patients and *Echinococcus granulosus*-specific IgE positivity was detected in 8 of 17 patients. Surgery was performed in 31 patients with lung involvement and PAIR was performed in 13 patients who had liver involvement. Cyst excision was performed in two patients who had isolated spinal involvement. All patients were treated with albendazole, and additional praziquantel treatment was given to seven patients. Relapse occurred in seven patients in this period. The relapse frequency was higher in patients who had organ involvement other than in the lung and liver ($p<0.05$), and these patients' treatment durations were longer compared with the others ($p<0.05$).

Conclusion: Hydatid cysts can involve different organs in children. Patients with organ involvement other than the lung and liver should be followed up carefully in terms of recurrence.

Keywords: Children; hydatid cyst; organ involvement

Öz

Amaç: Kist hidatik dünyada yaygın görülen endemik bir parazitik hastalıktır. Çalışmamızda kist hidatikli çocuk hastaların verilerinin gözden geçirilmesi, hastalık bulguları ve verilen tedaviler ile tedavi yanıtının değerlendirilmesi, tedavi yanıtını etkileyen etmenlerin saptanması amaçlanmıştır.

Gereç ve Yöntemler: Ocak 2006 ve Aralık 2016 yılları arasında kist hidatik nedeniyle izlemde olan hastaların dosyaları gözden geçirildi. Hastaların tanı yaşları, cinsiyetleri, yaşam alanları (kırsal/kent), köpek temas öyküsü, ailede başka bireylerde kist hidatik varlığı, yakınmaları, tutulan organları, boyutları, laboratuvar sonuçları, uygulanan tedaviler ve tedavi sonrası yanıtları kayıt edildi.

Bulgular: On yıllık sürede 50 çocuk hasta kist hidatik tanısı ile izlendi. Hastaların 33'ü (%66) erkekti. Ortalama tanı yaşı 9,3±0,5 yıldı. Hastaların 15'i kırsal kesimde yaşarken; 35'i kentsel kesimde yaşıyordu ve %10'unda ailede başka bireyde kist hidatik öyküsü vardı. Hastaların 36'sında akciğer tutulumu, 25'inde karaciğer tutulumu vardı. On dört hastada hem akciğer hem karaciğer tutulmuştu. Altı hastada akciğer ve karaciğer dışı organ tutulumu vardı. Kist hidatik indirekt hemaglutinasyon testi bakılan hastaların %60'ında pozitif iken, kist hidatik spesifik IgE 17 hastanın 8'inde pozitif saptandı. Hastaların tümü albendazol tedavisi almıştı. Yedi hastaya ek olarak praziquantel tedavisi verilmişti. Akciğer tutulumu olan 31 hastaya cerrahi, karaciğer tutulumu olan 13 hastaya PAİR (perkütan aspirasyon, enjeksiyon ve reaspirasyon) yapılmıştı. Spinal tutulumu olan iki hastada operasyonla kistler çıkarılmıştı. Akciğer ve karaciğer dışı organ tutulumu olan hastalarda yineleme sıklığı fazlaydı ($p<0,05$) ve bu hastaların tedavi süresi daha uzundu ($p<0,05$).

Çıkarımlar: Kist hidatik çocuklarda farklı organ tutulumları ile karşımıza çıkabilir. Akciğer ve karaciğer dışı organ tutulumu olan hastaların izleminde yineleme açısından daha dikkatli olmak gereklidir.

Anahtar sözcükler: Çocuk; kist hidatik; organ tutulumu

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Introduction

Hydatid cystic disease (HD) is an endemic parasitic disease that is observed commonly in the world and in our country. The parasite that most commonly causes infection in the human lung is *Echinococcus granulosus* (1). There is no specific clinical finding and different symptoms may occur depending on the location and size of the cyst. In children, lung involvement is observed most frequently, whereas liver involvement occurs most frequently in adults. However, any organ may be involved. Most hydatid cysts are asymptomatic and may regress spontaneously (2). The diagnosis is made through clinical findings, radiologic imaging methods, and serologic tests. In treatment, albendazole is used alone or in combination with surgical treatment and percutaneous interventions (3–8). The clinical, radiologic and serologic tests of each patient are addressed separately and treatment response is evaluated because controlled clinical studies related to the type of treatment and a standard protocol are lacking (9, 10). Different studies from our country and the world have presented the data of children with HD, but these data change by the age, socioeconomic status, and place of residence of the patients.

In our study, we aimed to review the data of pediatric patients with HD who were followed up in two centers in the Central Anatolia region, to evaluate the manifestations of the disease, and treatments administered and treatment responses, to determine the factors that influenced treatment response and to contribute to the literature in terms of diagnosis, treatment, and follow-up.

Material and Methods

The files of the patients who were followed up between January 2006 and December 2016 in two Pulmonology Outpatient clinics in the Central Anatolia region because of HD, were reviewed.

The patients' ages at the time of diagnosis, sexes, places of residence (rural/urban), dog contact history, presence of hydatid cyst in other family members, symptoms, organs involved, dimensions, and number of cysts were recorded.

In the laboratory findings, indirect hemagglutination (IHA) test, *Echinococcus granulosus*- specific immunoglobulin (Ig)-E, and the eosinophil count and percentages in complete blood count were recorded.

The medical treatments administered to the patients and their durations, the mean hospitalization and follow-up times of patients who were applied percutaneous aspiration, injection, and reaspiration (PAIR) or who underwent surgery were recorded. Treatment complications were recorded. All findings of the patients who did and did not have recurrence in the long-term follow-up were compared with each other.

Table 1. Demographic characteristics of patients with hydatid cyst

	Number (n)	Percentage (%)
Age (years)	9.3±0.5	
Sex (male)	33	66
Place of residence		
Rural area	15	30
Urban area	35	70
Positive history of dog contact	15	30
HD in another member in the family	5	10

HD: Hydatid disease

The study was conducted in accordance with the principles of the 2008 Declaration of Helsinki with approval obtained from the Ethics Committee of the Faculty of Medicine (Date: 27/02/2017, Number: 36). Informed consent was not obtained because the study was conducted retrospectively.

Statistical Analysis

The Statistical Package for the Social Sciences v.16.0 program (SPSS Inc., Chicago, IL, USA) was used in statistical analyses. Descriptive data are presented as frequency, percentage, mean and standard errors. The Mann-Whitney U test was used in the analysis of continuous variables because parametric assumptions were not met. The Chi-square test was used in the analysis of nominal variables. Fisher's exact test was used when the distribution was not compatible with the Chi-square test in the analysis of nominal variables. A p value of <0.05 was considered significant.

Results

In a period of 10 years, 50 pediatric patients were followed up with a diagnosis of HD in two centers. Thirty-three of the patients (66%) were male. The mean age at the time of diagnosis was 9.3±0.5 years. The demographic characteristics of the patients are shown in Table 1. The most common symptom at the time of presentation was cough (46%), followed by fever, abdominal pain, chest pain, and dyspnea. One patient presented with numbness in the arm and one presented with an inability to walk.

Lung involvement was present in 36 patients (72%) and liver involvement was present in 25 (50%). Fourteen patients had both lung involvement and liver involve-

Table 2. The organs involved, number and sizes of cysts in the patients with hydatid disease

Organ involved (n)	Site (n)	Number of cysts (n)	Cyst size (cm)			
			<1	1–4	5–9	>9
Lung (36)	Right lung					
	Upper lobe (8)	10		2	7	1
	Lower lobe (10)	10			8	2
	Left lung					
	Upper lobe (10)	13		3	6	4
	Lower lobe (12)	15		2	8	5
Liver (25)	Right lobe (16)	26		15	8	3
	Left lobe (11)	13			10	1
Spinal (2)		2		2		
Spleen (1)		1		1		
Gallbladder (1)		1		1		
Brain (1)		1			1	
Adrenal gland (1)		1			1	

ment. Six patients had organ involvement other than the lung and liver. Five patients who had lung involvement had bronchial expansion. Among the patients who had bronchial expansion, the cyst was located in the right upper lobe in two patients, in the right lower lobe in one patient, in the left upper lobe in one patient, and in the left lower lobe in the remaining patient. The patients' organs that were involved and the cyst sizes are shown in Table 2.

In the diagnosis, an HD IHA test was performed in 40 patients and found to be positive in 24 patients (60%). Specific IgE was tested in 17 patients and found to be positive in 8 patients (47%). In the diagnosis, the mean eosinophil count of the patents was found as 558±258/μL and the mean percentage was 4.8±1.3%.

All patients received albendazole treatment. The mean treatment period was 15.5±1.5 months. Seven patients additionally received praziquantel treatment. An increase in liver enzymes was found in one patient who was receiving albendazole treatment, so the treatment was interrupted. In the other patients, no adverse effects were observed with medical treatment.

Surgical treatment was performed in 31 patients who had lung involvement and PAIR was performed in 13 patients who had liver involvement. The cysts were surgically removed in two patients who had spinal involvement. The mean hospitalization time after surgery was 12.8±6.6 days. The data related to the patients' treatments and follow-up are shown in Table 3.

The mean follow-up time was 26.4±3.8 months. During follow-up, recurrence was observed in seven patients. No difference was found between patients who did and did not have recurrence in terms of the age at the time of diagnosis, sex, cyst size, number of cysts, and laboratory findings (p>0.05), but the frequency of recurrence was higher in patients who had organ involvement other than in the lung and liver (p=0.033). The comparison of patients who did and did not have recurrence in terms of clinical characteristics is shown in Table 4. The mean age at the time of surgery was 6.2±2.4 years in patients who had organ involvement other than in the lung and liver, and 10.2±3.4 years in patients who did not have organ involvement other than in the lung and liver; the difference was statistically significant (p=0.026). Again, the albendazole treatment duration was significantly longer in patients who had organ involvement other than in the lung and liver (28.5±13.5 months) compared with patients who did not have organ involvement other than in the lung and liver (13.7±9.2 months) (p=0.007).

Table 3. Treatment and follow-up of the patients with cystic hydatid disease

	Number (n)	Percentage (%)
Medical treatment		
Albendazole	50	100
Praziquantel	7	14
Surgical treatment	33	66
PAIR	13	26
Recurrence	7	14
Mean follow-up time (months)	26.4±3.8	

PAIR: Percutaneous aspiration, injection and reaspiration

Table 4. Comparison of the patients with and without recurrence in the follow-up

	Recurrence (%) (n=7)	No recurrence (%) (n=43)	p
Age	7.1±0.9	9.7±0.5	>0.05
Sex[a] (male)	5 (71.4)	27 (64.3)	>0.05
Place of residence[a]			
Rural area	1 (14.3)	14 (33.3)	>0.05
Urban area	6 (85.7)	28 (66.7)	
Positive history of contact with dog[a]	1 (14.3)	14 (33.3)	>0.05
HD in another family member[a]	1 (14.3)	4 (9.5)	>0.05
Organ involvement other than lung and liver[a]	3 (42.9)	3 (7.3)	0.033
Albendazole treatment duration (months)	19.2±4.7	14.9±1.6	>0.05
Age at the time of operation (years)	7.8±0.9	9.9±0.7	>0.05

HD: Hydatid cystic disease; [a]Fisher's exact test was used

Discussion

Hydatid cyst disease is still an important public health problem in our country and worldwide. The larvae ingested by the oral route are transferred from the intestines to the liver by way of the portal vein and the most commonly involved organ is the liver (11). In children, however, the cyst is observed most commonly in the lungs, because the lungs enable rapid growth of the cyst due to their compressible structure, vascularization, and negative pressure (12). It has been reported that the lower lobes of the lungs are more frequently involved and the right lung is involved most commonly (13). In our study, we observed that the most commonly involved organ was the lung and the lower lobes were involved more frequently, in accordance with the literature. However, it was observed that the left lung was involved with a slightly higher rate compared with the right lung. It is known that organ involvement may show variance by regions and ages.

If the larvae pass through the liver and lungs, which are the primary filters, or skip these organs by using the lymphatics, they may cause the disease to spread via the blood or lymphatic pathways and thus may lead to infection in any part of the body (11, 14). In the literature, many studies have reported that the third most commonly involved organ is the spleen following lung and liver involvement (11, 15). However, there are also studies reporting different results (16, 17). In our study, spinal involvement (two patients) was observed in third place following lung and liver involvement, and also spleen, brain, gallbladder, and adrenal involvement was observed. Spinal involvement is observed very rarely in children, its frequency is considerably low (18–23). It is thought that its lower frequency may be related to a lack of consideration in the differential diagnosis in regions where HD is not endemic and due to difficulties in the diagnosis.

In our patients, HD IHA positivity was found with a rate of 60% and specific IgE positivity was found with a rate of 47%. In serologic studies conducted with patients who had HD, different serologic methods were compared with each other and it was shown that the most sensitive diagnostic method was specific IgG, followed by specific IgM and IHA, and the least sensitive diagnostic method was specific IgE (24–26). Specific IgE was not be evaluated because it could not be studied in the two centers where our study was conducted. However, the rate of IHA positivity was observed to be higher compared with specific IgE, in accordance with previous studies.

There is no perfect therapeutic option because controlled clinical studies comparing different therapeutic approaches are lacking. The treatment approach is determined according to the patient's age, the cyst's structure, location, and size, the experience of the team who conduct the treatment, and the patient's long-term follow-up. Treatment approaches include surgical treatment, percutaneous interventions, medical treatment, and the watch-and-wait approach. In some patients, multiple approaches are used in combination (5). In a study related to childhood *Echinococcus granulosus* disease published recently, which included 187 children, an algorithm for the treatment approach in children was recommended. Accordingly, it was recommended to administer albendazole or mebendazole treatment for 1-4 weeks before surgery, to follow up patients for a long period following cystectomy in cases of uncomplicated cysts smaller than 10 cm, to continue medical treatment for 1-3 months following surgery including cystectomy and capitonnage in cases of uncomplicated cysts larger than 10 cm, to follow up patients for a long period following segmentectomy or lobectomy in cases of complicated cysts with any size, and to follow up patients with imaging in cases of inactive or calcified

cysts (27). In another study related to the treatment of lung HD in children, it was recommended that parenchyma-preserving surgery (cystectomy and capitonnage) should be preferred rather than lung resection due to a high risk of recurrence, especially in endemic regions and because of the high lung regeneration capacity in children (28). In our study, surgery was performed in 31 of 36 patients who had lung involvement, and medical treatment alone was administered in five patients. The patients who did not undergo surgery had multiple small cysts in both lungs (<5 cm) and they benefited from medical treatment.

In cases of liver cysts, surgical treatment, PAIR or medical treatment may be administered. PAIR was administered in 13 of 25 patients who had liver involvement and no surgery was performed in any of these patients in our study. Surgery is mostly preferred in patients with complicated cysts (ruptured cyst, cysts with biliary fistula, cysts compressing vital structures, cysts with secondary infection or hemorrhage), cysts larger than 10 cm and superficial cysts which could easily rupture (29). In our 12 patients, medical treatment was given alone because there were multiple small cysts located in different lobes of the liver. Medical treatment was discontinued in the patients who had inactive cysts and these patients were followed up clinically.

There are no clear data related to treatment approaches in cases of organ involvement other than in the lung and liver. In cases of cardiac and bone involvement, surgery is recommended primarily (5). However, there are also studies recommending the PAIR method as the primary option in cases of organ involvement other in than lung and liver (30). Surgery was performed in two patients who had spinal involvement in our study. The other patients were followed up with medical treatment and it was observed that the cysts progressed to an inactive form. However, there are no definite recommendations related to the duration of treatment and drug choice in these patients. The fact that recurrence was observed more commonly in our patients who had organ involvement other than in the lung and liver was a notable outcome. Similarly, recurrence was observed more commonly in patients who had organ involvement other than in the lung and liver in a study conducted with adults (31).

It was thought the fact that recurrence was observed more commonly in our patients who had organ involvement other than in the lung and liver in our study might be related to both delayed diagnosis and to the low bioavailability of albendazole, which caused failure of the drug to reach effective doses in these organs (32, 33). It was concluded that physicians should be more careful in the follow-up of these patients.

Our study had some limitations. Our study was conducted retrospectively only in two centers in the Central Anatolia region in our country. The number of patients was low and children who had both lung and liver involvement and who had involvement other than in the lung and liver were included in the study. It will be helpful to confirm these results with multi-center retrospective studies including higher numbers of patients.

In conclusion, HD is still a widespread problem in our country and may be manifested by involvement of different organs in children. It should be kept in mind that serologic methods are not always helpful in the diagnosis in suspicious cases and HD is observed commonly in our country. Treatment should be decided according to the organ involved, the number and size of the cysts, and complications. Physicians should be more careful in terms of recurrence in patients with organ involvement other than in the lung and liver.

Ethics Committee Approval: The study was conducted in accordance with the principles of the 2008 Declaration of Helsinki with approval obtained from the Ethics Committee of the Faculty of Medicine (Date: 27/02/2017, Number: 36).

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