



Relation between Serology and Grow-Up Time in Atypically Localized Hydatid Cysts

Atipik Lokalizasyonlu Kist Hidatiklerde Büyüme Hızı ve Seroloji İlişkisi

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ABSTRACT

Objective: Hydatid cyst is a parasitic disease caused by the larvae of *Echinococcus granulosus*. In the study, the aim is to evaluate the relation between serology and grow-up time in atypically localized cysts.

Methods: Retrospectively, all the patients with hydatid disease between December 2004 and May 2012 were screened from the hospital database. Hydatid cyst localization other than the liver and lungs were accepted as atypical localization.

Results: There were 325 patients with a diagnosis of hydatid disease. Most common localizations of the cysts were the liver (72.8%) and lungs (21%). Atypically localized cyst rate was 6.4% (n: 21). The most common atypical localization was the spleen (2.4%). 80.9% of atypically localized cysts were primary cases. In 3 cases with primary intramuscular hydatid cyst and 2 cases with primary subcutaneous hydatid cysts, serology was negative.

Conclusion: The relation between the hydatid cyst and the host is the main factor in serological tests and grow-up time. In tissues with a weaker cellular immunity like muscle and subcutaneous tissue, serology tends to be negative and grow-up time to be faster. In atypically localized cysts, hematogenous dissemination cannot explain the pathogenesis fully. Therefore, lymphatic dissemination should be kept in mind.

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Key Words: Hydatid disease, atypical, rare, localization

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ÖZET

Amaç: Hidatik hastalık, sıklıkla *Echinococcus granulosus* larvalarının sebep olduğu parazitik bir hastalıktır. Bu çalışmada hidatik kistin atipik lokalizasyonu ile seroloji ve kistin büyüme hızı arasındaki ilişkinin araştırılması amaçlanmıştır.

Yöntemler: Aralık 2004 ile Mayıs 2012 tarihleri arasında hastanemizde hidatik kist nedeni ile tedavi edilmiş olan tüm hastalar hastanemiz veri tabanından retrospektif olarak tarandı. Hidatik kistin karaciğer ve akciğer dışı yerleşimi atipik lokalizasyon olarak kabul edildi.

Bulgular: Bu tarihler arasında hastanemizde hidatik kist nedeni ile 325 hasta tedavi edilmiş idi. En yaygın yerleşim yerleri karaciğer (%72,8) ve akciğerler (%21) idi. Karaciğer ve akciğer dışı yerleşim (atipik lokalizasyonlu hidatik kist) ise %6,4 (n=21) idi. Atipik lokalizasyonlu hidatik kist en sık dalakta (%2,4) gözlenmiştir. Primer kas içi hidatik kist olan 3 olguda, primer subkutan hidatik kisti olan 2 olguda seroloji negatiftir.

Sonuç: Hidatik kist ile konakçı savunma sistemi arasındaki ilişki seroloji pozitifliğini ve kist büyüme hızını belirleyen ana unsurdur. Hidatik kist kas dokusu, subkutan doku gibi hücrel immünitenin daha zayıf olduğu dokularda serolojinin negatif olması ve daha hızlı büyüme eğilimindedir. Atipik lokalizasyonlu hidatik kistler için hematojen yol patogenezi izah etmek için yetersiz olup, bu olgularda lenfatik yayılda söz konusu olabilir. (*Türkiye Parazitol Derg* 2013; 37: 257-61)

Anahtar Sözcükler: Kist hidatik, atipik, nadir, yerleşim

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INTRODUCTION

Echinococcosis (hydatidosis, hydatid disease) is a zoonosis caused by the larval (metacestode) stages of cestodes (flat worms) belonging to the genus *Echinococcus* and the Family *Taeniidae*. Humans are an accidental, intermediate host and become infected when they accidentally ingest eggs of the tapeworm. The eggs hatch in the duodenum, and the released oncosphere penetrates the mucosa and reaches a blood vessel. The bloodstream can carry the oncosphere to any part of the body, but it most frequently settles in the liver and lungs. Once settled, the parasite develops its larval stage, the hydatid cyst, the clinical presentation of *E. granulosus*. The cellular response of host tissue is an attempt to encase the parasite in fibrous tissue. A developing cyst usually survives, with a steady increase in size of about 1 to 1.5 mm in diameter per month, depending on the site and adjacent structures (1).

The aim of this study is to evaluate the relation of atypical localization of the cyst and serological markers and grow-up time.

METHODS

Between December 2004 and May 2012, all the patients administered to hospital with a diagnosis of hydatidcyst were screened from hospital records. Patient information and localization of the cysts were recorded. The number of cysts, treatment modality and complications were defined.

Liver and lungs were accepted as typical localizations. Any localization other than the liver and lung were accepted as atypical localizations. The cases with atypically localized cyst and liver and/or pulmonary cyst were accepted as secondary cysts. Also, the cases with previously treated liver and/or pulmonary hydatid cysts were accepted as secondary cases. Atypically localized hydatid cyst without existing or previously treated liver and/or pulmonary hydatid cysts were accepted as primary cases.

In cases with a doubt in the diagnosis, echinococcus indirect hemagglutination (IHA) test was used (Echinococcosis Fumouse, France). In cases with a definitive diagnosis, the test was not used. An IHA level 1/160 and above was accepted as positive. However, in some cases the diagnosis was made by pathological examination after surgery (Intramuscular and subcutaneous hydatid cysts).

Preoperative ultrasonography was used in all the patients. In the diagnosis, computed tomography and/or magnetic resonance imaging were used as advanced studies. Patients were staged according to Gharbi staging in ultrasonography.

According to hospital records, patients' duration of complaints, serological test results and the diameter of the cysts were recorded. In secondary cases, atypically localized cyst diameter was accepted as the cyst diameter. Treatment methods, mortality, morbidity and recurrences were also recorded.

The patients were called and checked by phone whether they had any complaints or recurrences.

All the patients used albendazole (100 mg/kg) for 3 months.

A literature search was done and atypically localized hydatid cysts were evaluated in terms of being primary or secondary, localization, duration of complaints, serological tests and cyst diameter.

Statistical analysis

In this study IBM SPSS Statistics version 20 was used. The data was given as mean \pm standard deviation.

RESULTS

In this period, there were 325 cases with hydatid disease. There were 211 (64.9%) female and 114 (35.1%) male patients. Their mean age was 41.3 ± 19.1 .

The most common localization of the hydatid cyst was the liver (72.8%, n=236), followed by the lungs (21%, n=68). The rate of atypically localized cysts was 6.4% (n=21). The distribution of hydatid cysts according to localization was given in Table 1.

Atypically localized cysts were mostly localized in the spleen (2.4%) (2 secondary and 6 primary cases). In second place were 4 intraabdominal hydatid cysts (3 primary and 1 secondary cases). Other rare localizations were given in Table 1. Interestingly, 80.1% of the atypically localized cysts (17 in 21) were primary cases.

In 3 splenic cysts, IHA was used and 2 were negative. The IHA test was positive in 2 secondary hydatid cysts (intraabdominal+liver and intraabdominal+liver+subcutaneous). In 2 of 3 primary intramuscular cysts and 2 primary subcutaneous cysts, IHA was negative (Table 2).

In splenic hydatid cysts, 3 cases were treated by PAIR (puncture, aspiration, injection, and reaspiration). In one case splenectomy was performed due to intraoperative bleeding and the other 4 cases underwent partial cystectomy. In renal hydatid cysts, one was treated by PAIR (Gharbi stage 1) and the other by partial cystectomy (Gharbi stage 4). Pancreatic hydatid cyst and the cyst in psoas muscle were treated by PAIR. The other cysts (intraabdominal, intramuscular and subcutaneous) were totally removed (Table 2).

Table 1. Localization of the hydatid cysts

Localization	n	%
Liver	236	72.8
Lung	68	21.0
Spleen	6	1.9
Spleen + Liver	1	0.3
Spleen + Lung	1	0.3
Intraabdominal	3	0.9
Intraabdominal + Liver	1	0.3
Intraabdominal + Subcutaneous + Liver	1	0.3
Intramuscular (Rectus abdominis - gluteus maximus - psoas)	3	0.3
Kidney	2	0.6
Subcutaneous	2	0.6
Pancreas	1	0.3
Total	325	100

In 2 cases, there were wound infections and they were treated conservatively. In one case, there was abscess formation in the cyst pouch and it was percutaneously drained. There was no mortality and recurrence in the follow up.

DISCUSSION

Hydatid disease is endemic in countries where husbandry is common, such as the Mediterranean, Middle Asia, South America, New Zealand and South Africa (2-4). Most commonly, the liver (70%) and lungs (10-15%) are affected. Other than these organs, it is very rare (2, 3). The rate of hydatid cyst of the peritoneal cavity is 10-16% and they are secondary to minimal rupture of liver cysts or implantation during previous surgery. Sixty one percent of them are seen with liver cysts and primary intraperitoneal hydatid cysts are very rare (2, 4). Furthermore, hydatid cysts can be seen in muscular tissue, soft tissue, kidneys, spleen, bone and rarely in the brain, thyroid, breast and pancreas. Atypically localized hydatid cysts can be primary or secondary (2-4). In this study, the rate of intraperitoneal hydatid cyst is very low and most of the cases are primary cases (75%). All those data in the literature are from small series; therefore, the rates are very different.

Atypically localized hydatid cysts other than the peritoneal cavity are explained by the escape of the embryos from the liver and pulmonary filter mechanisms and dissemination by the systemic circulation. However, primary atypically localized cysts are diffi-

cult to be explained by systemic dissemination. In our study, 80% of atypically localized cysts are primary cases. Therefore, lymphatic dissemination besides systemic dissemination may be an effective mechanism (5). Hydatid cyst after a bee sting also supports this mechanism (6).

Serological test are useful in diagnosis. They rely on the basis of specific antibodies in the patient's plasma. There are many serological tests; however the most commonly used is the indirect hemagglutination test. IHA is a very sensitive test and is positive in 80% of hepatic hydatid cysts. Yet, a negative result cannot rule out the diagnosis. IHA has a high negativity rate in tissues other than the liver (7). Especially, in most of the muscular and subcutaneous hydatid cysts it gives negative results and has no diagnostic value (4, 8). In the literature, there are studies giving 66% serological positivity rates in atypically localized hydatid cysts (9), but generally it has very limited diagnostic value, as in this study.

Negative serology and absence of a primary focus (liver and lung) in atypically localized hydatid cysts are interesting findings. Those findings show that the etiopathogenesis of the disease has not been fully understood yet.

Hydatid cysts used to be known as slowly growing lesions. The yearly growth rate is reported as 1 cm in some reference books and 4-5 cm in some studies (10, 11). Recently, the growth rate is determined as much higher than it previously known (12). In the

Table 2. Clinical details of atypically localized hydatid cysts

Localization	Serology (IHA>1/160)	Cyst diameter	Gharbi stage	Duration of symptoms (month)	Treatment
Spleen	Negative	4x4	1	6	PAIR
Spleen	Negative	3x3	2	12	PAIR
Spleen	Negative	3x2	2	24	Partial Cystectomy
Spleen	None	6x5	1	3	PAIR
Spleen	None	4x3	1	6	Partial Cystectomy
Spleen	None	4x3	1	6	Partial Cystectomy
Spleen + Liver	None	3x5	3	6	Splenectomy
Spleen + Lung	None	4x5	1	5	Partial Cystectomy
Intraabdominal +Liver	Positive				Cystectomy
Intraabdominal	None	15x10	4	6	Cystectomy
Intraabdominal	None	10x10	2	12	Cystectomy
Intraabdominal	None	3x1	3	3	Cystectomy
Intramuscular (Rectus abdominis)	Negative	5x4	2	12	Cystectomy
Intramuscular (Psoas)	Positive	7x8	2	1	PAIR
Intramuscular (Gluteus maximus)	Negative	3x5	3	8	Cystectomy
Intraabdominal + Subcutaneous + Liver	Positive	20x20	3	1	Cystectomy
Kidney	None	7x8	1	18	PAIR
Kidney	None	10x10	4	24	Partial Cystectomy
Subcutaneous (Back)	Negative	8x10	1	4	Cystectomy
Subcutaneous (Face)	Negative	4x3	1	0,5	Cystectomy
Pancreas	Negative	4x3	1	3	PAIR
PAIR: puncture, aspiration, injection, reaspiration					

Table 3. Atypically localized hydatid cysts in the literature

Author	Primary/ secondary	Localization	Duration of symptoms	Serology	Cyst diameter (cm)
Kouskos E et al 2007 [13]	Primary	Right thigh (between muscle and subcutaneous tissue)	Recent years	Positive	5x10
Dirican A et al 2008 [14]	Primary	thigh (subcutaneous)	1 year	Negative	8x9
	Primary	Palm (subcutaneous)	?	Negative	2x3
Bilgic S et al 2009 [15]	Primary	Paraspinal	5 months	Negative	5x5
Eryılmaz MA et al 2010 [16]	Primary	Right gluteal (intramuscular)	2 months	Negative	5x3
Şehitoğulları A et al 2006 [17]	Primary	Latissimus dorsi (intramuscular)	6 months	?	10x15
Demirel AH et al 2007 [18]	Primary	Right trapezius muscle (intramuscular)	?	Negative	3x3
	Primary	Below clavicle (subcutaneous)	?	Negative	4x5
	Primary	Retroperitoneal	?	Positive	15x15
Battany I et al 2011 [6]	Primary	Right popliteal region (subcutaneous)	Lower than 7 days	?	3x4
Ölmez A et al 2010 [19]	Primary	Right lumbar region (subcutaneous)	?	Positive	4x3
Öcalan K et al 2011 [20]	Primary	Right thoracic region (subcutaneous)	?	Negative	15x10
Kurt A et al 2009 [4]	Primary	Left leg (intramuscular)	2 years	Positive	15x8
Ozsoy M et al 2011 [21]	Primary	Axillary region	2 months	Negative	3x3
Dirican A et al 2011 [22]	Primary	Lumbar region (intramuscular)	2 months	Positive	6x5
Masoodi MI et al 2011 [23]	Primary	Pancreas	6 months	Positive	7x6
Avcu S et al 2010 [24]	Primary	Thyroid and submandibular glands	2 years	Positive	3x2
Bhat NA et al 2011 [25]	Primary	Pancreas	4 months	Negative	15x7
?: not indicated in the study					

literature, the growth rate of hydatid cysts can be as high as in our study (6). Especially in subcutaneous and intramuscular cysts, the duration of complaints can inform us about the growth rate.

As a result of the reaction between the hydatid cyst and the host, immune mechanisms try to limit the cyst. This cellular and humoral reaction causes the formation of the fibrinous pericyst. Moreover, as a result of the humoral defense mechanism, antibodies are formed. Serological evaluation of those antibodies can help us in diagnosis. The main detector of the growth rate is the relation between the cyst and the host (1). Being asymptomatic in the liver and lungs finding a relation between the duration of complaints and the growth rate is difficult. However, in subcutaneous tissue, duration of the symptoms can inform us about the growth rate of the cyst.

A high serological positivity in solid organs like the liver and lungs and negativity in tissues with weaker cellular immunity like muscle and subcutaneous tissue is exciting. Atypically localized hydatid cysts are very rare and are reported as case studies. In Table 3, serological results, duration of symptoms and cyst diameters of atypically localized hydatid cysts in the literature are presented. As the duration of the symptoms increases, the positivity rate of serology increases. Moreover, in cases with shorter duration, almost all are serologically negative. The results of this study are similar to the literature. Furthermore, the case with a 3x4 cm subcutaneous cyst shows that the growth rate can be very high and probably it is proportional to the escape from the immune response of the host.

CONCLUSION

The relation between the cyst and the host is the main factor in determination of serological positivity and the growth rate. In subcutaneous and muscular tissue, hydatid cysts tend to grow faster and the serological tests tend to be negative. In atypically localized hydatid cysts; hematogenous dissemination is not sufficient to explain the pathogenesis, and lymphatic dissemination may play an important role. The main limitation of the study is that atypically localized hydatid cysts are very rare and all data about them are from small case series.

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