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(REVIEW ARTICLE)

The importance of indirect hemagglutination assay test and eosinophilia in follow-up of calcified liver hydatid cyst: A Retrospective Study

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Abstract

Introduction: Calcified liver cystic echinococcosis(C-LCE) does not require interventional treatment but necessitates regular monitoring. The assessment of C-LCE commonly involves radiological, serological and hematological examinations. This study investigates the correlation between eosinophilia and serological test results in patients with radiologically confirmed C-LCE.

Materials and Methods: This retrospective study included 25 patients diagnosed with C-LCE through radiological imaging who were treated in surgery departments between 2010 and 2017. The levels of indirect hemagglutination assay (IHA) and peripheral eosinophilia counts were analyzed. Patients with an IHA titer of ≤1/320 and negative peripheral eosinophilia were not administered chemotherapy, while those with higher titers received treatment and follow-up care.

Results: The majority of patients were female. All cysts were solitary and localized in the right hepatic lobe. Imaging results were consistent with C-LCE. IHA positivity was observed in 22 patients, with seven of them exhibiting eosinophilia. A direct association was noted between high IHA titers and the presence of eosinophilia.

Conclusion: Interventional treatment for C-LCE carries significant risks, including infection and fistula formation. Therefore, non-invasive follow-up strategies using radiological, hematological and serological tests are recommended. Evaluating peripheral eosinophil levels alongside serological markers can enhance treatment decision-making

Keywords: Cystic echinococcosis; Calcified cyst; Eosinophilia; Serology; Liver

1. Introduction

Liver cystic echinococcosis(LCE) is a parasitic infection caused by Echinococcus granulosus, with endemic prevalence in South Central Europe, South America, Australia, and Alaska [1,2]. Typically, LCE remains asymptomatic unless cysts grow large enough to exert pressure on adjacent structures, become infected or rupture [3,4-6]. The primary treatment objective is scolocidal inactivation. Depending on the classification by Gharbi, management options include anti-helminthic chemotherapy, percutaneous aspiration under radiological guidance, surgery, or observational follow-up [1,3]. Cysts classified as calcified (Type V in the Gharbi system) should be followed-up with or without chemotherapy

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primarily managed through periodic monitoring [2]. Biannual assessments involving radiological imaging, hematological, and serological tests are essential for early detection of cyst reactivation [2-3].

This study aims to retrospectively analyze the relationship between peripheral eosinophil counts and serological test results in patients with radiologically confirmed C-LCE.

2. Material and methods

A retrospective review was conducted on 25 patients diagnosed with C-LCE between 2010 and 2017 at two medical institutions(Sakarya Toyota Hospital and Tekirdag University Research Hospital). Patient records were assessed for demographic data, hematological and serological test results, cyst localization, and cyst dimensions. Descriptive statistics were used to evaluate findings, with results presented as numerical values and percentages.

IHA was utilized as the primary serological test, employing Hydatidose Fumouze Sofibel kits (Levallois Perret, France). Peripheral eosinophil counts were determined using ABX Pentra DX 120 (Horiba, Montpellier, France). An IHA titer exceeding 1/320 was considered positive, while eosinophilia was defined as a serum eosinophil count above 0.7 × $10^3/\mu L$.

Patients were managed with or without chemotherapy based on IHA and eosinophil findings. Albendazole (15 mg/kg per day) was administered in divided doses for three weeks, followed by a one-week drug-free interval. This cycle was repeated over 6–12 months, with liver function monitored monthly.

2.1. Statistical Analysis

Data were analysed using the PASW (PASW Statistics 18.0.0, SPSS Inc., Chicago, IL) statistics program. Values for $p \leq 0.05$ were considered statistically significant.

3. Results

Among the 25 patients, 72% were female. The mean age was 38.8 ± 22 years, with an age range of 24–55 years. A statistically significant gender difference was observed ($p<0.05$). However, no significant difference in IHA titers was found between male and female patients ($p>0.05$). All cysts were solitary and located in the right lobe of the liver, classified as Type V based on radiological imaging.

IHA positivity (>1/160 titer) was detected in 88% of patients. Severe positivity (>1/1280 titer) was identified in 20% of cases, all of whom exhibited eosinophilia. A statistically significant correlation was noted between high IHA titers and eosinophilia ($p<0.05$). However, cyst size did not demonstrate a significant relationship with either IHA titers or eosinophilia ($p>0.05$). Throughout the follow-up period, no scolocidal activation or new cyst formation was observed, and no cases of morbidity or mortality were reported.

Table 1 The distribution of Indirect Hemagglutination Assay(IHA) titers and eosinophilia

Titer of IHA	**Number of Cases**	**Eosinophillia**	
		+	**-**
Negative (under 1/160)	3 (12%)	0	3 (12%)
Suspect Positive (1/160-1/320)	3 (12%)	0	3 (12%)
Mild positive (1/320)	6 (24%)	0	6 (24%)
Medium positive (1/640)	8 (32%)	2 (8%)	6 (24%)
Severe positive (1/1280 and up)	5 (20%)	5 (20%)	0
Total	25 (100%)	25 (100%)	

Table 2 The distribution of cysts by IHA, eosinophilia and size

Size of Cyst	Calcified Cyst	Number of Case	IHA			Eosinophillia		
			+		-	+		-
> 4 cm	+	15 (60%)	13	P=0,654	2	3	P=0,700	12
≤ 4 cm	+	10 (40%)	9		1	4		6
Total	25	25 (100%)	25			25		

4. Discussion

LCE is a parasitic disease with widespread hepatic involvement [1,2,7]. In many cases, cysts are identified incidentally during imaging for unrelated symptoms. LCE are usually don't give signs unless the pressure reaches a size that causes symptoms, infection or rupture [2]. Literature indicates that 80% of hydatid cysts are solitary and localized in the right hepatic lobe, consistent with our findings [1,8,9]. It is seen that our study is compatible with the literature.

Echinococcal cysts are usually seen asymptomatic, but the development of some important complications, such as lung infection, cholangitis, rupture, and anaphylaxis, provides a good reason for patients to consider treatment [2].

The management of LCE varies from conservative chemotherapy to percutaneous drainage or surgical intervention [1]. For radiologically confirmed C-LCE, invasive treatment is generally unnecessary due to associated risks such as infection and/or fistula formation [10,11,12,13]. Instead, patients should undergo long-term follow-up involving radiological, serological, and hematological assessments every six months [2]. Deep-seated small cysts (≤four cm) may be managed conservatively unless complications arise [12].

Serological testing remains a valuable diagnostic and monitoring tool [1,2]. Available tests include IHA, enzyme-linked immunosorbent assay (ELISA), Weinberg test, and Casoni skin test [10]. Due to their low sensitivity, Weinberg and Casoni tests are no longer widely used. ELISA has high sensitivity (>90%) but may yield false-positive results for up to a year post-treatment [2,11]. IHA, while reliable, has a sensitivity of 85% and may persist for years, reducing its efficacy in endemic regions [1,2].

Peripheral eosinophilia is usually detected in about half of patients [7]. Eosinophilia (> 3%) occurs in 25% to 40% of patients with hydatid cyst in western countries, but it appears as a non-specific finding in endemic locals [2]. In this study, eosinophilia was observed in accordance with the literature. Eosinophilia was observed in seven (28%) patients with a high IHA titer (> 1/640). These findings align with existing literature, suggesting a correlation between elevated eosinophil counts and serological markers.

Different degrees of calcification may be present in all cyst forms, from active classic unilocular or multivesicular cysts to the more complicated stages, such as advanced and highly degenerate phases where the parasite wall appears massively calcified [14]. Cyst calcification is regarded as the terminal phase of parasite degeneration, restricted to five Type and believed to be an index of cyst inactivity. All cyst types with signs of calcification increasing as the degenerative process progresses. Nevertheless, the detection of calcification is not in itself sufficient to evaluate parasite activity and can be misleading, since this process may coexist with still active cysts, and partial calcification is not always indicative of parasite death [15]. In this case, other supporting methods such as serological tests and peripheral eosinophils are needed.

5. Conclusion

The long-term follow-up of C-LCE should incorporate hydatid serologies, periodic imaging, and eosinophil assessments. Conducting peripheral eosinophil counts alongside serological testing enhances the accuracy of scolocidal activity monitoring. Our findings suggest that chemotherapy may not be required for patients with IHA titers ≤1/320 and negative eosinophilia. However, further large-scale randomized studies are necessary to establish definitive treatment guidelines.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest was declared by the authors.

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Statement of informed consent

Informed Consent was not received due to the retrospective nature of the study.

Author contributions

Surgical&medical practices: Duran Y, Polat FR Concept-, Design-, Supervision-, Resource-, Materials- Duran Y , Polat FR, Data Collection &/or Processing-, Analysis- Duran Y , Polat FR, , Polat IF; Analysis or Interpretation-, Literature Search-, Writing-, Critical Reviews- Duran Y , Polat FR, , Bali İ, Benek S, Çaglayan K, Sagiroglu T, Gurdal SÖ Drafting &/or Revising: Duran Y , Polat FR Writing: Duran Y , Polat FR Final Approval:Duran Y, Polat FR, Polat IF, Benek S, Çağlayan K, Sağıroğlu T, Özkan Gürdal S, Bali İ.

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