

Surgically managed human cystic echinococcosis in north-eastern Iran: a single center's experience from 2001 to 2008

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Abstract Cystic echinococcosis (CE) is a zoonotic parasitic disease caused by the tapeworm *Echinococcus granulosus*. Although CE has a large geographic distribution, data are lacking on the frequency of infection and epidemiology of CE in many endemic areas of the world, including the Middle East. Demographic and clinical information on surgically managed human CE cases were evaluated from a referral hospital in north-eastern Iran for the years 2001–2008. Of the 400 CE cases, 218 (54.5%) were male. The median age of patients was 35 years (range 2–83 years). The lungs (41.0%) and liver (37.7%) were the most commonly infected organs. However, 12.7% of patients had multiple organ involvement. The majority of cases (54.3%) were diagnosed using ultrasound, with only 12.0% diagnosed with the help of serology. Total white blood cell count was elevated in 26.8% (107/400) of patients, neutrophil count was elevated in 24.0% (96/400) of patients, and eosinophil count was elevated in 13.3% (53/400) of patients. Lymphocyte count was the only complete blood count (CBC) value that differed based on organ location ($P = 0.001$). Despite some successes in the control of CE, the number of surgical CE cases in north-

eastern Iran remains high. Although not diagnostic alone, CBC values allow for clinicians to obtain a more complete clinical picture of CE before, during, and after treatment. While serology has its place, the use of diagnostic imaging continues to be the most commonly used tool for the diagnosis of CE cases.

Keywords Cystic echinococcosis (CE) · Complete blood count (CBC) · Surgery · Iran

Introduction

Cystic echinococcosis (CE), caused by the zoonotic parasite *Echinococcus granulosus*, is globally distributed, with a number of highly endemic regions located in the Middle East. Intermediate hosts, including livestock species such as sheep, goats, and camels, are infected via ingesting eggs released in the feces of infected dog definitive hosts (Eckert 2001; Fallah et al. 1995; Razmi et al. 2006). Humans can also act as aberrant intermediate hosts if they accidentally ingest the parasite eggs. In intermediate hosts, the parasite's larval stage (metacestode) can develop in any organ system, with the liver and lungs being the most commonly infected. Due to the condition's chronic nature and socioeconomic impact, CE is considered an important Neglected Tropical Disease in endemic countries, including Iran (Budke et al. 2006; Craig et al. 2007; Fasihi Harandi et al. 2012).

Clinical manifestations associated with CE are largely dependent on organ involvement and cyst size (Eckert 2001). Diagnosis is most commonly based on diagnostic imaging and serology (Rokni 2009; Sadjjadi et al. 2001; Wuestenberg et al. 2014). The usefulness of ancillary tests, such as the complete blood count (CBC), as a prognostic tool in CE patients has been evaluated in several studies

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(Cappello et al. 2013; Cicioglu Aridogan et al. 2009; Hernández-Pomi et al. 1997). In addition, eosinophil count has been shown to be elevated in some patients with confirmed CE (Cicioglu Aridogan et al. 2009; Panaitescu 1970; Pautrizel and Gosman 1953), with a greater eosinophilia reported in patients with multiple or ruptured cysts (Pautrizel and Gosman 1953). Additional studies are needed to determine if CBC parameters may be useful as part of a diagnostic profile for CE patients and especially those patients with low antibody production. The current study provides demographic and clinical information on surgically managed CE patients treated at a referral hospital in an endemic area in north-eastern Iran from 2001 to 2008.

Materials and methods

Patients

The medical records of CE patients who were surgically managed at Ghaem Hospital, a referral hospital in Mashhad, the capital of Razavi Khorasan Province in north-eastern Iran, from 2001 to 2008 were reviewed after obtaining ethics approval. A form was developed and used to collect information on patient demographics, pre-operative laboratory data, diagnostic imaging, and organ involvement.

Statistical analysis

Descriptive statistics were performed for collected data, with non-normally distributed continuous variables expressed as medians and ranges, while frequency of infection was expressed as percentages. The Chi squared test was used to evaluate difference in CBC values (low, normal, or elevated) by organ involvement, with values categorized based on normal ranges provided by the Iranian Association of Clinical Laboratories (<http://iaclid.ir/en/>). For CBC values statistically significant by the Chi squared test, post hoc assessment was conducted by calculating adjusted standardized residuals using crosstabs. Cell-specific z-scores were then transformed to Chi square values and then to *P* values. A Bonferroni correction was performed, resulting in an adjusted *P* value of 0.00333. All data were analyzed using SPSS software (version 22, Chicago, IL, USA), with a *P* value of 0.05 or less considered statistically significant unless otherwise noted above.

Results

A total of 400 surgical CE cases were managed between 2001 and 2008, with cases originating from the provinces of North Khorasan, Razavi Khorasan, and South Khorasan.

Out of these 400 cases, 218 (54.5%) were male. The median age of patients was 35 years (range 2–83 years). The frequency of CE patients in different age groups is shown in Table 1. The most commonly involved organs were the lungs (164/400, 41.0%) and liver (151/400, 37.7%). Multiple organ involvement was seen in 12.7% (51/400) of cases. Magnetic resonance imaging (MRI) was primarily used in patients with brain or spinal cord involvement (*n* = 8), with the majority of patients receiving an abdominal ultrasound (*n* = 217). Out of 48 cases diagnosed with the aid of serology, 44 (11.0%) and 4 (1.0%) cases were evaluated using an indirect hemagglutination assay (IHA) and enzyme-linked immunosorbent assay (ELISA), respectively. Frequency of use of the different diagnostic methods is shown in Fig. 1.

Total white blood cell (WBC) count was elevated in 26.8% (107/400) of patients. Neutrophil count was elevated in 24.0% (96/400) of patients and 13.3% (53/400) of patients presented with an eosinophilia. Lymphocyte count was the only CBC value that differed based on organ location of the cyst(s) (*P* = 0.001) (Table 2). Post-hoc assessment indicated that the proportion of patients with elevated lymphocyte counts was significantly higher than expected in those patients with cysts in the liver plus another organ system (*P* = 0.00004).

Discussion

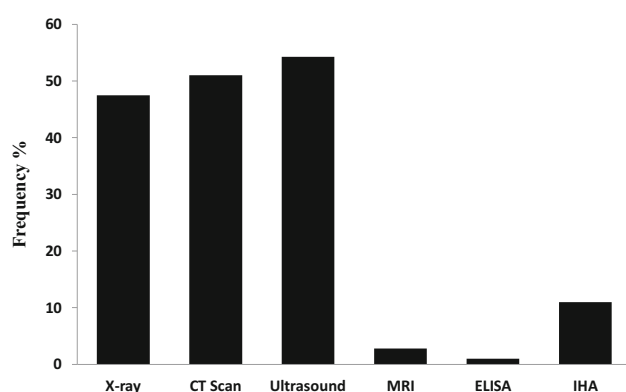
Human CE is an endemic parasitic zoonosis in north-eastern Iran, with up to 3.27 surgical cases per 100,000 population reported in this region (Ebrahimipour et al. 2016; Rokni 2009; Spotin et al. 2016). As with previous studies, in the current study, the majority of surgically treated cases had lesions in the liver or lungs (Andalib Aliabadi et al. 2015; Cappello et al. 2013; Conchedda et al. 2010; Karim et al. 2015; Pezeshki et al. 2007; Rokni 2009; Salama et al. 2014; Vahedi and Vahedi 2012; Yolasigmaz et al. 2006). In addition, 12.7% of cases had cysts in more than one organ system. This finding is also in line with previous reports from Iran and other endemic countries. Multiple organ involvement was reported in 11.1% of CE patients in Italy (Chalechale et al. 2015) and 15.6% of CE patients in Egypt (Salama et al. 2014), while other studies in Iran have reported 0–14.6% of patients with multiple organ involvement (Ahmadi and Hamidi 2008; Esfandian et al. 2010; Mansour-Ghanaei et al. 2012; Moosazadeh et al. 2016; Pezeshki et al. 2007; Sarkari et al. 2010; Zibaei et al. 2013).

Diagnosis of CE is largely based on serological and imaging techniques (Giri and Parija 2012; McManus et al. 2012; Muhtarov et al. 2015; Sadjjadi et al. 2001). In the current study, ELISA and IHA were used to diagnose CE in

Table 1 Frequency of single and multiple organ CE infection in different age groups

Age group (in years)	Lung no. (%)	Liver no. (%)	Liver and lung no. (%)	Liver and other organs no. (%)	Other organs no. (%) ^a	Total no. (%)
<10	6 (37.5)	4 (25.0)	3 (18.8)	0 (0.0)	3 (18.8)	16 (100)
10–19	41 (65.1)	17 (27.0)	4 (6.3)	0 (0.0)	1 (1.6)	63 (100)
20–29	39 (45.3)	27 (31.4)	10 (11.6)	3 (3.5)	7 (8.1)	86 (100)
30–39	29 (41.4)	28 (40.0)	7 (10.0)	1 (1.4)	5 (7.1)	70 (100)
40–49	18 (34.0)	25 (47.2)	3 (5.7)	2 (3.8)	5 (9.4)	53 (100)
50–59	15 (41.7)	13 (36.1)	4 (11.1)	2 (5.6)	2 (5.6)	36 (100)
60–69	8 (17.8)	24 (53.3)	7 (15.6)	1 (2.2)	5 (11.1)	45 (100)
>70	8 (25.8)	13 (41.9)	3 (9.7)	1 (3.2)	6 (19.4)	31 (100)
Total	164	151	41	10	34	400

^a Other organs infected were the kidney (9), spleen (4), gallbladder (3), bone (3), brain and spinal cord (8), abdominal cavity (6), and pancreas (1)

**Fig. 1** Frequency of use for the various diagnostic methods

a sub-set of patients ($n = 48$). However, the usefulness of serology is limited due to poor sensitivity and the possibility of cross-reactions occurring with other parasitic infections (Chaya and Parija 2013; Dubey et al. 2011; Schantz et al. 1980; Swarna and Parija 2012; Wuestenberg et al. 2014). Because of these reasons, patients are typically not diagnosed based on serology alone. Imaging techniques, such as ultrasonography and computed tomography (CT) scans, can be used in conjunction with serological methods to obtain a diagnosis of CE (Sadjjadi et al. 2001).

The choice of imaging technique is largely dependent on the stage and location of the cyst(s) (Prakash et al. 2016; Stojkovic et al. 2012). Staging of cysts was not conducted for patients in the current study, even though diagnostic imaging was used more frequently than serological methods. This may, in part, be due to the fact that cyst staging is a fairly new practice among physicians and these patients were treated in the early 2000s. As with previous studies, ultrasonography was the most commonly used method for diagnosing CE (Ahmadi and Hamidi 2008, 2010; Ćulafić et al. 2007; Sadjjadi et al. 2001), while MRI was used

primarily in cases with brain or spinal cord involvement (Prakash et al. 2016; Teke et al. 2015).

Certain CBC findings, such as eosinophilia, are known to be associated with helminth infections (Muller 2002). While CE patients can present with eosinophilia, this alteration must be evaluated together with imaging and serological findings (Cicioglu Aridogan et al. 2009; Karadam et al. 2009). In the current study, elevation in total WBC count, neutrophil count, and eosinophil count were observed in CE patients. However, eosinophilia was present in only 13.3% of cases. Lymphocyte count was the only CBC value that differed based on organ location, with the proportion of patients with elevated lymphocyte counts significantly higher than expected in those patients with cysts in the liver plus another organ system. A possible reason for high lymphocyte counts in these patients could be due to secondary infection (Zhang et al. 2003, 2008). Additional studies are needed to evaluate if lymphocyte count could be used to assess disease severity in CE patients.

This study had a number of limitations, including researchers only having limited access to patient data, which did not include post-surgical bloodwork and surgical records. Evaluation of changes in CBC values over time, and especially after surgery, could help to evaluate the effectiveness of the intervention and post-surgical anthelmintic treatment (Cappello et al. 2013). For example, a decrease in eosinophil count after beginning treatment with albendazole could be indicative of a positive response to drug therapy (Cappello et al. 2013; Kakkos et al. 2007). Future studies are also needed to see if CBC values differ by World Health Organization-Infomal Working Group on Echinococcosis (WHO-IWGE) cyst stage, with the goal of helping guide treatment decisions to optimize outcome and costs (Group 2003).

Table 2 CBC parameters for pre-surgical CE patients based on organ involvement

Blood values	Lung no. (%)			Liver no. (%)			Liver and lung no. (%)			Liver and other organ(s) no. (%)			Other organs no. (%)		
	Low	Normal	Elevated	Low	Normal	Elevated	Low	Normal	Elevated	Low	Normal	Elevated	Low	Normal	Elevated
Total WBC count	9 (5.5)	108 (65.9)	47 (28.7)	12 (7.9)	107 (70.9)	32 (21.2)	4 (9.8)	22 (53.7)	15 (36.6)	1 (10.0)	6 (60.0)	3 (30.0)	2 (5.9)	22 (64.7)	10 (29.4)
Neutrophils	4 (2.4)	117 (71.3)	43 (26.2)	5 (3.3)	118 (78.1)	28 (18.5)	2 (4.9)	28 (63.8)	11 (26.8)	1 (10.0)	8 (80.0)	1 (10.0)	0 (0.0)	21 (61.8)	13 (38.2)
Eosinophils	60 (36.6)	79 (48.2)	25 (15.2)	53 (35.1)	79 (52.3)	19 (12.6)	13 (31.7)	22 (53.7)	6 (14.6)	4 (40.0)	6 (60.0)	0 (0.0)	17 (50.0)	14 (41.2)	3 (8.8)
Monocytes	83 (50.6)	81 (49.4)	0 (0.0)	74 (49.0)	77 (51.0)	0 (0.0)	19 (46.3)	22 (53.7)	0 (0.0)	4 (40.0)	6 (60.0)	0 (0.0)	16 (47.1)	18 (52.9)	0 (0.0)
Lymphocytes*	93 (56.7)	63 (38.4)	8 (4.9)	67 (44.4)	71 (47.0)	13 (8.6)	26 (63.4)	14 (34.1)	1 (2.4)	5 (50.0)	1 (10.0)	4 (40.0)**	20 (58.8)	12 (35.3)	2 (5.9)
Platelets	5 (3.0)	145 (88.4)	14 (8.5)	14 (9.3)	123 (81.5)	14 (9.3)	3 (7.3)	31 (75.6)	7 (17.1)	0 (0.0)	9 (90.0)	1 (10.0)	4 (11.8)	28 (82.4)	2 (5.9)
Hematocrit	100 (61.0)	61 (37.2)	3 (1.8)	96 (63.6)	51 (33.8)	4 (2.6)	22 (53.7)	19 (46.3)	0 (0.0)	7 (70.0)	3 (30.0)	0 (0.0)	19 (55.9)	14 (41.2)	1 (2.9)

* Overall statistically significant ($p = 0.001$)** Statistically significant on post hoc assessment ($p < 0.001$)

Conclusion

Despite some success in the control of CE, the number of surgically managed human cases remains high in north-eastern Iran. While not a stand-alone diagnostic method, it is important to evaluate CBC values in patients with suspected CE, as well as those patients who have undergone therapy for CE. Blood counts and serological methods can be used to supplement information obtained through diagnostic imaging for the diagnosis and monitoring of CE cases.

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Compliance with ethical standards

Conflict of interest The authors declare that there is no conflict of interest.

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