

# REVIEW OF 311 CASES OF ALVEOLAR ECHINOCOCCOSIS AND CRITERIA FOR CLASSIFICATION OF HEPATIC ULTRASOUND IMAGES

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**Abstract.** A review of data on 311 human alveolar echinococcosis (AE) cases detected in mass abdominal ultrasound screening in western Sichuan during the period 1997-2003 revealed that herders of livestock constituted the majority of infected persons, and the proportion of infected females was higher than males. Furthermore, most AE cases (92.3%) were detected in persons >20 years old, and the highest proportion (21.9%) in persons in the age group *ie* 31-40 years. Epidemiological data indicated that infection was associated with the practice of raising and handling dogs, drinking water from unsafe sources, and related behaviors. Based on a review of ultrasound images of 311 AE cases, we established criteria for ultrasound classification of AE, which are highly useful for mass screening. According to the size of the lesion and features indicative of the stage of disease, we propose classification of AE ultrasound images into three types and eight sub-types. Serum specimens of 195 of the 311 persons with positive hepatic AE images were tested for antibodies in the Em18 (ELISA and immunoblot); 169 (86.7%) were positive. Rates of positivity were related to the size and stage of the parasite lesions.

## INTRODUCTION

Alveolar echinococcosis (AE), caused by the larval stage of *Echinococcus multilocularis*, is a serious zoonotic parasitic infection with broad circumpolar distribution in much of the Northern Hemisphere (Schantz *et al.*, 1995). In China, AE is primarily distributed in the western region, including the Xinjiang Uygur Autonomous Region, Qinghai Province, Gansu Province, Ningxia Hui Autonomous Region, Sichuan Province and the Tibet Autonomous Region (Jiang, 1998). As in most of these regions, both AE and cystic echinococcosis (CE, or *E. granulosus* infection) are co-endemic. Review of prior published data (clinical records and results of mass screening) in China through the year 1996 (Jiang, 1998) disclosed only 584 reported AE cases. However, recent diagnostic surveys among rural populations have documented high overall prevalence of both forms of echinococcosis at 4.0% (CE 2.1%; AE 1.9%) (Qiu *et al.*, 2000). Among individuals engaged in livestock herding, the prevalence of both forms of infection was

as high as 10.5% (CE 5.1%, AE 5.4%) (Qiu *et al.*, 2000). Epidemiologic data indicate that females, especially women in the age group 19-38 years, were at highest risk of acquiring AE, and prevalence was associated with older age, contact with dogs, unsafe water sources, and related health behaviors (Wang *et al.*, 2001).

During the years 1997 to 2003, epidemiological surveys of echinococcosis were carried out in Tibetan communities in four counties of western Sichuan Province. A total of 7,566 volunteer participants was screened by abdominal ultrasound and serum antibody assays, and 311 AE cases were diagnosed. Here we report the epidemiological findings, ultrasound images, and serodiagnostic (Em18 antigen) findings. In addition, we propose an ultrasound image criterion of AE based on ultrasound images of 311 AE cases, which is especially suitable for mass screening in the field.

## MATERIALS AND METHODS

### Subjects

Volunteer participants from pasturing areas and the urban areas of Shiqu, Ganzi, Baiyu, and Seda Counties.

### Methods

Every participant underwent a questionnaire survey, upper abdominal ultrasound examination, and serum assays including Dot-ELISA (Zhen *et al.*, 1996),

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Em18-ELISA (Ito *et al*, 1997) and Em18-immunoblot (Ito *et al*, 1993a).

### Diagnostic criteria for AE

All those cases having hepatic; 1) space-occupying masses with echogenic content as well as irregular or indistinct boundary, markedly characterized by calcification sign; or 2) space-occupying masses with central necrotic fluid, characterized by peninsular sign or dentation sign; or 3) granular echogenic areas with or without acoustic shadow, as well as positive serum antibody using Dot-ELISA, were diagnosed as AE.

## RESULTS

### Epidemiological analysis

**Diagnosis of AE cases in 1997-2003.** Screening for echinococcosis among 7,566 volunteer participants was carried out in Shiqu, Ganzi, Seda, Baiyu counties of western Sichuan Province. 311(4.1%) cases of AE were diagnosed, of which 212 were from Shiqu (212/4453, 4.8%), 70 from Ganzi (70/1381, 5.1%), 18 from Baiyu (18/900, 2.0%), and 11 from Seda (11/832, 1.3%).

**Distribution by sex and age groups** (Table 1). Of 311 persons with AE detected by ultrasound screening, 180 (57.9%) were females and 131 (42.1%) were males. The highest proportion of infected persons (21.9%) was in the age group of 31-40 years, and the age group of 41-50 years with 19.6% (Table 1).

**Ethnicity.** Among the 311 persons detected with AE, 97.4% were Tibetan, 1.9% Han Chinese, 0.3% Hui ethnicity, and 0.3% other ethnic groups.

**Occupation.** Of the 311 AE cases, the dominant

occupation was pastoralist herdsman (249), others indicated public servants (13), students (12), businessmen (5), housewives (4), farmers (3), part-time farmers (3), and employees (2), others (20) included lamas and teachers.

**Dog contact and living conditions.** 1) Rearing dogs: only 39 persons among the 311 infected persons did not own dogs, 87.5% (272/311) of AE cases kept dogs, of whom 111 owned one dog, 105 owned two dogs, and 38 owned three dogs, 12 owned four dogs, 5 owned five dogs, and 1 had six dogs. 2) Rearing dogs by neighbors: 298 cases out of 311 (95.8%) had neighbors who kept dogs, and only 13 cases had no neighbors with dogs. 3) Fox skin products: 243 AE cases out of 311 (78.1%) had fox skin products with them, while just 68 cases had no fox skin products. 4) Sources of drinking water: among 311 cases, 263 (84.6%) cases got their drinking water from ditches, 41 from wells, while only 7 cases had running water.

**Behavior.** 1) Washing hands before meals: only 7.1% (22/311) AE cases reported the habit of washing hands before meals, whereas 77.2% (240/311) said they did not wash their hands at all, and 15.8% (49/311) washed their hands sometimes. 2) Drinking un-boiled water: 32.8% (102/311) of AE cases did not drink un-boiled water, 37.3% (116/311) seldom drank unheated water, and 29.9% (93/311) usually drank unheated water. 3) Contact with dogs: 23.5% (73/311) of AE cases always had contact with dogs, 66.6% (207/311) sometimes had contact with dogs, and 10% (31/311) never had contact with dogs.

### Ultrasound classification

Based on ultrasound findings in the 311 AE cases, a key criterion for ultrasound classification of AE, which was particularly suitable for mass ultrasound screening in the field, was considered.

Alveolar echinococcal lesion in the liver was always characterized by: 1) space-occupying masses with echogenic content, as well as with irregular or indistinct boundary, mostly with calcification sign (Fig 1); 2) space-occupying masses with central necrotic fluid, along with specific sign of peninsula or dentation (Fig 2); 3) granular echogenic areas with or without acoustic shadow (Fig 3), which were divided in to 3 main types according to lesion size.

According to these criteria, the ultrasound classification of 311 AE cases is shown in Table 2.

The results in Table 2 show that 29.9% (93/311) of AE cases had lesions with diameters of less than or equal to 5.0 cm, 46.0% (143/311) had lesions with diameters ranging from 5.0-10.0 cm, 24.1% (75/311)

Table 1  
Distribution by sex and age groups of 311 AE cases detected by ultrasound screening.

Age group (year)	Gender		Total of case	Percent of total
	Male	Female		
10	2	6	8	2.6
11-20	7	9	16	5.1
21-30	20	30	50	16.1
31-40	25	43	68	21.9
41-50	28	33	61	19.6
51-60	25	29	54	17.4
>60	24	30	54	17.4
Total	131	180	311	100.0

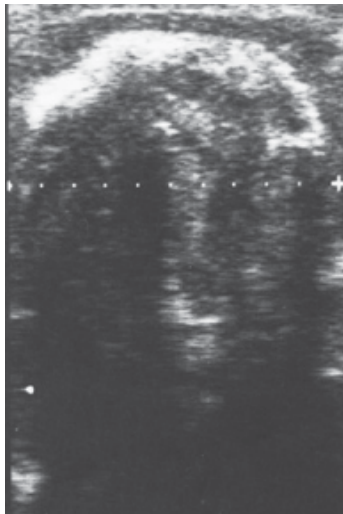


Fig 1- Ultrasound image of AE, showing space-occupying mass.

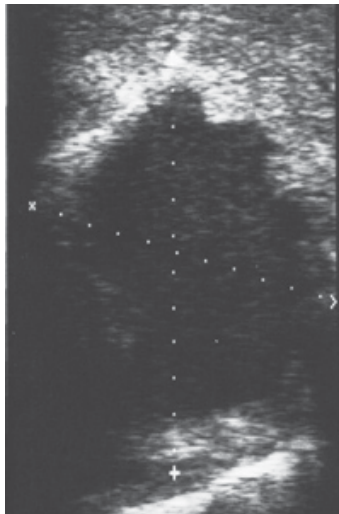


Fig 2- Ultrasound image of AE, showing space-occupying mass with necrotic fluid.



Fig 3- Ultrasound image of AE, showing granular echogenic area with an acoustic shadow.

- Type I: Maximum diameter of the lesion in the liver is less or equal to 5.0 cm ( 5.0 cm).
- Type Is: Single space-occupying mass.
- Type Im: Multiple space-occupying masses.
- Type II: Maximum diameter of the lesion in the liver ranges from 5.0 cm to 10.0 cm (5-10 cm).
- Type IIs: Single space-occupying mass.
- Type IIm: Multiple space-occupying masses without central necrotic fluid.
- Type IIIf: Single or multiple space-occupying masses with central necrotic fluid.
- Type III: Maximum diameter of the lesion in the liver is larger than 10.0 cm (>10 cm)
- Type IIIs: Single space-occupying mass.
- Type IIIIm: Multiple space-occupying masses without central necrotic fluid.
- Type IIIIf: Single or multiple space-occupying masses with central necrotic fluid.

Table 2  
Ultrasound classification of 311 AE cases.

Type I	No. cases	Type II	No. cases	Type III	No. cases
Is	71	IIs	70	IIIs	24
Im	22	IIm	19	IIIIm	3
		IIIf	54	IIIIf	48
Total	93		143		75

s=single mass; m=multiple masses; f=mass with necrotic fluid.

had lesions larger than 10.0 cm, 32.8% (102/311) had lesions characterized by a space-occupying mass with central necrotic fluid, while 21.9% (68/311) of AE cases had multiple masses.

**Serodiagnosis**

Serum samples from 195 AE cases (n=311) were checked using Em18 (Em18-ELISA and Em18-immunoblot) and sera of 169 (86.7%) of the infected persons tested antibody-positive (Table 3); 100% (65/65) of sera of infected persons having space-occupying masses with central necrotic fluid were antibody positive. Among 54 serum samples from cases that belonged to Type I, 17 were smaller than 2.0 cm, and 37 cases ranged 2.0-5.0 cm, 70.6% (12/17) of the former were antibody-positive, whereas 78.4% (29/37) of the latter were. The results in Table 3 revealed that 75.9% (41/54) of Type I cases were positive against Em18, Type II cases 87.6% (85/97), and Type III cases 97.7% (43/44).

**DISCUSSION**

For human echinococcosis, ultrasonography has become the key means of diagnosis for symptomatic and asymptomatic cases, particularly for mass

Table 3  
Correlation between different types and positive rates with Em18 in 195 AE cases.

Type I	No.cases	Em18		Type II	No.cases	Em18		Type III	No.cases	Em18	
		No. pos	%			No. pos	%			No. pos	%
Is	39	30	76.9	IIs	49	38	77.6	IIIs	10	9	90
Im	15	11	73.3	IIm	14	13	92.9	IIIm	3	3	100
				IIf	34	34	100	IIIf	31	31	100
Total	54	41	75.9		97	85	87.6		44	43	97.7

screening in endemic communities. For CE, a common classification, useful in different settings, has been elaborated by the WHO-Infomal Working Group on Echinococcosis (WHO-IWGE,2001). However, a comparable ultrasound classification scheme for AE has not been reported. In 1997, the WHO Informal Working Group elaborated a 'Classification of Alveolar Echinococcosis at Diagnosis' (WHO-IWGE,1997) and in 2001, the PNM system for classification of human AE was put forward by WHO/OIE (Eckert *et al*, 2001). Both classification criteria were mainly used in clinically-advanced cases and required CT-scan and magnetic resonance (MR) imaging. Furthermore, these two criteria just follow the classification of the TNM system for cancer. As we know, even cancer resulting from the same organ may have various pathologic characters and different malignant degrees, which grow at different speeds and have metastases in different stage of disease. On the contrary, the mass of AE, which has the same pathologic character, grows very slowly, and in general it metastasizes in the advanced stage of disease. To recognize the stage of each case, and to provide more detailed information for epidemiological surveys, the establishment of an ultrasound classification criterion for human AE is urgently needed. By our criteria, Type I suggests cases in the early stage of disease. Type Is may be inactive, whereas Type Im is active. Type II identifies cases in the middle stage, and cases categorized as Type III are in the terminal stage. Sub-Type classification (s, m, f) will offer further information applicable to selection of appropriate treatment. Among the 311 AE cases, 29.9% belonged to Type I, 46% to Type II, and 21.9% to Type III. In addition, of the 311 AE cases, 32.8% had lesions with necrotic fluid, and 21.9% had multiple masses in the liver.

Distinguishing AE from CE is important in areas where both AE and CE are co-endemic, because the prognoses and treatments are different. Serology using Em18 has been shown useful for identifying the

majority of AE cases; positive Em18 antibody detection is also a sign of disease activity (Ito *et al*, 1993a,b; Wen *et al*, 1995; Qiu *et al*, 1999; Craig *et al*, 2000; Jiang *et al*, 2001). In the current study, we analyzed the correlation between different ultrasound image types and the Em18 positive rate, and the results showed 75.9% of Type I cases were responsive against Em18, Type II 87.6%, and Type III 97.7%. The positive rate against Em18 with sera from Type I cases was statistically significantly different from Type III cases ( $\chi^2=9.31$ ,  $p<0.01$ ). One hundred percent of cases belonging to Type IIf or Type IIIf were antibody-positive to Em18. The result also revealed that 83.4% (126/151) of cases in the early and middle stages had detectable Em18 antibody. Consequently, serodiagnosis using Em18 is also useful for early diagnosis and specific identification of AE. Analysis of epidemiological data collected on 311 AE cases diagnosed in Ganze Prefecture, western Sichuan Province during the period 1997-2003 indicated that 57.9% were female, whereas 42.1% were male, and the highest proportion of AE cases occurred in the 31-40 year age group. People in various occupations could suffer from AE disease, but 80.1% of cases were herdsmen. In addition, 87.5% of the AE cases owned dogs and nearly all the patients (95.8%) had neighbors who owned dogs. Furthermore, 78.1% of AE patients owned fox skin products and 84.6% collected their drinking water from ditches (surface sources). Analysis of data obtained by questionnaire on related health behaviors revealed that only 7.1% habitually washed hands before meals. These findings are consistent with those in our previous report (Wang *et al*, 2001).

The highest prevalence of AE in the world has been documented in China (Ito *et al*, 2003), and some explanations have been given for such high prevalence, for example, high density of small mammals, dog ownership, and landscape (Giraudoux *et al*, 1998; Craig *et al*, 2000; Zhou *et al*, 2002). However, in western Sichuan Province, other major factors, such

as the high prevalence of *E. multilocularis* in animals (Qiu *et al.*, 1995), large numbers of dogs and a high rate of dog ownership, unsafe water sources, together with lack of related positive health behaviors, have been considered to play an important role in increasing the risk of suffering from AE (Wang *et al.*, 2001).

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