Cystic Echinococcosis of the Liver Associated with Repeated International Travels to Endemic Areas

Enrico Brunetti, Rosario Gulizia, Anna Lisa Garlaschelli, and Carlo Filice

Cystic echinococcosis (CE) is increasingly seen in immigrants from endemic areas to Western countries; however, it is rarely reported in short-term travels to endemic areas. This is partly because the echinococcal cyst typically grows slowly and may long remain clinically silent. We describe a case of cystic echinococcosis in a man born and living in a nonendemic urban area in North Italy that was acquired during a period of frequent travels in highly endemic countries.

Cystic echinococcosis (CE) is an infection caused by the larval stage (metacestode) of *Echinococcus granulosus*. In humans it may result in a wide spectrum of clinical manifestations, ranging from asymptomatic infection to severe, even fatal disease. *E. granulosus* has a worldwide distribution; areas of highest prevalence are those where dogs are used for sheep grazing. In recent times cystic echinococcosis is increasingly seen in immigrants from endemic areas to Western countries, where the disease is either virtually unknown or has a low prevalence. However, it is rarely, if ever, reported as a travel-related disease, that is, in short-term travel to endemic areas. This is partly because the echinococcal cyst typically grows slowly and may long remain clinically silent.

Case Presentation

A 56-year-old Caucasian man, born and living in Milan, North Italy, underwent an abdominal sonographic scan in November 2002 because of abdominal discomfort and elevated γ-glutamyltransferase (109 U/L [normal 11–50 U/L]) and alkaline phosphatase (383 U/L [normal 98–279 U/L]) blood levels.

The sonogram showed three cystic lesions in the II–III, IV, and VI–VII hepatic segments that were 68, 86, and 105 mm in diameter, respectively (Figure 1). A working diagnosis of hepatic hydatid disease was confirmed with serology (indirect hemagglutination titer 1:8,192 [normal < 1:64]) and computed tomographic imaging. The cysts, all type CE1 according to the World Health Organization classification,[1] were treated surgically in December 2002; then the patient was referred to our institute for follow-up.

Two facts make this observation worthy of interest:

1. The patient had undergone a previous ultrasound examination in December 2000 because of vague abdominal symptoms, but it showed no sign of focal lesions in the liver.
2. The patient reported recent travels to areas highly endemic for hydatid disease. From September 1999 to May 2002, he had traveled six times to Algeria (3-day trips), once to Iran (30 days), and six times to Kazakhstan (7- to 15-day trips). He also reported no international travel outside Europe in the 10 years preceding these trips.

Discussion

Pathophysiology

In the intermediate animal host, the oncosphere embryo is found in its final site of development—usually the liver—within 3 hours of the infection; during

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An abridged version of this article was presented as a poster at the 52nd Meeting of the American Society of Tropical Medicine and Hygiene, Philadelphia, PA, USA, December 3–7, 2003.

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J Travel Med 2005; 12:225–228.

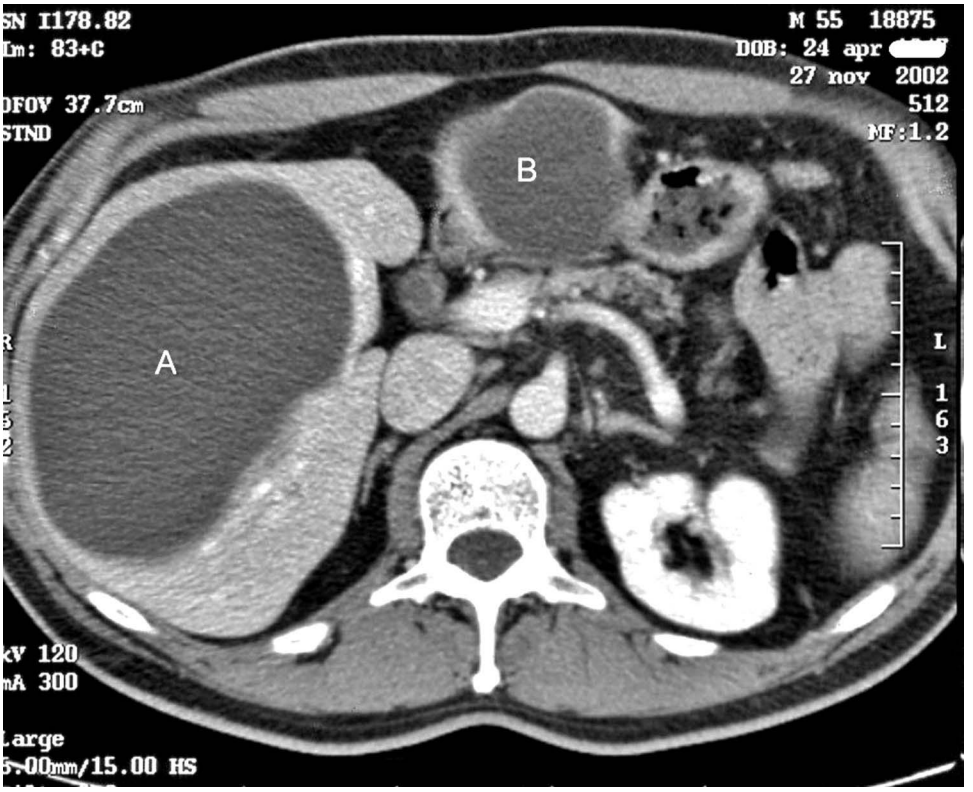

Figure 1 Computed tomography examination revealed cystic lesions of the liver. *A*, large cyst in the right lobe; *B*, cyst in the left lobe of the liver.

the subsequent 10 to 14 days, a series of reorganizational events occurs involving cellular proliferation, degeneration of oncospheral hooks, muscular atrophy, vesicularization and central cavity formation, and development of both germinal and laminated layers of the cyst wall. The minimum time required for the development of protoscolices in human cysts is not known exactly, but based on data from animals, it is expected to be 10 months or longer after infection.[2]

Liver cysts may remain asymptomatic for years or permanently. However, if the cysts grow, they can cause a variety of tumor-like symptoms related to their number and size and to the organ site. The growth rate of cysts is highly variable and may depend on strain differences and location. Estimates of the average increase of cyst diameter vary (range approximately 1–15 mm/yr).[3]

Epidemiology

E. granulosus has a broad geographic range and occurs in all continents and in circumpolar, temperate, subtropical, and tropical zones. The highest prevalence of the parasite is found in parts of Eurasia, Africa, Australia, and South America.[4] Within the endemic zones, the prevalence of the parasites varies from sporadic to high, but only a few countries can be regarded as being free of *E. granulosus*.

The true incidence is difficult to determine because of the slow rate of growth and variable clinical presentation. Most epidemiologic reports are based on hospital- and surgery-based surveys that are known to greatly underestimate the actual rates of infection, a distortion compounded by limited access to hospital care in many endemic countries.

The principles of epidemiology and control of *E. granulosus* have been studied in great detail and described in recent reviews. Current control programs are predominantly based on control of dog populations, regular dosing of dogs with praziquantel to eliminate *E. granulosus*, improved control of animal slaughter, and health education. Control programs are costly and may require > 30 years for substantial control to be achieved, depending on the control strategy employed in a given area.

Highest prevalences of hydatid disease in humans are found among populations involved in sheep raising, thus emphasizing the public health significance of the dog-sheep cycle and the sheep strain of *E. granulosus*.[5]

Epidemiology in countries visited by the patient. For Italy, the official reports indicate < 4 cases per 100,000 inhabitants per year, with a major peak of 23 cases per 100,000 in Sardinia. An epidemiologic multicenter study employing abdominal ultrasound screening showed that prevalence in Italy was 0.16% with a maximum of 2.09 in Sardinia and a minimum of 0.07% in North Italy.[6]

From 1970 to 1979, the annual incidence in Algeria per 100,000 population (hospital cases) was 3.4 to 4.6.[7]

In all of Iran, more than 5,000 patients with cystic echinococcosis were treated surgically in a 14-year period (1980–1993), corresponding to an annual average of 357 cases and an estimated annual incidence of at least 0.5 per 100,000.[4]

In Kazakhstan, the political changes and the deterioration of the financial situation and of the veterinary field services seem to be associated with an increased transmission of *E. granulosus* to humans and an alarming resurgence of cystic echinococcosis (from 1.4 surgical cases/100,000 in 1991 to 5.9/100,000 in 2000).[8] This increase in incidence has been most marked in the south of the country in the Zhambyl Oblast, from 3.8 in 1990 to 10.3 per 100,000 in 1997, and in the South Kazakhstan Oblast, from 2.7 in 1990 to 3.6 per 100,000 in 1997.[8]

Date and Destination of Patient's Recorded Trips

The dates and destinations of the recorded trips of the patient are as follows:

- Algeria: 1-day stays in Algiers and 3-day stays in Hassi Messaoud (village in the desert) in September 1999, February 2000, February 2001, and January, March, and May 2002
- Iran: August 2000, 30 days spent traveling throughout the country
- Kazakhstan: September 2000, March and August 2001, and January and July 2002; 7-day stays in Almaty (the capital) and Aksay (close to the Russian border), and 15-day stays during August 2001 (Figure 2). (Packs of stray dogs were reportedly seen by the patient, roaming in the destinations of all trips in Kazakhstan.)

Acquisition of Disease

When we take into account the epidemiologic data of the countries visited, the timetable of the trips (see Figure 2), the negative sonographic scan in December 2000, the low prevalence of cystic echinococcosis in Northern Italy, the patient being a resident of an urban area, the absence of previous trips in European countries and regions with high cystic echinococcosis prevalence (ie, Spain, Greece, Sardinia, and South Italy), the frequent trips to highly endemic areas, and the cystic stage (CE1) at the time of diagnosis, it is highly likely that cystic echinococcosis was acquired during one of the patient's sojourns abroad, most likely in Kazakhstan. Indeed, when the timing of the trips and the average growth rate of cysts are considered (1–15 mm/yr),[3] it is unlikely that trips to Algeria in September 1999 and in February 2000 were the source of infection. They were short trips, with limited potential for exposure to infective material. Acquisition of the infection in Iran is possible, since at 4 months the results of the sonographic scan could still have been negative. On the other hand, even considering a very

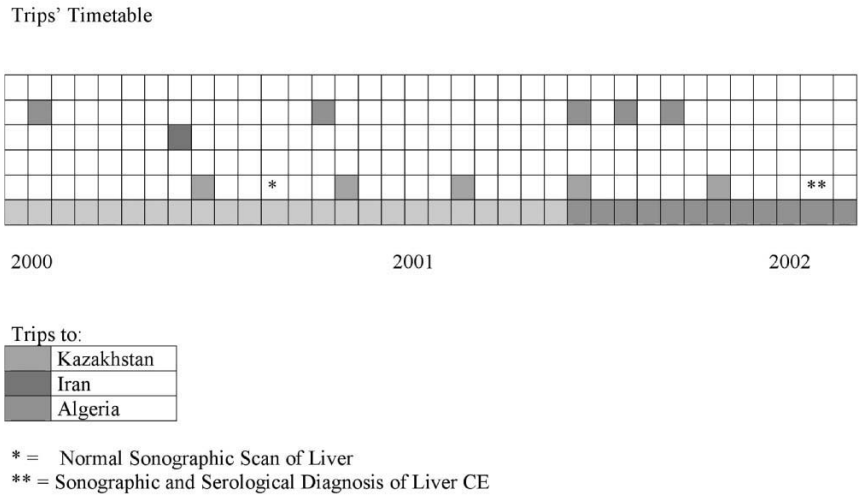

Figure 2 Timetable of trips taken. CE = cystic echinococcosis.

rapid cyst growth, trips taken after January 2002 seem unlikely to be the source of exposure. This narrows the possible sources of infections to four trips to Kazakhstan, one to Iran, and to two trips to Algeria (possibly less likely because of the short period of time—2 d). The current resurgence of cystic echinococcosis in Kazakhstan makes this country the most likely source of infection.

No fluid from the cysts treated surgically was available when we examined the patient, so, unfortunately, no genetic analysis was possible.

This case is also interesting because it shows that cyst growth can be dramatically fast. The estimated rate of growth of these cysts could be between 70 and 120 mm/yr. In one of the few studies available on the natural history of hepatic echinococcal cysts,[3] only 3 of 44 cysts studied for at least 12 months grew 50 to 134 mm/yr (maximum mean growth 11 mm/mo), whereas 11 grew about 10 mm/yr, 12 grew about 20 mm/yr, 3 grew 40 mm/yr, and the remainder either did not grow or collapsed and disappeared.

Our patient denied any direct contact with dogs in Italy or during his trips to the three endemic countries. We speculate that he might have been infected via ingestion of food soiled with *E. granulosus* eggs.

Conclusions

To the best of our knowledge, this is the first report of a travel-related cystic echinococcosis infection. We have shown, based on the history of recent travels, that the highest likelihood of infection occurrence was in Kazakhstan in the years 2000 to 2001.

In a world where the frequency of international travel has reached levels previously unknown,[9] control programs and prevention are crucial, not only for the resident populations but also for international travelers to endemic areas who may be from regions that are geographically remote from these areas. This should prompt infectious diseases and travel medicine consultants to add cystic echinococcosis to the list of very rare diseases that can be acquired during international travels.

From a clinical viewpoint, we believe that the differential diagnosis for patients who have traveled extensively in cystic echinococcosis–endemic countries and who have cysts should include cystic echinococcosis.

Acknowledgments

We are grateful to Dr. Peter Schantz and Dr. Thomas Junghanss for their time and patience in reading the manuscript and providing helpful comments and criticism.

Declaration of Interests

The authors have no financial or other conflicts of interest to disclose.

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