THE MAGNITUDE OF HUMAN HYDATIDOSIS IN EGYPT USING DIFFERENT EPIDEMIOLOGICAL APPROACHES

Thesis

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ABSTRACT

Human cystic hydatidosis (cystic echinococcosis) is a chronic zoonotic disease that results from infection with the dog tapworm Echinococcus granulosus. In Egypt, cystic echinococcosis (CE) is recognized in slaughtered livestock by veterinarians, however, there is little information about human CE infection rates. We describe an immunological assay useful for the diagnosis of human cystic hydatidosis. Sera were collected form surgically confirmed hydatid (38) case, nonendemic subjects free from parasitic infection (12) case and from (63) subjects infected with other helminthes (Hymenolepis nana, Schistosoma, fasciola hepatica and Ancylostoma duodenale).Hydatid cyst fluid (HCF) of camel origin was used as antigen in an ELISA format to measure total E. granulosus specific IgG antibodies and IgG subclasses. Sensitivity measurements of total IgG, and IgG1-4 were 100, 100, 79.4, 61.8 and 55.9%, respectively, whereas respective specificity reached 65.1, 97.7, 98.4, 96.1 and 83.7%. the diagnostic value of measuring IgG1 (97.7%), as assessed by a rating index (J) for combined sensitivity and specificity, was superior to total IgG (65.1%) and IgG2-4 (77.8, 57.9 and 39.6%, respectively). These findings set the stage for field evaluation of the IgG1 assay in areas endemic with human cystic hydatidosis.

We performed a retrospectives study to determine annual clinical incidence of human cystic echinococcosis (CE) in 14 Egyptian hospitals between January 1997 and December 1999. From 492 353 records examined, 133 (0.027%) new human CE cases were recorded. Of these, 50 (37.6%), were from Alexandria and Matrouh hospitals, 33 (24.8%) from Giza Chest Hospital and 50 from other regions. Matrouh governorate had the highest annual clinical incidence (1.34-2.60 per 100.000) followed by Giza governorate (0.80-1.16 per 100.000). About a third of those affected were aged < 20 years. Liver and lungs were the organs most affected. Although human CE is of low endemicity in Egypt, It may represent a public health concern in Matrouh and Giza Governorates.

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INTRODUCTION

Cystic Echinococcosis (CE) or hydatidosis is an important parasitic disease caused by a specific tapeworm, *E. granulosus.* It is a major public health problem in many countries around the world, concentrated in the major sheep-raising and pastoral areas ***Flisser (1998).*** In Egypt, the distribution of *E. granulosus* is of focal occurrence and the incidence of human CE is less than 1 per 100,000 per annum ***Shambesh (1997a).***

Humans who ingest ova accidentally develop hydatid cysts. The disease may produce serious clinical symptoms that vary depending on the site and size of hydatid cyst ***Shambesh et al.(1997b).***

There is an apparent variability in susceptibility of people to *E. granulosus* infection ***Lightowlers et al. (1993).*** Individuals who contract the infection can be categorized into a group who develop CE (susceptible to disease) and a group in whom CE cannot be detected (resistant to disease) ***Craig et al.(1996).*** In resistant individuals, a proportion of hydatid cysts die sometime after initial establishment and 13.6 % of cysts disappear or collapse spontaneously ***Romig et al.(1986).***

Variation in innate resistance to parasite infection is important in determining the prevalence

and intensity of infection in the population. As such, the factors that influence innate resistance may play crucial roles in the success of parasite control and vaccination programs *Lightowlers et al.(1993).*

Human cystic echinoccosis is a chronic process, the growth of hydatid cysts in humans is slow and variable, and the disease may not become clinically a major public health problem that causes severe morbidity and mortality in humans. It has its great impact on the health of rural residents, especially of developing countries because of the close proximity with domestic animals *Carmona et al. (1998).* In addition, echinococcosis is a disease of livestock, leading to further economic losses. Nevertheless, echinococcosis is a disease that can be controlled and even eradicated *Gemmell (1990).*

To date, diagnosis of human CE is achieved by means of imaging methods *Sinner (1991)* supported by the demonstration of specific serum antibodies. Imaging methods for detection of space occupying masses (i.e. x_ray, ultrasound, CT scan, or MRI) are the primary approaches for clinical diagnosis of CE *(Schantz and Gottstein, 1986; Sinner, 1991).* Even when cyst structures suggestive of *E. granulosus* (e.g. daughter cysts and laminated layer) can be imaged, confirmation by serology is still frequently requested. In many cases, however, characteristic cyst structures do not present as a clear image or are

absent ***Rogan et al. (1990).*** In these later cases, immunodiagnostic confirmation may be extremely important.

The serological diagnosis in a routine laboratory depends mainly on the detection of immunoglobulin class G (IgG) antibodies directed against different antigens of *E. granulosus.* Sensitivity and specificity of serological tests depend on the stage of the disease, the localization of the parasites, the antigens and the techniques used ***Gottstein (1992).***

In Egypt, veterinarians frequently recognize cystic hydatidosis in slaughtered livestock animals including sheep, camels and pigs ***(Helmy and Ramzy unpublished).*** Moreover, studies examining stray dogs in different parts of the country observed 1-10% prevalence rates of *E. granulosus* infection ***Hegazi et al. (1986).*** However, there is little information about human CE infection rates, therefore, mass screening using reliable diagnostic tools to assess CE endemicity among high-risk population is of immense importance ***Ramzy et al. (1999).***

REVIEW OF LITERATURE

Historical notes on Echinococcus

Although Hippocrates, Aretaeus and Galen were familiar with hydatid cysts Redi (1684), Hartmann (1685) and Tyson (1691) Quoted from Rausch, R.L. (1997): first suspected their animal nature. Palls (1776) Quoted from Rausch, R.L. (1997):, first mentioned the similarity of hydatids in man and other mammals. In 1776, Pallas recognized cysts of Echinococcus granulosus as living organisms and observed the taniid form of the protoscolices. Goeze (1782) first studied the scolices of the larva and recognized their relationship to those of Taenia. Hartmann (1695) Quoted from Rausch, R.L. (1997) first studied the adult worms in the dog's intestine.

The mid 1850s marked a period of exceptional accomplishment in the study of helminthes and might be considered to have been the time of the beginning of modern helminthology. Through the efforts of several investigators, including Von Siebold, Kuchenmeister and Leukart, cycles of Taenia spp, were traced experimentally, and Von Siebold (1853), fed scolices of cysts from domestic animals to dogs and observed developments of the adult worms of E. grnaulosus in

dog's intestine. Later Naunyn in Germany (1863), Krabbe in Iceland (1863), and Thomas in Australia (1885) Quoted from Rausch, R.L. (1997), obtained adult worms in dogs from scolices of human origin.

Kuchenmeister (1855) distinguished 3 growth forms of the larval stage (scoleciparіens, altriciparіens, and multilocular echinococcal cysts). The last characterized by an alveolar structure represented the taxon now designated *E. multilocularis.* ***Leukart (1863)*** considered *E. granulosus* to be the only species of *Echinococcus occurring* in Europe

Vogel (1957) evidently was the first to distinguish infraspecific taxa in the genus *Echinococcus.* ***Cameron (1960)*** observed that significant biological differences existed between the synanthropic form of *E. granulosus* and that indigenous to the northern regions of North America. The thorough investigations of ***Verster (1965)*** led to determination that few morphological characters were reliable for distinguishing subspecies.

Most recently, the discrimination of taxa has been attempted on the basis of differences in "strains" as determined by means of molecular/biochemical methods. ***Thompson et al. (1995a)*** have proposed to revise the genus *Echinococcus* so as to elevate such variants to the rank of independent species.

Larval cestodes belong to the phylum Platyhelminthes that are acoelomate metazoan with an elongated, dorsoventrally flattened body in their adult stage and a vesicular bladder in their larval stage. According to the most recent revision ***(Rausch, 1994)***, the systematic arrangement of cestodes in the subfamily Echinococcinae is accepted as follows:

Phylum: Platyhelminthes
Class: Cestoda
Subclass: Eucestoda
Order: Cyclophyllidea
Suborder: Taeniata
Family: Taeniidae
Subfamily: Echinococcinae
Genus: Echinococcus

E. granulosus
Northern biotype
European biotype
Other intraspecific categories

E. oligarthus
E. multilocularis
E.vogeli

The 4 recognized species of *Echinococcus* based on mitochondrial DNA, were found to be genetically

distinct, while differences among populations of *E. granulosus* have been demonstrated by means of molecular methods, their significance has not been established to any degree at present that would justify generic revision. It is not expected that such differences would be reflected in the macromorpho-logical characteristics of intraspecific populations ***Bowles et al.(1992).***

In the strobilar stage of *E. granulosus*, all the populations of the European (synanthropic) biotype correspond morphologically to the northern (nonsynanthropic) biotype. The larval stages are identical in fundamental structure, but that of the European biotype is subjected to host induced modifications ***Rausch (1995)***. However, ***Flisser (1998)*** stated sheep, dog-horse, dog-pig and dog-cattle) differ morphologically, developmentally, in DNA hybridization, in restriction site analysis, in their infectivity and pathogencity to human.

The species of E. granulosus is currently recognized as being of at least 9 different host adopted strains which vary in their genographical distribution ***Thompson et al.(1995a).*** At lest 5 of these strains are thought to occur in Africa (Fig. 1 and Table 1). The genographical distribution of the strains in North Africa varies and is shown in Fig. 2.