Fifteen year surveillance of echinococcal heart disease from a referral hospital in Greece

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Ten cases of hydatid heart disease were treated over a 15-year period (1980–1995). Cysts were located in the left ventricular wall (four patients), right ventricular wall (one patient), interventricular septum (one patient), interatrial septum (one patient), right atrium (one patient), pericardial cavity (one patient) and in multiple loci (one patient). Apart from two asymptomatic cases, clinical manifestations included chest pain (four patients), anaphylactic shock (one patient), constrictive pericarditis (one patient), congestive heart failure (one patient) and arterial embolism (one patient). Computed tomography was found useful in the detection of hydatid cysts and also in the determination of their morphology. Magnetic resonance was performed in three patients, with satisfactory imaging. Three out of the 10 patients died: rupture of pulmonary echinococcal cyst (one patient), massive pulmonary hydatid embolism (one patient) and rupture of an undiagnosed hydatid cyst of the right atrium during cannulation for cardiopulmonary bypass (one patient). One other patient experienced recurrent systemic embolism and became hemiplegic. Six patients were successfully treated. In five patients, the cysts were excised by open heart surgery, while in one by pericardectomy. In addition, antiparasitic drugs were successfully used in two patients with long-term satisfactory results.

In conclusion, cardiac echinococcosis is associated with an increased risk of potentially lethal complications. Newer techniques of cardiac imaging have helped locate the cysts while surgical removal may offer cure. Some patients responded to specific long-term drug treatment.

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Introduction

Echinococcus infestation is known to be endemic in some parts of the world[1,2]. This parasitic disease, from the time of ingestion of the ova, or larvae by man, until clinical manifestations begin, may evolve insidiously over several decades. In some cases, it may lead to conditions which constitute a medical emergency, again without any previous history of the disease, or any symptoms. The endemic nature of the disease is due largely to poor hygienic measures in these areas. Man is infected from contaminated dogs (intermediate host), which have been infected by eating sheep’s liver containing hydatid cysts. Another source of contamination is the abundant consumption of raw vegetables growing in naturally fertilized (contaminated) soil. After ingestion by man the worms and/or ova of the parasite reach the liver, evolve to hexacanthic embryos and enter the right circulation through either the venous or lymphatic route. Some pass the lung barrier and enter the systemic circulation. The involvement of the heart itself is reported to range between 0-5 and 2% of cases of echinococcosis[3]. Today, the incidence and prevalence of hydatid cyst disease in Greece, although not accurately known because it is not reportable, are estimated to be high. The disease will hopefully be completely eradicated with improved hygiene measures, which are coming into force. Nevertheless, Greek hospitals, as well as those of other European countries, may admit patients with echinococcosis presenting as difficult cardiological diagnostic or therapeutic problems.

We report all the clinical, laboratory, diagnostic and therapeutic data of 10 cases of echinococcal infestation involving the circulatory system. It is a retrospective study extending back about 15 years in the hospital’s records and hence not every case will have been studied on the basis of contemporary knowledge, equipment, and diagnostic and therapeutic modalities.
Materials and methods

This report concerns a retrospective clinico-laboratory study of 10 patients (six male and four female), with a mean age of 46.5 years (range 22–72), who were admitted to our hospital between 1980 and 1995. Depending on the year of admission, some of the patients presented here lack the more detailed imaging investigations available nowadays. All the patients were handled in a standard and classical way by the specific department to which they were admitted. Because most of them constituted difficult diagnostic problems, all the available diagnostic means and modalities were freely utilized: imaging techniques, biochemical, haematological, skin and serological tests, as well as, interventional diagnostic methods (see Table 1). A short description of the specific tests follows.

Casoni’s test

This is one of the oldest diagnostic tests for echinococcosis. It consists in injecting intradermally a minute quantity of hydatid cyst fluid, which as an antigen produces redness of the skin where it is injected. Despite the simplicity, however, in performing the test, there are many disadvantages. Its major limitation is that the test is not specific. False-positive reactions are very common in sufferers from other parasitic and even non-parasitic diseases.

For the above reasons, several tests which aim at searching for titres of anti-echinococcal antibodies in the serum of these patients have been developed. These include: complement fixation (CF), indirect haemagglutination (IHA), indirect immunofluorescence (IFA), latex agglutination, immunoelectrophoresis, ELISA, etc. The sensitivity and specificity of these tests vary and it is suggested that in suspected cases, more than one test should be performed. It is reported, however, by some [14] that these tests may be used in patients following surgical, or pharmacological treatment. The positivity of the tests is influenced mainly by the location and the condition of the cyst. Pulmonary cysts very frequently give false-negative results [15]. Also, the immuno-antigenic titres are low when the cysts contain clear liquid, or when they are calcified. However, they are very high if...
the fluid is turbid, or contaminated, or if the wall is destroyed. In addition, cross-reactions in sufferers from other parasitic diseases and mainly from cysticercosis, are not uncommon. This may occur even with the electrophoresis where the arc 5 is considered as specific for the diagnosis of hydatid disease[6].

The tests which were used in our hospital included: Casoni's (positive, or negative), Weinberg's (titres ≤ 200), ELISA (titres ≤ 200), indirect haemagglutination (titres ≤ 40).

Recently, a new immunoblotting method by which hydatid disease can be diagnosed by searching specific antibodies, no. 8 and 116 KDa, has been developed[7,8]. This method is highly specific, does not cross-react with cysticercosis and is considered as confirmatory of the clinical diagnosis.

As far as surgical treatment is concerned, all these patients were treated in the Department of Cardiac Surgery. A short description of the methodology and special precautions applied in these cases follows. The cysts, once diagnosed, were either drained, or excised, even in asymptomatic patients, because of fear of serious, or even fatal complications. After median sternotomy, the pericardial sac was opened. This endeavour may sometimes be extremely difficult because of adhesions. If the cysts lie within the pericardial sac they are excised together with the pericardium, with special care to avoid severing the phrenic nerves. If the hydatid cysts lie on the superficial myocardial layers their enucleation is rather easy. The cyst was wrapped with compresses soaked in 33% hypertonic solution of sodium chloride, or silver nitrate. The contents of the cyst were drained (sucked) in order to avoid rupture of the cyst and spilling of its contents on the surrounding tissues; simultaneously an attempt was made to excavate the cyst. The complete cyst wall was excised and the remaining cavity washed with 33% hypertonic sodium chloride solution, or with 0.5% solution of silver nitrate. The solution was left in the cavity for a few minutes in order to sterilize it. Although this solution is considered safe and non-toxic and is preferred to formalin, we observed myocardial oedema in one of our cases (no. 7) from the use of this hypertonic solution. After excision of the cyst, the hole was sutured in layers (marsupialization) in the cavity. When the cysts were within the myocardium, for reasons of safety all the previously described steps were performed under extracorporeal circulation. Sometimes, if the location of the cyst allowed, myocardial tissue could be excised and the cavity closed, or, when the ventricle was thin and fibrotic the same technique as for aneurysmectomy was applied, i.e. the sutures were reinforced with teflon.

Cases where surgery cannot be performed (chronic and neglected cases, cases with low life expectancy and those with multicaerbral lesions or with frequent relapses) are treated with a drug (albendazole). This drug may also be given following surgical treatment. It interferes with the uptake of glucose by the parasites, thus decreasing their glucagon content and killing them.

**Discussion**

Echinococcosis is a human parasitic disease, caused by the larval stage of *Echinococcus granulosus*. Echinococcus cysts were known to Hippocrates, who mentioned the serious manifestations and consequences of rupture of hydatid cysts of the liver. Human infection with echinococcus is not so rare, when one takes into consideration that, in certain areas, this parasitic disease exists in endemic form. The disease is common in the sheep-raising countries primarily Uruguay, Australia, New Zealand, Greece, the Middle East, North Africa and the Balkans[12]. In some of these places, those affected may be carriers of the parasite in a 'quiescent clinical form' for several years, even decades. This is understandable, since the cysts of the parasite, even if they reach a significant size (5–10 cm diameter), and if they do not exert pressure on organs and structures, or do not rupture, may be present without any symptoms at all[3]. The larvae, may survive within the cyst for 4–5 years. About this time, their capsule becomes calcified, the larvae die and they may be found incidentally during life, or at post-mortem. The usual loci where cysts may develop are the parenchymal organs (liver, kidney, spleen) as well as the lungs, the omentum, the peritoneal cavity etc. Of course, if a cyst ruptures, or even if it leaks, the most common symptoms are anaphylactic reactions, with chills and fever, skin exanthem, bronchospasm and dyspnoea, and sometimes circulatory collapse with death.

A great variety of symptoms, depending mainly on the location of the parasitic cyst, have been described. It is understandable that, if the cyst ruptures suddenly, the patient may present as a medical emergency. Besides all the anaphylactic symptoms, which are the consequence of the foreign protein molecules entering into the circulation of the patient, severe and fatal circulatory collapse may occur. In the first three patients of this series the cysts ruptured and insufficient time was given for therapeutic interventions. The first patient died of massive pulmonary embolism during cannulation for cardiopulmonary bypass for replacement of the mitral valve. The second patient developed 'vomique'. This French word is derived from the word vomitus and describes the situation where a pulmonary cyst is ruptured within the bronchial tree and a torrent of liquid containing parts of the echinococcus is expelled like vomitus. The third patient died suddenly after becoming cyanotic and dyspnoeic and was found at autopsy to having suffered massive pulmonary embolism from hydatid cyst remnants. It is clear that rupture of the cyst is a real medical emergency, frequently killing the patient.

The involvement of the pericardium may be manifested by: (1) silent rupture and the appearance of the echinococcus cyst some months later; (2) acute pericarditis with or without cardiac tamponade; (3) constrictive pericarditis[9–11].

Disturbances in rhythm are attributed to interference with the conduction system[10,13]. Murmurs
may be caused by valve insufficiency, when the echinococcus invades the papillary muscles or by partial obstruction of the right ventricular outflow tract, by an intruding cyst. Clinical pictures mimicking subaortic stenosis, pulmonary stenosis, mitral stenosis, and involvement of the tricuspid valve, have all been described. Sometimes the first manifestations are destructive and may even be fatal.

Biochemical and haematological investigations may not reveal anything else except an abnormal differential white blood count with an impressive increase of the eosinophilic series of the white cells. In this series, all the patients exhibited an increased eosinophilic count as an indication of the anaphylactic reaction to the parasite.

Whenever a case is met, which does not fit into the symptomatology and the general manifestations of a known disease, particularly if the patient originates from a geographical area where echinococcus is common, the physician has to think about the possibility of echinococcal disease. If, within the frame of the initial routine blood tests, eosinophilia above 6–7% is noted, then the physician should proceed with specific tests. We are fortunate today to live in the era of several diagnostic imaging techniques. Even if one performs ‘blindly’ echocardiograms, computed tomography (CT) scans, Magnetic Resonance Imaging (MRI) scans, or if one applies various radionuclide imaging techniques it is quite probable that one might come across findings which will illuminate the diagnosis. However, these techniques should not encourage the clinician to omit, or pay scant attention to the history. On the contrary, the very careful and detailed recording of the patient’s symptoms frequently render some very important and essential information which may lead to the correct diagnosis. Only when the patient is asymptomatic, or the symptoms are very mild and not specific, or they vary in different time periods, may the physician decide to use ‘blindly’ the above mentioned diagnostic modalities, but again, with moderation and scientific reasoning.

The myocardium is affected mainly via the coronary and arterial circulation. A few weeks or months after the implantation of the hexacanthic embryo, the hydatid cyst develops. The latter is encapsulated by a fibrous structure, which is often becoming calcified. Within 1–5 years the cyst may degenerate (die), unless it ruptures, with all the consequences.

In this series, the hydatid cyst was found in the left ventricle (four times) or other myocardial site (four times) and in the pericardial sac (once). Cysts in multiple loci were encountered in one case. The locations of the cysts indicate the possibility of the disease appearing with a great variety of symptoms.

All five patients of this series who complained of chest pain gave a rather vague and undetermined description of their symptoms. Even in the patient in whom the coronary arteriogram demonstrated obstructive compression of the circumflex artery (case no. 5), the pain did not resemble that of angina. According to Murphy et al., the precordial pains are usually the result of the partial rupture of the cyst into the pericardial sac, while Rivera and Delcan attribute the chest pain to coronary insufficiency, as a result of compression of coronary arteries. As a matter of fact, they suggest angiographic examination of all cardiac echinococcosis suspects. It is advisable to submit every case of cardiac echinococcosis to coronary arteriography, particularly if they are above the age of 40, and possible candidates for open heart surgery.

Routine haematological examinations may reveal some degree of eosinophilia, which was a stable and common finding in this series, and impressively high in case nos 2 and 3 (38 and 27%, respectively).

Certain changes in the electrocardiogram, although neither the electrocardiogram, nor the chest film contributed any specific findings in the cases reported here. While the chest film was entirely negative, quite often the electrocardiogram would exhibit non-specific (or pathognomonic) changes.

The contribution of echocardiography, particularly in two dimensions, has to be underlined. In this series, echocardiography proved more sensitive and more specific than computed tomography. However, the sensitivity of the method is reduced in relation to: (1) the size and number of cysts (difficulty in the location of cysts less than 0.5 cm in diameter); (2) the contents of the cyst, when these have degenerated and include remnants of membranes and necrotic material (case no. 5); and (3) in distinguishing between a single and a multilocular cyst.

Computed tomography, is a sensitive modality in the diagnosis, but lags behind the echocardiogram in the precise location of a hydatid cyst. In case nos 2 and 3 the echocardiogram accurately determined the location of the cardiac cysts, but the computed tomography scan did not. Also, in case no. 9 in whom the right pulmonary artery was occluded, the computed tomography scan could not locate the cyst, while with the magnetic resonance imaging scan its intraluminal location was ascertained. These peculiarities are illustrated in Figs 1 and 2.

We conclude from these last observations that a history of non-specific symptoms (mainly atypical chest pain), combined with a lack of physical findings and eosinophilia, should raise the suspicion of echinococcal involvement of the heart, and lead to meticulous and careful echocardiographic investigation. If, from such an approach, enough information is gained indicative of such involvement, then (and only then) should one proceed to further studies such as magnetic resonance imaging and cardiac catheterization and angiography, aiming at more detailed information, which will contribute to a more accurate and precise diagnosis and better planning of surgical treatment for the condition.

Concerning treatment of cardiac echinococcosis, it is evident that this must always be immediate and aggressive, in order to prevent morbid complications from ruptured cysts.
In this series, the outcome of all four patients who were not operated on, was very poor (three died, one became hemiplegic); note that patient no. 1 died of massive pulmonary embolism from the rupture of an undiagnosed cyst of the right atrium during cannulation for total cardiopulmonary bypass for mitral valve replacement.

Treatment with albendazole (Zentel 400 mg) should be applied in patients with low life expectancy, such as those with multiple cerebral lesions, or cases with frequent relapses. The result of albendazole treatment in our patients (case no. 6 with a cerebral echinococcus cyst and case no. 8 with multiple small cysts in both lung fields) was spectacular and the cysts disappeared after treatment. However, in patient no. 8, there was a relapse 3 years later and the drug had to be administered again. The usual way this drug is given is as follows: Zentel 800 mg daily, in two equal divided doses during meals, for 28 days. This 28-day treatment can be repeated after an interval of 14 days, for a total of three cycles.

In conclusion, to diagnose hydatid disease of the heart, a high degree of suspicion is necessary. However, if the patient comes from an area where the disease is endemic, if the symptomatology is not quite 'typical', and most importantly, if significant eosinophilia is present, the patient should be submitted to a most careful and meticulous investigation with all the available diagnostic modalities, to rule out the presence of hydatid disease infestation of the circulatory system. If the disease is diagnosed with certainty, its surgical management may be curative and life saving.

References