Medical and surgical management of a rare and complicated case of multivisceral hydatidosis; 18 years of evolution

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SUMMARY

Hydatidosis (echinococcosis) is a parasitic disease caused by the development in the human host of the larval form of the *Echinococcus spp.* tapeworm. Among the parasitic diseases transmitted from animal to human, hydatidosis represents the main Romanian helminthic zoonosis in humans, due to the severity of the clinical presentation and the complications of this illness. Before 1995-2000, surgical care was considered the only treatment available for the disease in Romania. Recently, the association of surgical procedures with pre and postoperative benzimidazolic drugs has been imposed.

We describe the case of a patient diagnosed in 1995, when he had already presented a form of multivisceral hydatidosis, and we also emphasize the development of this disease in this transition period, which concerns the change in the hydatidosis approach.

KEY WORDS: Multivisceral hydatidosis, Management, Long evolution.

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INTRODUCTION

Hydatidosis is often encountered in rural areas, but it can also affect urban populations due to the presence of stray dogs (Craig *et al.,* 2006; Neghina *et al.,* 2010; Otero-Abad *et al.,* 2013). The illness was relatively recently included on the list of "neglected tropical diseases" by the World Health Organization (Budke *et al.,* 2009; Giri *et al.,* 2012). Apart from these strictly medical aspects, echinococcosis has a socio-economic impact (Budke *et al.,* 2006; Hotez *et al.,* 2011). Echinococcosis is not common in the EU: 783 cases were confirmed in 2011, most of them in Bulgaria, Germany, Romania, Spain and the Netherlands (ECDC, 2013). The overall case rate (0.18 cases per 100 000 in 2011) stabilized between the years 2009 and 2011 (ECDC, 2013). The disease frequently manifests in humans through hepatic and pulmonary localizations (Brunetti *et al.,* 2010; Conchedda *et al.,* 2010; Geraci *et al.,* 2012). We describe a rare and complicated case of multivisceral hydatidosis, with a long history.

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CASE REPORT

The patient, a 55-year-old man from an urban area (without an established risk of acquiring hydatidosis) was admitted to another hospital in June 1995 for right organized pleural effusion of known tuberculous nature. A cyst was excised through axillary thoracotomy. No medical antiparasitic treatment was administered.

Two years later, the patient returned for a giant tumoral mass in the right axillary region. Surgi-

cal intervention was warranted and a right lateral thoracic wall cystectomy was performed, with the evacuation of a giant cyst with numerous degenerated hydatids inside.

Multiple cysts with individualized walls were revealed (thoraco-abdominal) by imaging methods. After 8 months, a surgical intervention was performed to eliminate a 4/5 cm cystic formation of the thoracic wall.

In January 2000 a right parietal relapsed hydatid cyst was excised. In February 2000 the patient underwent another surgical intervention due to a fistula of the anterior third of the thoracotomy incision through which hydatid content (fluid and membranes) were exteriorizing.

After another 2 years, the results of a CT scan compared to those from 1997 showed a greater number of enlarged pulmonary, pleural and pericardial hydatid cysts. Only the subdiaphragmatic cyst located above the right kidney was smaller, with a denser content.

The patient presented to hospital only after 6 years, in 2008, due to symptoms of cardiac failure. Under medical treatment for cardiac insufficiency the symptoms improved. CT chest scan showed (Figure 1):

- a spontaneously solid inhomogeneous mass with multiple air levels exerting traction on the superior mediastinum, situated in the apical portion of the right pulmonary parenchyma;
- a spontaneously liquid mass with polylobulated contour, with a thin wall from which several interior septa emerged, exerting a mass effect over the right cardiac cavities, the right pulmonary veins and inferior vena cava, situated in the right lower pulmonary parenchyma;
- a paravertebral liquid collection with a 3/2 cm diameter on the right-hand side;
- pleural effusion at the base of the right lung.

Abdominal CT scan showed (Figure 2):

- gigantic liquid masses with liquid densities, with interior septa, which exerted a mass effect over the hepatic vessels, at the level of the hepatic parenchyma in the IV, V, VI, VIII hepatic segments;
- wall microcalcifications at the level of the cyst in the VII hepatic segment.

The colleagues at the Cardiology section referred the patient to the Clinical Parasitology Unit of Colentina Hospital for positive diagnosis and antiparasitic treatment. The titre of anti-*Echinococcus granulosus* antibodies was elevated, being 7.5 (a minimum positive of 1.1) and routine laboratory tests did not show evi-

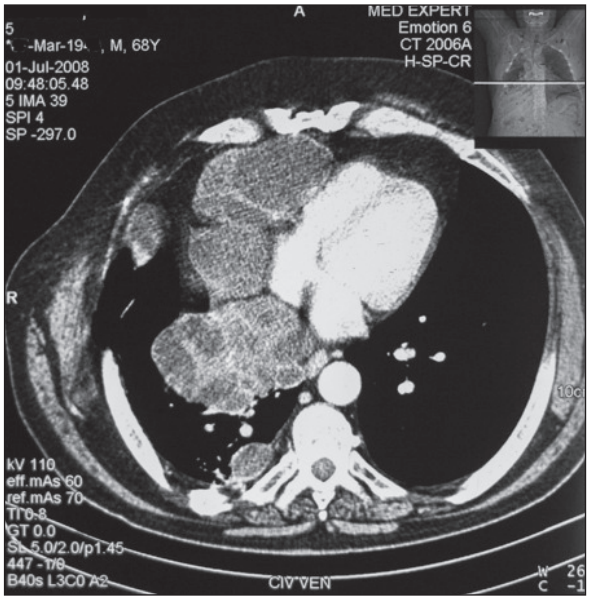

FIGURE 1 - *Cystic mediastinal-pulmonary mass lesions situated at the right paracardiac border and adjacent to the right thoracic wall (2008).*

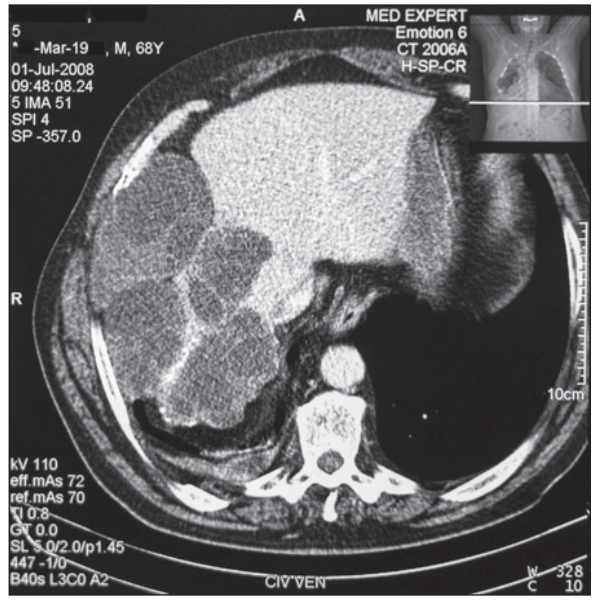

FIGURE 2 - *Peritoneal and hepatic cystic mass lesions (2008).*

dence of significant modifications, with the exception of a biological inflammatory syndrome. Antiparasitic treatment was instituted with Albendazole 800 mg/day given in two doses, postprandial (postprandial absorption after a "fatty lunch" improves 4-9 times) (Horton, 1997) and liver protective medication was associated.

The patient received multiple medical treatments with antiparasitic agents; over the course of the first year regimens of 90 days (interspaced by 30 days of treatment rest) were established and, as the lesion images started to stabilize and become more dense, the treatment was switched to 30 day regimens (interspaced by a pause of 15 days) over the next 2 years. Throughout the course of treatment, liver function and hemogram were monitored monthly. Medication was well-tolerated, no allergic reactions were noted, nor were hepatic cytolysis or medullary inhibition.

The CT scan of May 2009 showed hepatic and peritoneal hydatid cysts which had diminished in size as well as a smaller paracardiac hydatid cyst in the right lung and the almost complete resorption of the pulmonary cyst found in the anterior segment of the right lower lobe. The largest cyst was localized in the VII liver segment, being 8 cm in diameter.

A CT scan performed in 2010 disclosed the same number and dimensions of the cysts, without new calcifications and with a denser aspect of virtually all hydatid cysts (indicating a favorable evolution under treatment); the persistence of the posterior and basal pleural effusion was noted.

A CT scan performed in 2011 showed no modifications of the lesions in comparison with the CT in 2010; consequently, the antiparasitic therapy was halted.

In June 2013, the patient presented for control. A chest CT scan was performed (Figure 3). At the base of the right lateral hemithorax two lesions were noted with direct contact between them (one of 3.4 cm with parafluidic but also solid densities and one of 7 cm with parafluidic densities). There was a persistence of the paracardiac lesion at the mediastinal level 7/3.7 cm in size, presenting at this point solid and parafluidic densities and adjacent to this the persistence of the 5.4 cm lesion in direct contact with the VIII hepatic segment, but with thick walls and solid and parafluidic densities.

Abdominal CT scan showed (Figure 4): normal-sized liver, presenting 3 peritoneal and hepatic lesions; a 2.5 cm one with frank liquid density, a 4 cm one with parafluidic density and an 8 cm

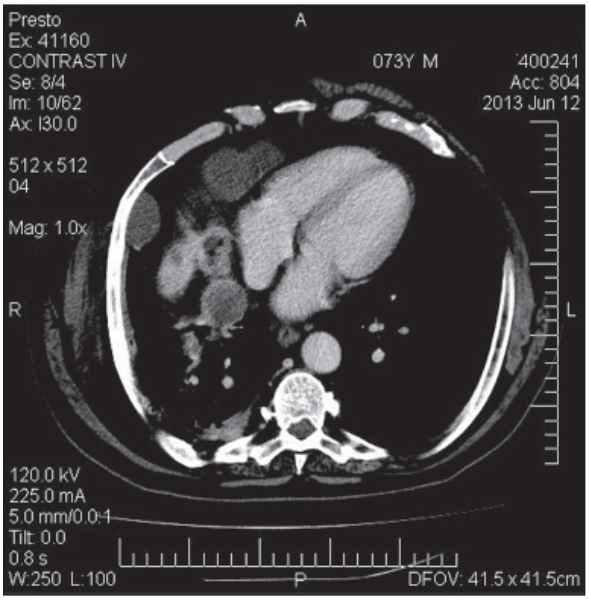

FIGURE 3 - *Cystic mediastinal-pulmonary mass lesions situated at the right paracardiac border and adjacent to the right thoracic wall (2013).*

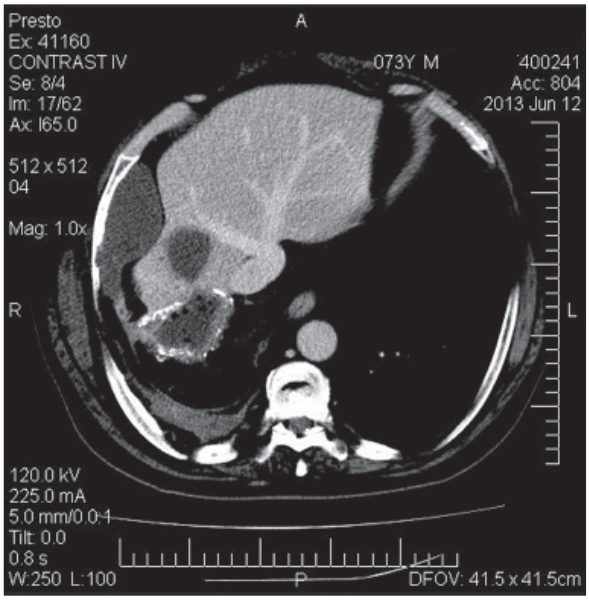

FIGURE 4 - *Peritoneal and hepatic cystic mass lesions (2013).*

one presenting with a thick wall, calcifications and parafluidic and solid densities.
Antiparasitic treatment was restarted due to the appearance of a hepatic lesion with the aspect of a liquid density, which was considered to be a relapse.

DISCUSSION

The presented case has a history of hydatid cyst disease spanning 18 years. During this time the patient underwent 5 surgical interventions, all of them palliative. We consider that the patient was in the phase of secondary hydatidosis even before undergoing the first surgery. Our theory is based on the existence of a giant pulmonary cyst with multiple vesicles, and the fact that the CT done after 2 years showed a right subdiaphragmatic cyst with partially calcified walls, it being known that calcium needs time to accumulate.
This case illustrates the extremely complex nature hydatidosis may present, being a rare form of disseminated multivisceral disease, with multiple complications (fissure, infected hydatid cysts with secondary hydatid pleural effusion, mediastinal localization with secondary compression on the heart and great vessels, retroperitoneal localization, multiple liver localizations, paravertebral localizations, toxic condition and septic risk).
For the past 5 years, since he has been cared for in our clinic, the patient has systematically refused a new surgical intervention. He presented for clinical, imaging and routine laboratory tests twice yearly in the first three years and subsequent annual tests.
In this time interval, the patient has received multiple antiparasitic drug regimens, with slow favorable evolution for the majority of cysts; yet it has been noted that a new lesion with frank liquid densities has appeared and continued to expand after treatment was stopped. In addition, it was noted that there were cysts which did not solidify even after 5 years from the start of specific therapy. All of these imaging findings as well as the rise in the specific antibody titre were arguments for restarting antiparasitic therapy.
In this interval, the titre of anti-*Echinococcus granulosus* (ELISA) varied considerably (7.59 in 2008, 6.11 in May 2009, 7.09 in October 2009, 4.63 in May 2010, 4.67 in November 2010, 12 in June 2011 and 11 in June 2013). The rise in the titre of antibodies could be correlated with the appearance of new hepatic lesions after the halt of medication, without neglecting the limits of serological diagnosis in hydatid cyst disease (useful in confirming some cases, but not very important in follow-up).
Each hydatid cyst is a unique entity, with individual response to antiparasitic therapy (in regards to age, viability and thickness of the adventitial membrane). This was confirmed by imaging follow-up in our case.
In hydatid cyst disease the administration of antiparasitic treatment is required before and after the surgical intervention to prevent the dissemination of protoscolices through the bloodstream and to prevent secondary hydatidosis in situ and at a distant site. Using Albendazole 10 mg/kg/day, 4 days preoperatively (Eckerd *et al.*, 2002) the viability of protoscolices is altered and the effect is enhanced if the duration of the treatment spans 1 month preoperatively (Filippou *et al.,* 2004).
Although antiparasitic treatment is recommended to be continued for at least 3 months postoperatively for intact hydatid cysts (Koulas *et al.,* 2006) and at least 6 months for complicated cysts (fissured, infected) (Dziri *et al.,* 2004), the patient had not undergone pre- and post-operative therapy (the patient was admitted to our clinic 8 years after his final surgical intervention) which had led to the dissemination of the infection and the complications presented above.
The evolution of this case confirms the need for follow-up for at least 5 years postoperatively (preferably as long as possible) to prevent relapses (Cretu *et al.,* 2012). We emphasize the need for future enhancements in serological diagnosis and the need to monitor the evolution of the disease under antiparasitic treatment (the combination of serological and imagistic methods) in Romanian hospitals, by studies of viability, genotyping, and the procurement of new diagnostic kits with recombinant antigens (for a greater sensitivity and specificity).
We can assume that surgical intervention would have been (partially) avoided by the appropri-

ate and timely use of Albendazole chemotherapy since the beginning of the management of this case. Albendazole could be a unique and definitive solution for the cysts up to 5-6 cm, but its support of surgery in terms of prevention of surgical spillage diffusion might be relevant.

CONCLUSIONS

Hydatid disease leads to the risk of severe, sometimes life-threatening complications, which may subject the patient to a long period of suffering through repeated surgical interventions due to relapses with multivisceral dissemination, infections, and last but not least, the risk of anaphylactic shock. Active attempts to implement the screening for this disease are also important as it can be asymptomatic for a long time (until the cysts have reached major dimensions). In these cases, associated medical treatment takes a long time (requiring repeated workup to monitor hepatic function and to rapidly diagnose a bone marrow inhibition), and accounts for considerable expense, as do the costs of the surgical interventions and the impact on work capacity. The patient with hydatidosis must be followed for a period of at least 5 years after the end of therapy to rapidly diagnose any relapses. Interdisciplinary collaboration is very important.

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Conflict of interest:
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REFERENCES

Brunetti E., Kern P., Vuitton D.A. Writing Panel for the WHO-IWGE. (2010). Expert consensus for the diagnosis and treatment of cystic and alveolar echinococcosis in humans. *Acta Trop*. **114**, 1-16.

Budke C.M., Deplazes P., Torgerson P.R. (2006). Global socioeconomic impact of cystic echinococcosis. *Emerg. Infect. Dis*. **12**, 296-303.

Budke C.M., White A.C., Garcia H.H. (2009). Zoonotic larval cestode infections: Neglected, neglected tropical diseases? *PLoS Negl. Trop. Dis*. **3**, e319.

Conchedda M., Antonelli A., Caddori A., Gabriele F. (2010). A retrospective analysis of human cystic echinococcosis in Sardinia (Italy), an endemic Mediterranean region, from 2001 to 2005. *Parasitol. Int*. **59**, 454-9.

Craig P., Larrieu E. (2006). Control of cystic echinococcosis/hydatidosis. *Adv. Parasitol*. **61**, 443-508.

Cretu C.M., Codreanu R., Mastalier B., Popa L.G., Cordos I., Beuran M., Ianulle D.A., Simion S. (2012). Albendazole associated to surgery or minimally invasive procedures for hydatid disease - how much and how long. *Chirurgia*. **107**, 15-21.

Dziri C., Haouet K., Fingerhut A. (2004). Treatment of hydatid cyst of the liver: where is the evidence? *World J. Surg*. **28**, 731-736.

Eckerd J., Gemmell M.A., Meslin F.X., Pawlowlovski S.Z. (2002). Manual on Echinococcosis in humans and animals: a public health problem of global concern. WHO/OIE. **2**, 20-71.

European Centre for Disease Prevention and Control. Reporting on 2011 surveillance data and 2012 epidemic intelligence data. Stockholm: ECDC. (2013). Annual Epidemiological Report 2013. http://www.ecdc.europa.eu/en/publications/Publications/annual-epidemiological-report-2013.pdf

Filippou D.K., Kolimpiris C., Anemodouras N., Rizos S. (2004). Modified capitonage in partial cystectomy performed for liver hydatid disease: report of 2 cases. *BMC Surgery*. **4**, 8.

Geraci G., Sciuto A., Lo Nigro C., Sciume C., Li Volsi F., Cupido F., et al. (2012). Bilateral lung and liver hydatid cysts. Case report. *G. Chir*. **33**, 229-33.

Giri S., Parija S.C. (2012). A review on diagnostic and preventive aspects of cystic echinococcosis and human cysticercosis. *Trop. Parasitol*. **2**, 99-108.

Horton RJ. (1997). Albendazole in treatment of human cystic echinococcosis: 12 years of experience. *Acta Trop*. **64**, 79-93.

Hotez P.J., Gurwith M. (2011). Europe's neglected infections of poverty. *Int. J. Infect. Dis*. **15**, e611-9.

Koulas S.G., Sakellariou A., Betzios J., Nikas K., Zikos N., Pappas-gogos G., Tsimoyiannis E.C. (2006). A 15-year experience (1988-2003) in the management of liver hydatidosis in northwestern Greece. *Int. Surg*. **91**, 112-116.

Neghina R., Neghina A.M., Marincu I., Iacobiciu I. (2010). Epidemiology and epizootology of cystic echinococcosis in Romania 1862-2007. *Foodborne Pathog. Dis*. **7**, 613-8.

Otero-Abad B., Torgerson P.R. (2013). A systematic review of the epidemiology of echinococcosis in domestic and wild animals. *PLoS Negl. Trop. Dis*. **7**, e2249.