A case of hepatic alveolar echinococcosis contracted in Belgium

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Abstract

We report herein the case of a Belgian 76-year-old woman who developed a hepatic tumour suspected to be a breast cancer metastasis. Radiological imaging and guided biopsies were not contributive. The patient underwent an explorative laparoscopy with frozen sections that did not provide further diagnosis, and an open left bisegmentectomy was performed during the same anaesthesia. Histopathological examination of the hepatic mass showed Echinococcus multilocularis metacestodes, demonstrating alveolar echinococcosis. As our patient denied any travel in foreign countries and has undergone regular abdominal ultrasonographies since her mastectomy, it is highly likely that this alveolar echinococcosis had been contracted in Belgium. If some imported cases may be seldom managed in Belgium, to our knowledge, this case is the first occurrence of alveolar echinococcosis contracted in Belgium. This report, added to the demonstration of E. multilocaris infection of 50% of red foxes in Southern Belgium, and the potential infection of domestic cats and dogs, should attract attention of the medical community on the possible outbreak of endemic alveolar echinococcosis in Belgium, and on the related public health concerns. (Acta gastroenterol. belg., **2002**, 65, **55-60**).

Key words : echinococcosis, zoonosis, liver, surgery, treatment, pathology, case report, review.

Introduction

Alveolar echinococcosis is a parasitic disease related to the development in the liver of cestodes larvae of Echinococcus multilocularis, and must be differentiated from the more common hydatid cyst, caused by Echinococcus granulosus. In this paper, we present a case of alveolar echinococcosis that had been contracted in Belgium. If some imported cases are seldom managed in Belgium, to our knowledge, this case is the first occurrence of alveolar echinococcosis contracted in Belgium.

Case Report

The patient was a 76-year-old female living in the Southern part of the province of Liège, with medical history including advanced rheumatoid polyarthritis controlled by prednisolone 7.5 mg/day and methotrexate 7.5 mg/day, and breast cancer treated by right mastectomy in 1993. Since this operation, she had undergone regular follow-up and yearly abdominal ultrasound. In 1998, an abdominal ultrasound detected a tumour in the left liver lobe. Abdominal computed tomography (CT) scanner confirmed a 7-cm large atypical mass in the left liver, with irregular geographical border and a central calcification (Fig. 1A). The diagnosis of metastasis was suggested, and confirmed by the magnetic resonance imaging (MRI) (Fig. 2). Liver blood tests showed normal bilirubin level, normal transaminases, but cholestatic enzymes were two fold the normal value. Tumour markers, including carcinoembryonic antigen, alpha-fetoproetin and CA125, were negative. The positron emission tomography showed a large hypo-metabolic mass in the left liver lobe, with a hyper-metabolic right border, compatible with a necrotic tumour (Fig. 3). Two biopsies of this liver mass were performed (Fig. 1B) but they only provided amorphous necrotic material without cellular analysable components. On March 24, 1999, the patient underwent diagnostic laparoscopy (Fig. 4) with surgical biopsies of the hepatic lesion, but frozen sections did not reveal further relevant information. It was therefore decided to performed an open left bisegmentectomy (segments II and III) during the same anaesthesia.

Macroscopically the resected tissue showed a solitary mass with a spongy aspect, microcystic like soft parts of bread (Fig. 5) surrounded by a thick stringy veinstone replacing the Glisson capsule. This lesion measured $10 \times 8.5 \times 5$ cm and showed unclear nodular limits extending into the residue of the parenchymatous tissue. Many whitish nodules also raised the Glisson capsule. Microscopically, these lesions corresponded to multiple territories, with granulated surroundings of various sizes, centred by a cystic cavity surrounded by a laminine ringed membrane (Fig. 6), this one being emphasised by a thick histiocystoid crown comprising a few giant cells. On various places, these cystic formations had scolex head equipped with the characteristic hooks of the E. multilocularis (Fig. 7). The residual hepatic parenchyma showed important lesions of cholangitis secondary to the biliary obstruction due to this lesion.

The postoperative course was uneventful and the patient left the hospital at postoperative day 6. She had been treated by albendazole 800 mg/day for six months. At 1-year follow-up, she was asymptomatic and thoracic and abdominal CT revealed no recurrence of the infectious process. The patient owned a domestic dog that could not tested for E. multilocaris because this animal
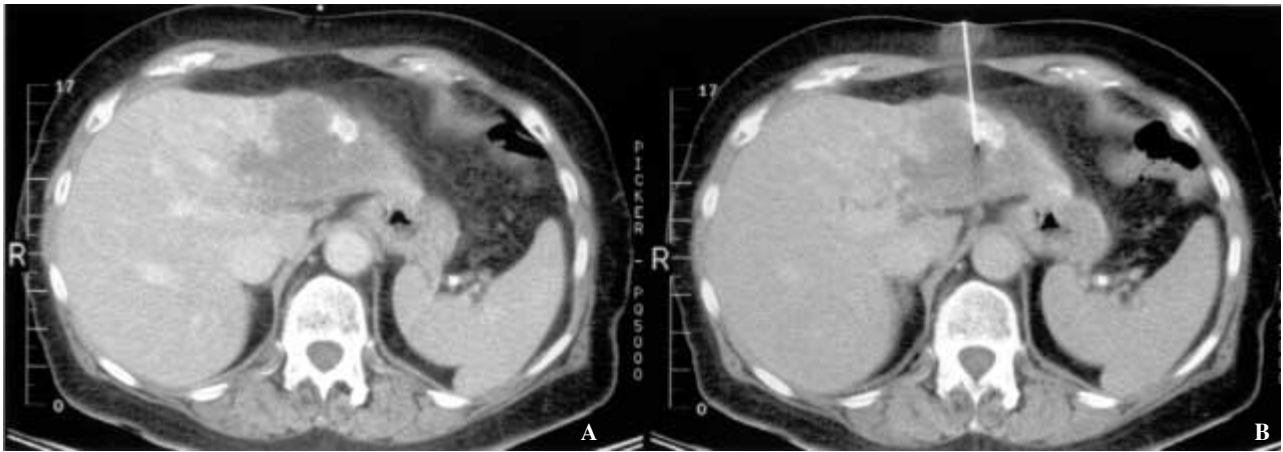
Fig. 1. — Computed tomography of the liver showing a necrotic mass in the left liver lobe, with calcification. A biopsy of the mass was performed (Fig. 1B).

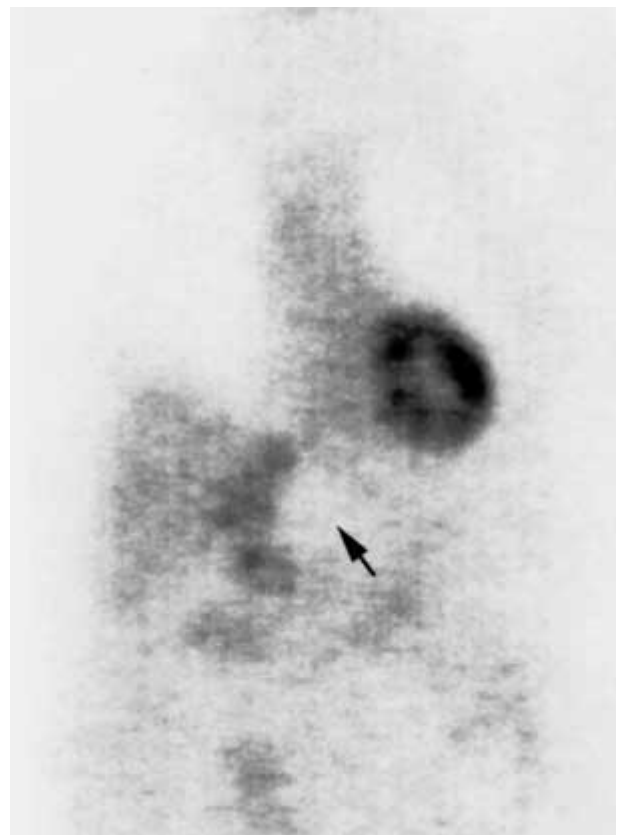Fig. 2. — Magnetic resonance imaging of the liver, confirming the computed tomography.

Fig. 3. — Positron emission tomography demonstrating a large hypo-metabolic mass in the left liver lobe (arrow), with a hyper-metabolic right border.

died shortly before the diagnosis of liver alveolar echinococcosis.

Discussion

Echinococcosis is a parasitic disease caused by the larval (metacestode) stages of various cestodes (tapeworm) species of the genus Echinococcus. Two of these parasite species are of medical and public health importance because they are widely prevalent and may cause severe diseases in humans : (a) E. granulosus, that is the causal agent of cystic echinococcosis, or cystic hydatid disease ; (b) E. multilocularis, that causes alveolar echinococcosis, or alveolar hydatid disease, in humans. Two other species of the genus Echinococcus, namely, E. vogeli and E. oligarthrus, are very rare in humans and may cause so called polycystic echinococcosis (1). The four species of Echinococcus are morphologically distinct in their adult and metacestode stages, geographic distribution and host specificity. The first description of alveolar

hydatid disease is attributed to Buhl in 1852, under the name "colloid alveolar cancer of the liver" (1). However, it was Virchow in 1855 who recognised the parasite nature of this disease and named it "Echinococcus ulcerous tumour". It is only in the 50's that Rausch and Schiller gave to one morphological parasite, different from the E. granulosus, the pathogen causing alveolar echinococcosis (2).
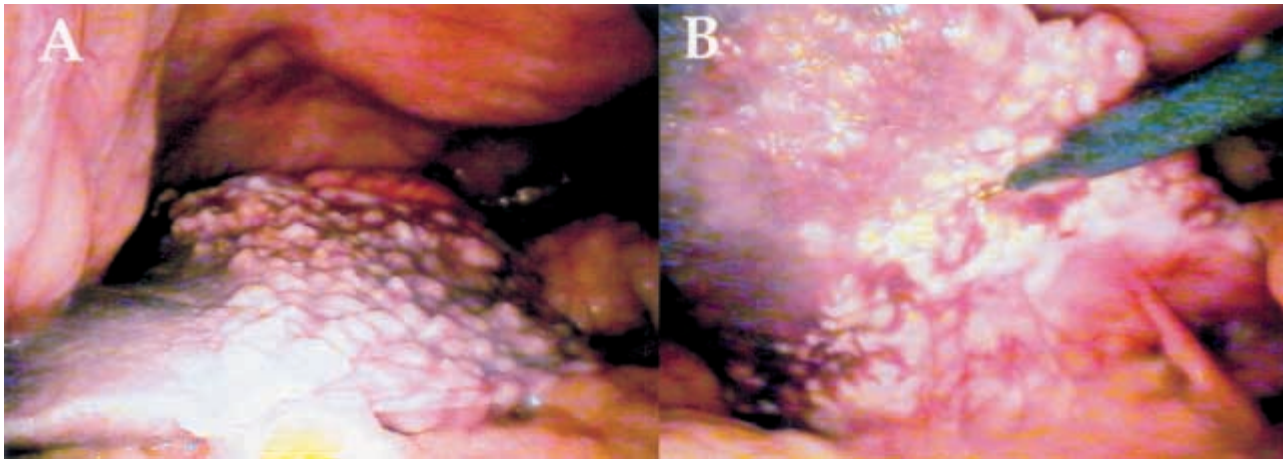
Fig. 4. — Per-operative view of the diagnostic laparoscopy. The upper surface of the segments II and III showed white nodules (Fig. 4A) that were also found at the lower surface (Fig. 4B).
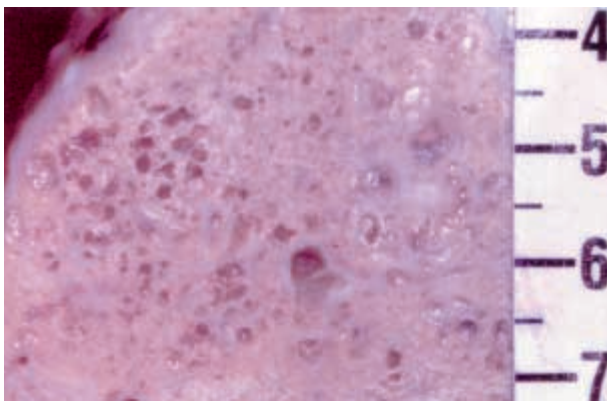

Fig. 5. — Gross photography of the resected liver section, showing a solid, white mass with spongy, microcystic aspect.

E. multilocularis seems to occur only in the Northern Hemisphere. Four world sources are known : Central Europe, (especially in Bavaria, from Tyrol extending to Switzerland, in Eastern France, Austria and Germany), North America (Alaska-Canada), Eurasia (Siberia and Turkey) and China (1,2,3). In Belgium, no pure human local case has ever been reported, to our knowledge. However, in a study on foxes in Belgian Luxembourg province in 1993 and 1995, it was shown that more than 50% of the foxes were E. multilocularis carriers (4). This finding was also confirmed in the Netherlands (5). It was also demonstrated that domestic cats and dogs may be carriers and definite host for this parasite in endemic regions (6), in urban regions (7) and in Belgium (8). Therefore it seems likely that the rate of cases contracted in Belgium may rise in the next future.

The adult E. multilocularis, whose life cycle is summarised in the Figure 8, is a tapeworm measuring from 1 to 3 mm and has 3 to 6 segments. The anterior part is composed of a rostrum with a double crown of hooks. The last segment (mature or gravid proglottid) contains an uterus full of ripe eggs. The adult lives attached to the small intestine of the definitive host, mainly the red fox,
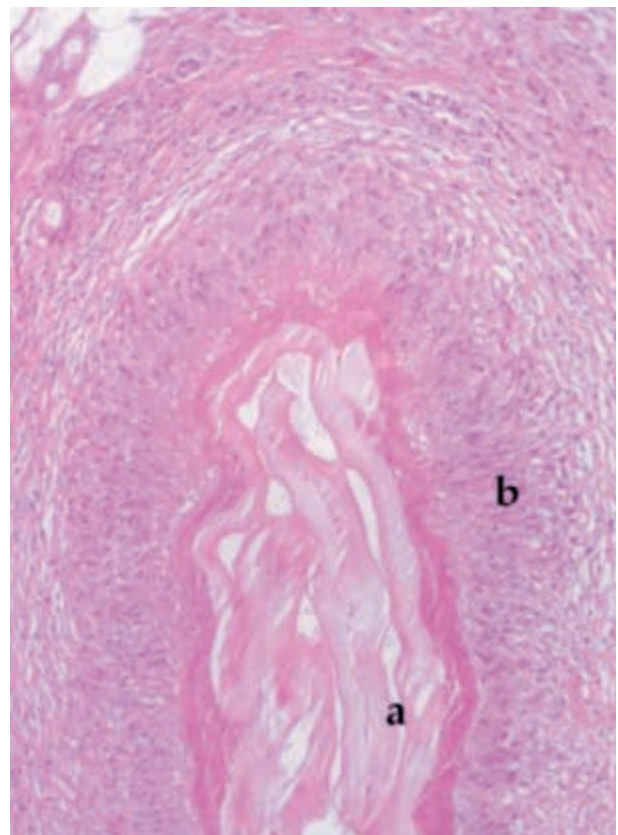

Fig. 6. — Pathology of the resected tissue (hematoxylin–eosin, 40 ×) showing a cystic formation surrounded by a laminine ringed membrane (a) and histocytoid, granulomatous reaction (b).

but dogs and cats are also vulnerable (Fig. 8) (6,7,8). When the gravid proglottid arrives to maturity, it is released in the faeces with 400 to 800 eggs. The eggs contain the oncospheres, which have six hooks surrounded by protective envelopes. The oncospheres are resistant and remain infectious from 15 to 110 days, depending on the outer conditions (2,9,10). The cycle
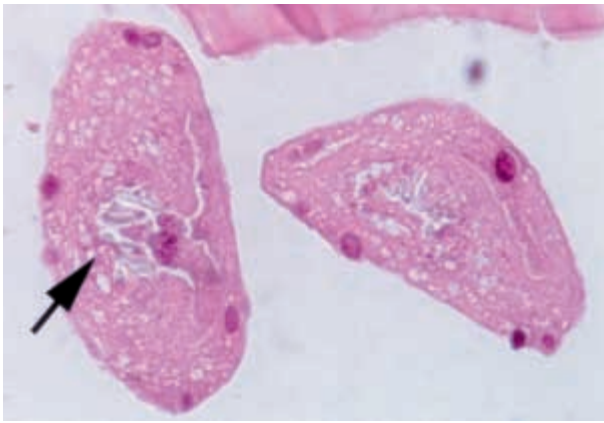
Fig. 7. — Pathology of the resected tissue (hematoxylin–eosin, 400 ×) showing the histological aspect of E. multilocaris with characteristic hooks (arrow).

continues if field rodents (intermediate carriers) ingest the eggs. Reaching the stomach of an intermediate host, the oncospheres are released from their protective coat, and by means of its larval hooks, penetrate the intestinal wall, reaching the lamina propria within 30 to 120 minutes. The oncospheres migrate via the portal circulation to the liver, where most are deposited. When the intermediate host dies and his vital organs are devoured, each consumed scolex may transform in an adult larva in the small intestine of the definitive host. Human beings are accidental intermediate hosts in this cycle, and may be contaminated mainly by eating wild berries such as wood strawberries, blackberries, blueberries soiled with foxes excrements, or by contacts with contaminated domestic animals (Fig. 8) (9). In humans, E. multilocularis metacestodes are found almost exclusively in the liver, but secondary lesions can form in the lung, brain, and other organs (10).

There are differences in the development of cysts of each of the various echinococcal species. In contrast to the development of the unilocular hydatid cyst of E. granulosus that grows slowly, about 1cm by 20 weeks, the alveolar hydatid of E. multilocularis develops rapidly with infiltrative and invasive abilities, characterised by rapid dissemination to adjacent tissue. The germinal layer of the metacestode proliferates both exogenously and endogenously. This form of development and infiltration of the host tissue is facilitated by the relative absence of pericyst and a very thin laminated layer. E. multilocaris metacestodes invade liver tissue much like a malignant tumour. The host response is variable. There may be a granulomatous reaction or an extensive peripheral rim of necrosis, fibrosis and focal calcification. The growth and the metastasis of hydatidosis in host tissues are always associated with an intense humoral and cell-mediated immune response. However, despite the persistence of inflammatory responses during the entire course of infection, the parasite grows in size until the host dies. Although a fibrous reaction is characteristic of
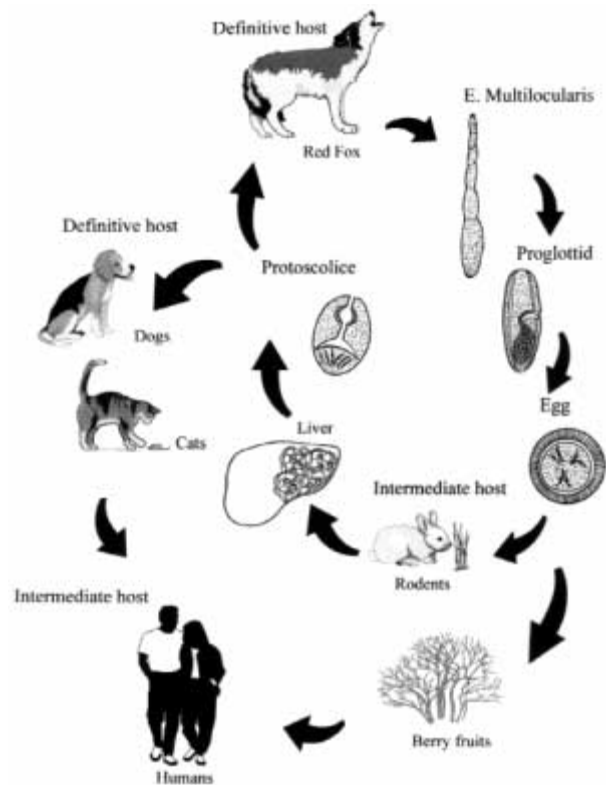

Fig. 8. — Scheme of the E. multilocaris cycle

the alveolar hydatic disease, there is no encapsulation by the host to restrict the growth of the parasite. Thus, the pronounced cell mediated responses are thought to be due to a close intimacy between the parasite and the host. This contrasts with E. granulosus infection in which there is encapsulation creating a partial barrier between parasite and host. Several mechanisms have been considered to explain the ability of the parasite to overcome the immune system of the host. With regard to alveolar echinococcosis, most human patients develop parasite-specific serum antibodies, including all types of immunoglobulins (11). Very few patients fail to demonstrate a humoral immune response (12). Antibodies are thought to be involved in immunopathologic mechanisms responsible for the occasional chronic granunulomatous course of the disease, including immune complex associated membranous nephropathy and histopathological changes related to the incidence of amyloid and immune complex deposits in the liver, as found in several patients. Parasitic- specific antibodies alone are unable to control parasite growth, and host tissue infiltration may be due partly to complement neutralising factors released by the metacestode that cause complement depletion at the host-parasite interface. In vitro experiments have demonstrated the ability of protoscolices of E. multilocularis to suppress murine T cell function including the proliferation of CD-8 + T cells while simultaneously inhibiting interleukin-2 (IL-2) production and IL-2 receptor expression (13,14). In

humans, alveolar hydatidosis is also associated with impaired T cell function by direct splenic T lymphocyte cytotoxicity to the metacestode as measured by in vitro assays and is characterised also by a decrease in total peripheral lymphocytes and in circulating B lymphocytes percentage. Moreover, the state of the host immune system influences probably the susceptibility to the disease (15). In our patient receiving immunosuppressive drugs, one may suggest that this immunosuppression may have influenced the parasite development and growth rate.

In humans, the incubation period is estimated between 5 and 15 years (16). Asymptomatic alveolar echinococcosis may be detected by an unrelated ultrasound or CT (17). Symptoms are generally the result of the enlarging hydatid disease on adjacent tissues and organs and may mimic the symptoms of hepatic carcinoma, cirrhosis, or other liver diseases (2,3). Jaundice and hepatomegaly may be present. The obstructive jaundice is most of the time incomplete and evolves in thrusts. Sometimes angiocholitis may occur. Without adapted therapy, the relapses are frequent, and the jaundice becomes permanent leading to invalidating pruritus. Usually the hepatomegaly is painless, but the palpation shows an irregular surface with nodules comparable to a metastatic liver. Compression of hepatic parenchyma with portal hypertension may also occur (2,3). The general state of health may be impaired, with asthenia, anorexia, and loss of weight in a few weeks. The parasitic disease can spread to the peritoneum and the abdominal organs, in particular to the spleen. Secondly, it can "metastasise" into the lungs, the brain, the kidneys, or bones. Untreated alveolar hydatidosis is fatal with 94% mortality within 10 years of diagnosis (2,3,).

Immunodiagnostic (ELISA) tests are more reliable in alveolar echinococcosis than in cystic echinococcosis, with more than 95% of sensibility and specificity (1,16,18,19). Radiological exams, either ultrasonography, CT or magnetic resonance imaging, may demonstrate the E. multilocaris lesions but are not very specific (17,20). The lesions are characterised by heterogeneous, hypodense masses, often associated with necrotic cavities, by lack of a well-defined wall and by irregular contours (16). Interestingly, calcifications within the liver or at the periphery of lesions are characteristic features of alveolar echinococosis and are present in 70% of the cases (Fig. 1A) (16). Positron emission tomography may show the metabolic activity of viable infection of E. multilocaris, with hypometabolic regions corresponding to necrosis, as in our case (Fig. 3). However, the diagnostic power of positron emission tomography and its role in the follow-up of these patients has still to be assessed (21). Percutaneous fine needle aspiration can be performed without risks of anaphylaxis or secondary echinococcal infection but is usually non contributive due to fibrosis or necrosis. In most cases, as in ours, the pathological exam of surgical specimen provides the diagnosis. Surgical resection is the base of alveolar

echinococcosis management (22,23). Without radical removal, the lesions inevitably spread out with complicated infections (angiocholitis, hepatic abscess) or mechanical complications (portal high blood pressure, spontaneous fistula) (22). After surgical resection anti parasite drugs are required. Many studies proved the efficiency of benzimidazole derivatives in reducing the size of the lesions and in improving of the clinical symptoms (24,25). Albendazole (10 -15 mg/kg/day) should be administrated during 6 to 12 months or more after the procedure. The non resectable lesions should be medically treated during a longer period (24). Liver transplantation may be a life-saving palliative measure in patients with non resectable hepatic lesions (26,27). Unfortunately, growth of residual parasitic tissue may be enhanced by the immunosuppressive therapy given to the transplant recipient (15), and recurrences after liver transplantation are not infrequent (28). Radiological and serological surveillance must be continued indefinitely to monitor for recurrence and/or progression of disease.

In conclusion, we report herein the first published case of alveolar echinoccocosis contracted in Belgium. This report, added to the demonstration of the presence of E. multilocaris infection in more than 50% of red foxes in Southern Belgium, and the potential infection of domestic cats and dogs, should attract attention of the medical community regarding the possible outbreak of endemic alveolar echinococcosis in Belgium, and the related public health concerns.

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