International Journal of Medical and Pharmaceutical Case Reports
3(4): 96-100, 2015; Article no.IJMPCR.2015.043
ISSN: 2394-109X

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Multiple Hypodense Liver Tumors: Unusual Case of a Spontaneously Healed Echinococcosis

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Authors' contributions

This work was carried out in collaboration between all authors. Author TF wrote the draft of the manuscript and managed the literature searches. Authors TF, NW, TJ and DK designed the figures, managed literature searches and contributed to the correction of the draft. Author CR provided the case and supervised the work. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/IJMPCR/2015/15136
Editor(s):
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(4) Anonymous, Turkey.
Complete Peer review History: http://www.sciencedomain.org/review-history.php?iid=994&id=38&aid=8707

Case Study

Received 8th November 2014
Accepted 17th March 2015
Published 6th April 2015

ABSTRACT

A 62 year old woman suffered from unspecific upper abdominal pain. Abdominal imaging showed multiple liver tumors highly suspicious for malignancy. Although a first needle biopsy was suggestive for an echinoccocus cyst, repeated serologic testing for echinococcosis was negative. Only after surgical resection of one tumor nodule, a spontaneously healed *Echinococcus multilocularis* could be diagnosed.
Therefore echinococcosis should always be considered as a possible differential diagnosis of liver tumors in Central Europe. Spontaneous death of *Echinococcus multilocularis* hydatids as described in this case is rare, but might be underreported in the literature.

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Keywords: Liver tumor; alveolar echinococcosis; Echinococcus multilocularis; alveolar hydatid disease.

1. CASE REPORT

A 62-year-old woman has suffered from irregular, unspecific upper abdominal pain since summer 2012. An ambulatory CT-scan showed multiple hypodense (not clearly cystic) liver lesions with diameters of approximately 1 cm. Due to contrast enhancement pattern and morphology the tumors were regarded as suspicious of malignancy, which was most probably related to carcinoid metastases or angiosarcoma. Metastases of an intestinal carcinoma were improbable based on the intial CT scan. Since chronic cholecystitis was also diagnosed, a cholecystectomy with a laparascopic biopsy of some liver lesions was performed elsewhere in November 2012, which showed an unspecific encapsulated necrosis.

After surgery, the patient was still suffering from the same pain and was therefore referred to our hospital for further examination in January 2013. The patient did not report weight loss, fever, night sweats or cutaneous flushing. Gastroscopy and colonoscopy, as well as repeated outpatient gynecological examinations were unremarkable. The patient did not drink alcohol and her BMI was 28 kg/m^2. Liver function tests (ASAT, ALAT, AP, GGT, total bilirubin) and standard laboratory values were all within normal range. There was no laboratory evidence for a carcinoid tumor. In addition, AFP, CEA and CA 19-9 were not elevated.

Ultrasound showed multiple hypoechoic tumors with washout in contrast enhanced ultrasound (Fig. 1).

A repeated CT and MRI scan showed multiple hypodense and round lesions in both hepatic lobes similar to the first CT scan (Fig. 2). The contrast enhancement pattern in early arterial phases and the absence of clearly cystic lesions in T2-weighted sequence were indicative for malignancy.

Next, we performed an ultrasound guided as well as an endosonographic biopsy in order to clarify the etiology of these hepatic tumors First histological results showed no signs for malignancy. Further specific examinations were suspicious for wall pieces of an echinococcus cyst. However, extensive serological testing, including Em2plus ELISA for an echinococcus infection, was negative. The patient negated contact to foxes or dogs and had not eaten any potentially contaminated berries.

Due to the negative blood results for echinococcosis we decided to do a diagnostic laparoscopy with resection of some of the hepatic lesions. Detailed histological examinations in several laboratories showed an encapsulated necrosis with multiple cysts with foreign material and granulomas in the walls of these cysts (Fig. 3). Despite the negative serology, these structural findings were typical for echinococcus cysts.

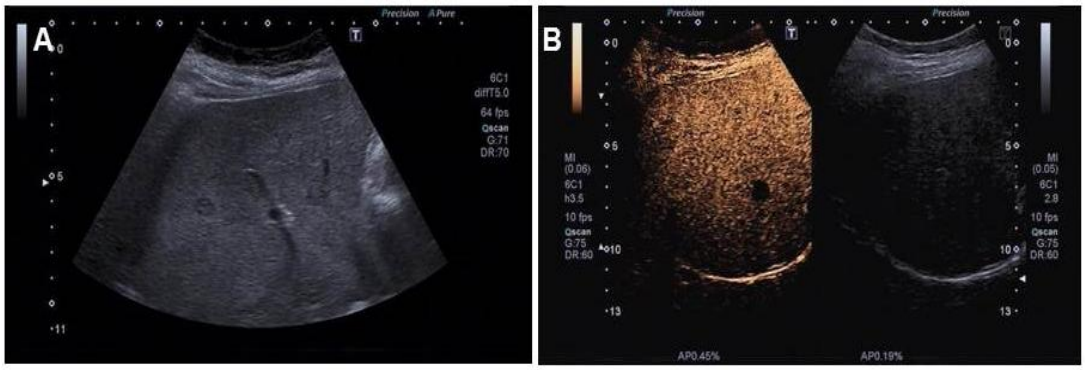

Fig. 1. (A) Abdominal ultrasound and (B) contrast enhanced ultrasound (CEUS): Hypoechoic, round lesions in the right hepatic lobe with washout suggestive for malignancy in CEUS

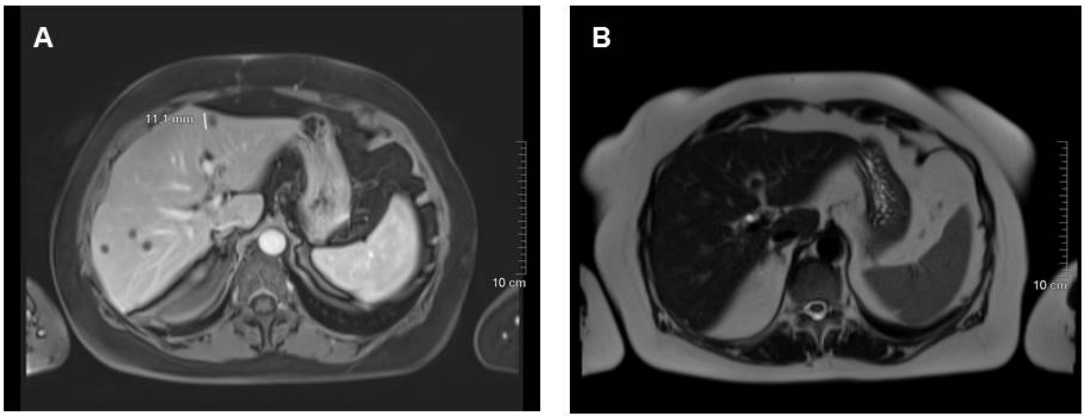

Fig. 2. MRI scan (T1w, T2w). (A) Multiple, round, hypodense liver lesions about 1 cm in diameter. (B) Absence ofcysticlesions in T2 weighted sequences

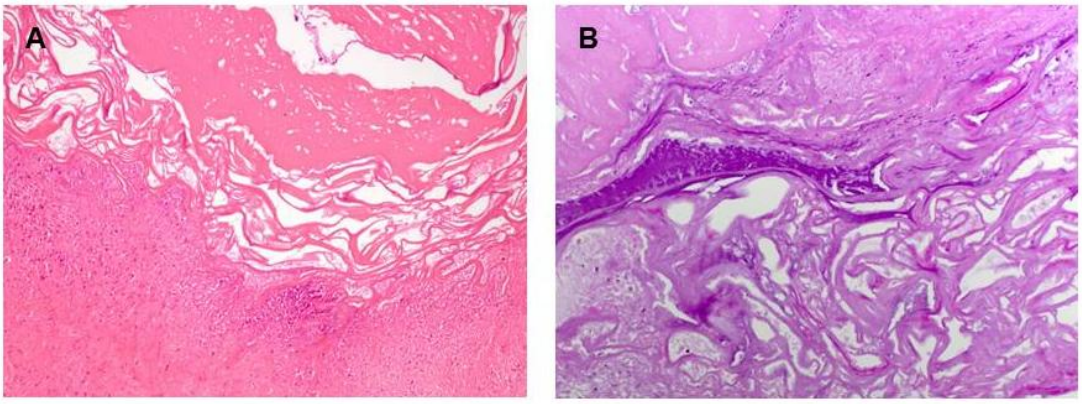

Fig. 3. (A) Volatile thick membranes (H&E stain). (B) Broadly PAS (Periodic-acid Schiff) negativity without germ layer

As the echinococcosis of our patient was completely necrotic, she did not need any systemic therapy or further surgery. Initially, we recommended follow up examinations, including contrast enhanced ultrasound and serological testing every 6 months. One year after the diagnosis, the patientis still in good health, the hepatic lesions are still unchanged in repeat imaging studies and specific serology is still negative.

2. DISCUSSION AND CONCLUSION

Alveolar echinococcosis (alveolar hydatid disease) is a very rare helminthic zoonosis caused by the larval stages of *Echinococcus multilocularis* (fox tapeworm). It is characterized by a chronically progressive liver infestation due to invasive tumor-like hydatids [1,2].

Echinococcus multilocularis is a small cestode whose definitive hosts are wild carnivores (mainly red and arctic foxes). The adult tapeworms live in the bowel of their definitive hosts. Gravid proglottids release eggs which are excreted with fox faeces. Aberrant hosts such as humans can become infected by direct contact to those eggs or indirectly by contaminated food or water. Oncospheres emerge from the ingested eggs, penetrate the mucosa of the small intestine andare transported through blood or lymph vessels to the liver. There oncospheres develop into a hydatid cysts (metacestodes), who proliferate in humans indefinitely and invade the surrounding tissue mimicking a malign tumor. The larval mass is able to spread into extrahepatic structures and even to metastasize to distant organs.

Although extrahepatic metastases are rare, they can occur (e.g. in the lungs and the brain).

Without treatment, 95 % of the patients die within 10 years after becoming symptomatic [3]. After a long asymptomatic period, symptoms like abdominal pain in the right upper quadrant, dyspepsia and cholestatic jaundice may occur. In the course of the disease, most of the patients die due to advanced chronic or acute hepatic failure.

A diagnosis is usually made by imaging studies (ultrasound, CT and MRI scan), serologic tests (with a sensitivity of up to at least 90% [4]) and/or histological examination.

Surgical removal of cysts combined with systemic therapy (e.g. albendazole) is the only curative treatment of alveolar echinococcosis [1]. Spontaneous death of *Echinococcus multilocularis* hydatids as described in this case is rare, but might be underreported in literature [5-7].

Piarroux et al. [5] examined retrospectively 387 cases of alveolar echinococcosis diagnosed in France between 1982 and 2007. Only 15 patients had dead echinococcus lesions and they were mostly incidental findings.

In 1987 Rausch et al. [6] reported about 9 cases of asymptomatic alveolar echinococcosis of the liver among Eskimos, diagnosed by an enzyme-linked immunosorbent assay (Em2 ELISA). Spontaneously died off echinococcus alveolaris lesions were found in 6 of these 9 Eskimos. Spontaneous death of *Echinococcus multilocularis* in humans has not been reported before that.

The unclear liver lesions in our patient were an infiltration of a long-lasting, completely necrotic and abortive, encaspsulated echinococcosis. Due to the histological pattern (infiltrative growth, bizarre membranes with volatile thickness), they were regarded more specific for an echinococcus alveolaris (*multilocularis*) infection. Complete spontaneous necrosis might have been the reason for the negative serological test results and the widely PAS-negativity.

False negative serological test results can also occur in patients with low antibody levels, who do not demonstrate a detectable immune response [8]. The sensitivity of serological tests is also influenced by the degree of sequestration of the echinococcal antigens. Thus, this means that intact or inactive cysts produce a weaker immune response than e.g. ruptured or leaking cysts. Besides, liver cysts are more likely to generate a significant immune response than pulmonary cysts [4].

In general, alveolar echinococcosis is mostly seen in the northern hemisphere e.g. Central Europe, Central Asia, China and North America. Only about 5 – 40 cases are registered yearly in Germany at the Robert Koch Institute. About 500 cases have been registered in the European Echinococcosis Registry during 1982 – 2000 in central Europe. So far, the highest prevalences (6.2%) have been found during a mass screening with portable ultrasound, combined with serodiagnostic tests among inhabitants of the Chinese province Sichuan [9].

A retrospective study in Switzerland based on case finding studies and databases of the 3 major echinococcosis treatment center has demonstrated an annual incidence increase from a mean of 0, 10 per 100.000 during 1993 - 2000 to a mean of 0,26 per 100.000 during 2001 – 2005 [10]. There is also evidence of parasites spreading from endemic to previously non-endemic areas due to the movement of foxes. Several cases have been reported from areas, which were considered to be non-endemic previously [4,11].

Thus, echinococcosis might become an emerging disease especially in certain areas in Central Europe [1].

In these regions, echinococcosis should always be a differential diagnosis of liver tumors and physicians need to know more about its clinical features, including atypical clinical presentation.

CONSENT

All authors declare that ‘written informed consent was obtained from the patient (or other approved parties) for publication of this case report and accompanying images.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sciencedomain.org/review-history.php?iid=994&id=38&aid=8707