

Recurrent multiple-organ involvement of disseminated alveolar echinococcosis in 3 patients

Case report

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Abstract

Rationale: Alveolar echinococcosis (AE) is a rare but highly malignant form of echinococcosis caused by *Echinococcus multilocularis*. There have been very few reports on multiple-organ AE, especially AE in bones. Here we report 3 rare cases of disseminated multiple-organ AE from western China and its neighboring areas.

Patient concerns: Patient 1 had back and left hip pain, headache, and weakness in left lower limb, often with minor epilepsy and fluctuation of blood pressure. Lower limbs Babinski sign was positive and muscular tension was above normal range. The second patient had pain in lower limbs and chest discomfort without fever, cough, sputum, chest tightness, or hemoptysis. Patient 3 had masses and pain in the back side of his right shoulder.

Diagnoses: The patients had been treated for AE multiple times and were positive for serum hydatid antigens. They were diagnosed as multiorgan AE involving liver, spinal cord, and many other organs.

Interventions: The patients had undergone surgeries to decompress the spinal cord, remove lesions from tissues as required, and were put on albendazole for at least 2 years.

Outcomes: The patients responded well and AE recurrence has not occurred.

Lessons: All 3 cases experienced multiple recurrences of AE due to missed diagnosis, misdiagnosis, or inappropriate treatment, which resulted in metastatic multiorgan AE. These cases demonstrated the need for more policy attention to battle AE endemic in western China.

Abbreviations: AE = alveolar echinococcosis, CT = computed tomography, EgB = hydatid cyst fluid native antigen B, EgCF = crude hydatid cyst fluid antigen, EgP = *Echinococcus granulosus* protoscolex antigen, Em2 = *Echinococcus multilocularis* metacestode antigen, MRI = magnetic resonance imaging.

Keywords: alveolar echinococcosis, bone, case report, multiorgan, recurrence

1. Introduction

Alveolar echinococcosis (AE) is a highly malignant form of echinococcosis caused by the larvae of parasite *Echinococcus*

multilocularis,^[1] and its prevalence has unexpectedly increased recently.^[2] AE commonly infects the liver and may invade other organs.^[3–6] The involvement of bone in AE is extremely rare.^[5–10] Here we report 3 cases of AE (Table 1) involving multiple organs, including bones, from Xinjiang Province of China where AE is endemic.

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2. Case report

The study was approved by the institutional review committee of The First Affiliated Hospital of Xinjiang Medical University. All patients provided a written informed consent.

2.1. Case 1

A 30-year-old Kazakhstan male, who had a history of close contact with dogs and sheep, was admitted to Orthopedics Center of Xinjiang Medical University in January 2016 because of back and left hip pain, headache, and weakness in left lower limb, often with minor epilepsy and fluctuation of blood pressure. Lower limbs Babinski sign was positive and muscular tension was above normal range. It was misdiagnosed as right lung tuberculosis for chest pain but found to be AE by pathological results after operation in June 2008 and another operation for

Table 1

Summary of major findings of 3 cases AE.

	Patient 1	Patient 2	Patient 3
Age, y	30	52	26
Gender	Male	Female	Male
Ethnicity	Kazakhstan	Khalkhas	Uyghur
First diagnosed	June 2008	2006	July 2005
Times operated previously	8	2	6
Hydatid test results	EgCF ⁺ EgP ⁺ EgB [±] EM2 [±]	EgCF ⁺ EgP ⁺ EgB [±] EM2 [±]	EgCF ⁺ EgP ⁺ EgB ⁺⁺ EM2 ⁺
Organs involved	Head, lungs, spleen, kidneys, liver, right scapula, left second costal arch, the left acetabulum, the third left rib, and T5-T8 thoracic vertebrae	L1-L2 lumbar vertebrae, lung, liver, and gallbladder	Right scapula, psoas major, rectus abdominis, and liver
Treatment	Decompress the spinal cord, removal of intracranial AE, 2 year albendazole	Decompress the spine, debride anterior focus, and remove and rebuild the fixation, 2 year albendazole	Excise the masses and the destructed part of 9 to 11 ribs, debride focus, repaired the pleura, 2 year albendazole

AE = alveolar echinococcosis, EgB = hydatid cyst fluid native antigen B, EgCF = crude hydatid cyst fluid antigen, EgP = *E. granulosus* protoscolex antigen, Em2 = *E. multilocularis* metacestode antigen.

oxter lesion in the same month in a Kazakhstan hospital. He had 3 more operations in 2009 and 2010 for liver AE. In July 2011, the patient was diagnosed as thoracic AE because of back pain and thoracic canal decompressed posteriorly. AE located between axillary region and scapular was operated in 2012. In July 2013, thoracic lesions were again treated with canal posterior decompression and fixed with hooks and rods.

MRI and CT scan showed lesions in head, lungs, spleen, kidneys, right scapula, left second costal arch, the left acetabulum, the third left rib, and T5-T8 thoracic vertebrae (Fig. 1). Abdominal ultrasound showed heterogeneous lesion within the right lobe cortex of liver and spleen. Dot Immunogold Filtration Assay (DIGFA) kit for human echinococcosis (Xinjiang Beisiming Biotechnology Development Co, Urumqi, China) was used to detect the presence of antibodies

against EgCF (crude hydatid cyst fluid antigen), EgP (*Echinococcus granulosus* protoscolex antigen), EgB (hydatid cyst fluid native antigen B), and Em2 (*E. multilocularis* metacestode antigen) in patient serum^[11] and the results were EgCF⁺ EgP⁺ EgB[±] EM2[±]. Blood tests indicated that tumor markers, blood counts, blood biochemistry, blood coagulation, and erythrocyte sedimentation rate were normal. C-reactive protein was 61.40 mg/L, which was significantly higher than the normal range of 0 to 8 mg/L. Based on clinical symptoms and test results, the patient was diagnosed as multiple-organ AE presented in liver, kidney, spleen, thoracic vertebrae, left acetabulum, and right scapula, and transcranial alveolar hydatid disease with epilepsy. Surgeries were performed to decompress the spinal cord, and patient was given a prescription of 2-year albendazole treatment.

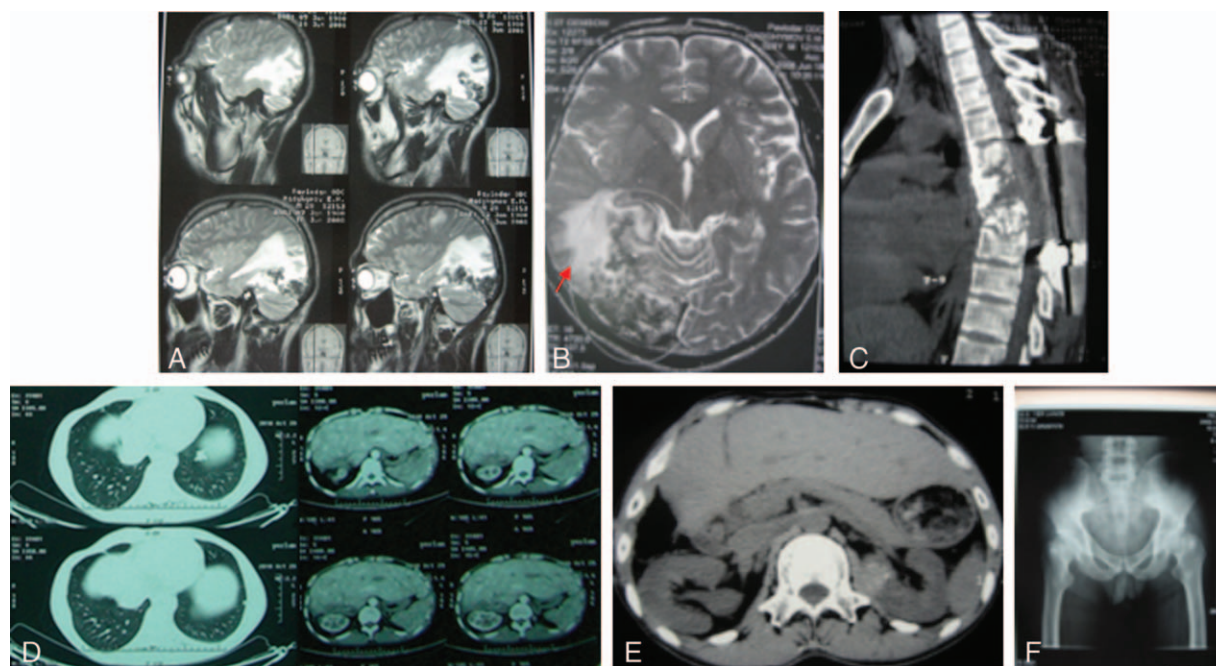


Figure 1. (A) T2 sagittal image showed focal lesions on right parietal. (B) T2 coronal image showed large patch lesions in right temporal lobe (arrow). (C) Vertebral sagittal MR imaging showed bony destruction of thoracic vertebral body and irregular low density lesions. (D, E) Lesions at the right and left lung. (F) Left acetabulum margin of local bone cortex continuity outages and local visible patchy bone density low dense area.

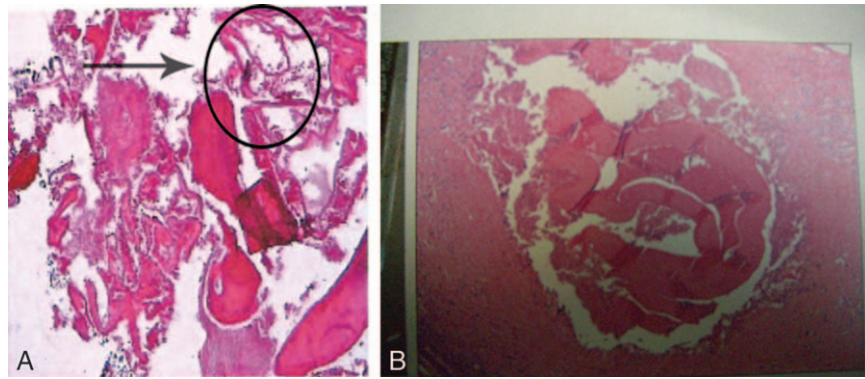


Figure 2. H&E staining showed hydatid lesions (arrow pointed circle) adjacent to the thoracic vertebrae (A) and brain (B) of the first patient. H&E = hematoxylin eosin.

The second lethal lesion was the brain AE but the patient refused operation on his brain in January 2016. He went back to Kazakhstan after back surgery. Ten months later, this patient came back due to the progression of intracerebral AE. In November 2016, the ninth operation was performed to treat brain AE. Pathological examination confirmed AE (Fig. 2).

2.2. Case 2

A 52-year-old Khalkhas female, who lived in pastoral areas in close contact with dogs and sheep, came to our hospital as lung lesions had been identified during medical examination. She had pain in lower limbs, and chest discomfort without fever, cough, sputum, chest tightness, or hemoptysis. She previously had operations for liver hydatid in 2006 and for tuberculosis of

lumbar spine in 2012. Physical examination did not find spine deformity, abnormality of thoracic or heart, abdominal pain, gastrointestinal symptom, abdominal varicose, limb muscle weakness, or abnormal breathing. However, there was lumbar spine tenderness and movement restriction of the waist. X-ray and CT scan identified lesions in lungs and liver (Fig. 3). EA hydatid test showed EgCF⁺ EgP⁺ EgB[±] EM2[±]. Blood test results were normal except for abnormally high erythrocyte sedimentation rate (56 mm/h compared to normal 0–20 mm/h). The patient was diagnosed as multiorgan AE involving L1-L2 lumbar vertebrae, lung, liver, and gallbladder.

Second stage surgery was performed through the original incision (Fig. 4A) to decompress the patient’s spine, undergo anterior focus debridement, and remove the fixation from previous operation. Second surgery was performed to correct

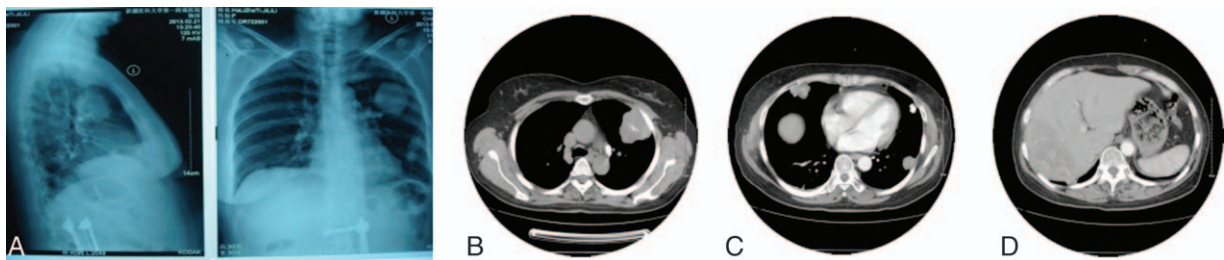


Figure 3. X-ray showed multiple lesions in bilateral lung (A) and CT scan showed spherical cystic and punctate calcification in the right and left lung (B), and lesions in the right lobe of liver (C, D) of the second patient.

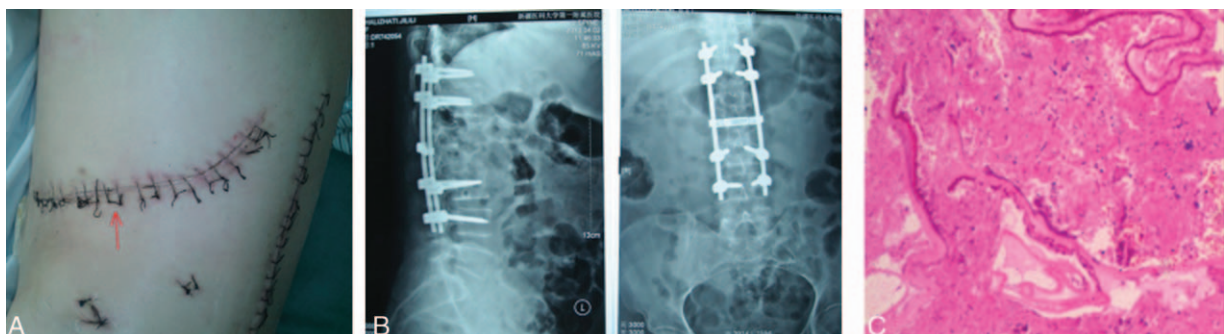


Figure 4. The incision site of surgery (A), x-ray showed postoperative fixations of spine (B), and H&E staining of spinal cord tissue (C) of the second patient. H&E = hematoxylin eosin.

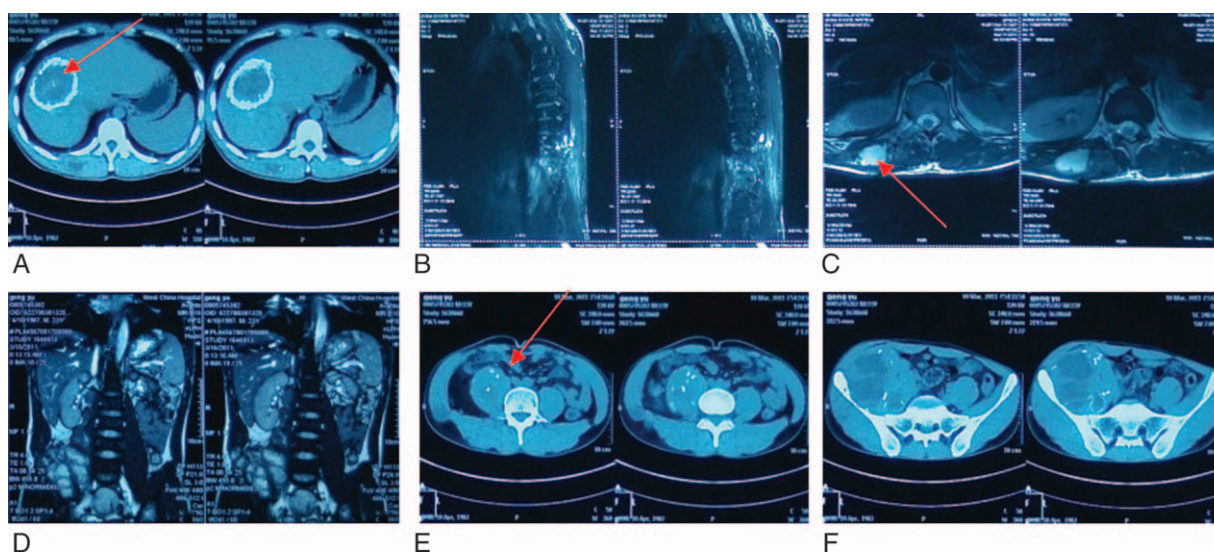


Figure 5. MRI showed multiple lesions (arrow) in liver (A), the right of the back (B, C), the upper right hip (D), the right psoas major (D, E), and within the iliacus (D, F) of the third patient.

posterior internal fixation and bone graft. Postoperative x-ray showed that the internal fixation was correctly positioned and properly fixed (Fig. 4B). Pathological examination confirmed EA (Fig. 4C). Albendazole was prescribed at 10 to 15 mg/kg body weight/d taken by 2 doses, recommended to be continued for at least 2 years to reduce the risk of AE recurrence.

2.3. Case 3

A 26-years-old Uyghur male, with masses and pain in the back side of his right shoulder, was admitted into our hospital, and diagnosed as right shoulder tuberculosis but confirmed as AE by postoperative pathological examination at Huaxi Hospital (Chengdu, China) in March 2011. This patient had undergone 5 surgeries since July 2005 to remove masses in upper back before he came to our hospital. MRI showed multiple EA lesions in liver, the right side of the back, the upper right hip, the right psoas major, and the iliacus (Fig. 5). Intraoperative and postoperative pathologic examinations confirmed AE. The patient had begun taking medicine for AE in 2011. Physical examination did not find spine deformity or abnormality in heart, thoracic, and abdomen. However, a 6 × 8 cm mass near the inferior angle of scapula could be felt by touching; skin was tender but temperature was not elevated. Hydatid test was EgCF+ EgP+ EgB++ EM2+. Blood tests were normal but erythrocyte sedimentation rate (45 mm/h) and C-reactive protein level (13.0 mg/L) were higher than normal ranges. This patient was diagnosed as multiple-organ AE involving lower part of the right scapula, psoas major, rectus abdominis, and liver.

As AE of this patient had recurred many times and imaging showed that a part of 9-11 ribs was destroyed; a surgery was performed to excise the masses and the destructed part of 9-11 ribs, then to repair the pleura with patch after focus debridement. After surgery, the patient was told to continue albendazole treatment for at least 2 years to reduce the risk of recurrence.

3. Discussion

AE is endemic in western China,^[12,13] especially in rural herding areas. Wild canines appear to be the definitive hosts, whereas

rodents, deer, moose, reindeer, and bison are the intermediate hosts of *E. multilocularis* in these regions. The lack of medical resources in rural areas of western China often results in missed diagnosis, misdiagnosis, or inappropriate treatment of AE. These problems were presented in all 3 cases reported here, which resulted in delayed diagnosis, inappropriate treatment, recurrences, and metastasis of AE.

AE is a rare but highly malignant form of echinococcosis, and it is caused by cyclophyllid tapeworm *E. multilocularis*. AE is generally presented in liver initially, and the majority of *E. multilocularis* infections is confined to the liver but may later spread to other organs,^[14] mainly via blood circulation or lymphatic system.^[13,14] In an analysis of 117 AE patients from eastern France, pulmonary metastasis occurred in about 20% of the patients whereas cerebral metastasis in only 1% and the simultaneous lung and brain metastases occurred in 1.1% of the patients.^[15] Among 159 AE patients from western China, 35 (22%) patients had extrahepatic metastasis; among them, 8 (5%) patients developed multiorgan AE and 2 (1.25%) patients had spine metastasis.^[13] Both multiorgan involvement and spine metastatic AE were rare, which made it unusual that these 3 cases had spine-related multiorgan-involved AE. At admitting time, the first patient had alveolar hydatid disease of brain, acetabular, liver, kidney, spleen, spine, and scapula. The second patient had infection in spine, liver, lung, and gallbladder, whereas the third patient had AE involving spine, scapula, liver, and psoas major and rectus abdominis. AE of the spine^[5-9] is rare; extraspinal bone AE is even rarer.^[10,16,17] The first patient had the most unusual diagnosis, with AE being currently identified in thoracic vertebrae, left acetabular, and right scapula besides other organs.

AE manifestations in liver always precede lung involvement, which is mainly through transdiaphragmatic migration of hepatic AE or occasionally due to intrathoracic rupture of hepatic cysts into the bronchial tree, pleural cavity, or mediastinum.^[18,19] Lung lesions of AE on CT scan generally have an irregular contour with intralésional and wall calcifications. Imaging studies are usually highly suspicious of carcinoma or sarcoma, and biopsy may provide the first confirmation of infection. The

overall condition of patients with AE is generally better than would be expected with a malignancy.^[18–21] CT images of patients with intracerebral AE are not specific. Increased intracranial pressure, epilepsy, neurological disturbances such as hemiparesis, skull deformity, and cranial nerve palsies have been reported.^[20] Intracerebral *E. multilocularis* on MRI is characteristically shown as a grape-like, multilocular cystic mass with definite margins. It is common to be accompanied by calcifications and surrounding edema. The inflammatory reaction around the cysts may produce a contrast enhancement.^[22] Multiple recurrence of AE in these 3 patients may be the cause of spreading AE in brain, spine, bones, lung, gallbladder, and liver, and also presented a complicated situation for management and treatment of the disease.

In conclusion, missed diagnosis, misdiagnosis, or inappropriate treatment resulted in multiple recurrence and multiorgan metastasis of AE. The 3 cases reported here had unusual or end-stage brain, spine, scapula, acetabulum, and muscle AE, and all had liver and lung AE (Table 1). These cases demonstrated the need for significant changes in health policy toward the rural areas of western China where minorities dwell and adequate medical resources to battle AE endemic in those regions.

References

- [1] Vuitton DA, Zhou H, Bresson-Hadni S, et al. Epidemiology of alveolar echinococcosis with particular reference to China and Europe. *Parasitology* 2003;127(suppl):S87–107.
- [2] Vuitton DA, Demonmerot F, Knapp J, et al. Clinical epidemiology of human AE in Europe. *Vet Parasitol* 2015;213:110–20.
- [3] Albayrak Y, Kargi A, Albayrak A, et al. Liver alveolar echinococcosis metastasized to the breast. *Breast Care* 2011;6:289–91.
- [4] Çakmak E, Alagozlu H, Gumus C, et al. A case of Budd-Chiari syndrome associated with alveolar echinococcosis. *Korean J Parasitol* 2013;51:475–7.
- [5] Keutgens A, Simoni P, Detrembleur N, et al. Fatal alveolar echinococcosis of the lumbar spine. *J Clin Microbiol* 2013;51:688–91.
- [6] Nell M, Burgkart RH, Gradl G, et al. Primary extrahepatic alveolar echinococcosis of the lumbar spine and the psoas muscle. *Ann Clin Microbiol Antimicrob* 2011;10:13.
- [7] Toussaint F, Pere P, Le Chaffotec L, et al. Alveolar echinococcosis of the spine. *J Clin Rheumatol* 2001;7:248–51.
- [8] Claudon M, Bracard S, Plenat F, et al. Spinal involvement in alveolar echinococcosis: assessment of two cases. *Radiology* 1987;162:571–2.
- [9] Merkle EM, Kramme E, Vogel J, et al. Bone and soft tissue manifestations of alveolar echinococcosis. *Skeletal Radiol* 1997;26:289–92.
- [10] Dorn R, Küsswetter W, Wunsch P. Alveolar echinococcosis of the femur. *Acta Orthop Scand* 1984;55:371–4.
- [11] Ye J, Zhang Q, Xuan Y, et al. Factors associated with echinococcosis-induced perioperative anaphylactic shock. *Korean J Parasitol* 2016;54:769–75.
- [12] Jianyong L, Jingcheng H, Wentao W, et al. Ex vivo liver resection followed by autotransplantation to a patient with advanced alveolar echinococcosis with a replacement of the retrohepatic inferior vena cava using autogenous vein grafting: a case report and literature review. *Medicine* 2015;94:e514.
- [13] Wang H, Lu C, Liu X, et al. Metastatic and prognostic factors in patients with alveolar echinococcosis. *Int J Clin Exp Pathol* 2015;8:11192–8.
- [14] Kayacan SM, Vatansever S, Temiz S, et al. Alveolar echinococcosis localized in the liver, lung and brain. *Chin Med J* 2008;121:90–2.
- [15] Bresson-Hadni S, Vuitton DA, Bartholomot B, et al. A twenty-year history of alveolar echinococcosis: analysis of a series of 117 patients from eastern France. *Eur J Gastroenterol Hepatol* 2000;12:327–36.
- [16] Hayasaka K, Aburano T, Tanaka Y. MR imaging in alveolar echinococcosis of bone. *Radiat Med* 1995;13:179–82.
- [17] Herrera A, Martínez AA. Extrapinal bone hydatidosis. *J Bone Joint Surg Am* 2003;85-A:1790–4.
- [18] Ammann RW, Eckert J. Cestodes. Echinococcus. *Gastroenterol Clin North Am* 1996;25:655–89.
- [19] Morar R, Feldman C. Pulmonary echinococcosis. *Eur Respir J* 2003;21:1069–77.
- [20] Nunnari G, Pinzone MR, Gruttadauria S, et al. Hepatic echinococcosis: clinical and therapeutic aspects. *World J Gastroenterol* 2012;18:1448–58.
- [21] Marrone G, Crino F, Caruso S, et al. Multidisciplinary imaging of liver hydatidosis. *World J Gastroenterol* 2012;18:1438–47.
- [22] Algros MP, Majo F, Bresson-Hadni S, et al. Intracerebral alveolar echinococcosis. *Infection* 2003;31:63–5.