Diagnostic Pitfalls of Spinal Echinococcosis

Xinghua Song, PhD, MD, Dapeng Liu, MD,* and Hao Wen, PhD, MD†*

Objective: To critically examine and elucidate the diagnostic pitfalls of spinal echinococcosis.

Summary of Patients: From October 1957 to June 2006, 25 consecutive cases drawn from 5721 cases of echinococcosis were collected in the First Affiliated Hospital of Xinjiang Medical University. The selected cases comprised 11 males and 14 females; all were treated with debridement operations. The average age was 28.3 years (15 to 56 y). The average duration of infestation with spinal hydatid disease was 3.2 years (0.5 to 12 y). Nineteen of the 25 cases underwent magnetic resonance imaging (MRI) scanning, which identified 17 out of 19 cases as having hydatid disease. The lesion was located in the cervical vertebrae in 3, the thoracic vertebrae in 11, the lumbar vertebrae in 5, and the sacrum in 6 cases.

Results: Eighteen cases were available for follow up; the period ranging from 0.5 to 15 years with an average of 3.6 years. The Casoni test was performed in 15 cases and was positive in 12 patients (80%). In addition, 4 cases were positive in all of the so-called 8 tests of immunodiagnostic methods. MRI examination was performed in 19 of the 25 cases and 17 of these were diagnosed as having spinal hydatid disease (89.47%). The typical MRI appearance is that of a multilocular cyst and the signal of the parent cyst is similar to that of muscle and higher than that of secondary cyst in the T^1Weighted image (WI). The signal of the secondary cyst is similar to water, either located in or overflowing or adjacent to the parent cyst. Both the parent and the secondary cysts showed high signals in the T^2W1 with either rose or wheel shapes. In the 18 cases, which were reviewed, 11 cases had relapsed (61.11%).

Conclusions: Although x-ray or computed tomography images of spinal echinococcosis are similar to tuberculosis, metastases, giant cell tumors, or cysts of the bone, MRI shows distinctive diagnostic features of spinal hydatid disease. Serologic examinations are important to confirm the correct diagnosis.

Key Words: echinococcosis, spine, diagnosis, pitfalls, clinical manifestation

(*J Spinal Disord Tech* 2007;20:180–185)

Received for publication June 29, 2006; accepted September 12, 2006.

From the *Department of Orthopaedics, the First Affiliated Hospital of Xinjiang Medical University, Urumqi, Xinjiang Province; and †Xinjiang Hydatid Clinical Research Institute, China.

Reprints: Hao Wen, PhD, MD, Xinjiang Hydatid Clinical Research Institute, The First Affiliated Hospital of Xinjiang Medical University, No. 1, LiYuShan Road, Urumqi, Xinjiang Province 830054, China (e-mail: wenh19@163.com).

Cystic echinococcosis (CE) and alveolar echinococcosis (AE) result from infestation with echinococcus granulosus and echinococcus multilocularis, respectively. Although 12 different species have been identified, only 2 of these, *Echinococcus granuosus* and *Echinococcus multilocularis* are known to affect man, the latter is extremely rare and it does not affect bone.[1] Hydatid disease is prevalent throughout most part of the world. CE occurs on every continent except Antarctica and may be transmitted in arctic, temperate, and tropical regions. Human infestation with CE is caused by the larval stage of *Echinococcus granuosus* and is cosmopolitan in distribution in Northern and northwestern China, parts of South America, East Africa, Australia, Central Asia, the Mediterranean littoral (including North Africa), and Russia. CE is also endemic in parts of Western Europe and the southern United States.[2] By 2002, 2 countries, Iceland and New Zealand, and 1 island state, Tasmania, had already declared that hydatid disease had been eliminated from their territories. Other hydatid programs implemented in South America (Argentina, Chile, Uruguay), in Europe (mid-Wales, Sardinia) and in East Africa (northwest Kenya), showed varying degrees of success, but some were considered as having failed.[3]

Hydatid disease may develop in almost any part of the body. The overall incidence of organ infestation is greatest in the liver (50% to 77%) and lungs (8.5% to 43%).[4] Importantly, the incidence of bone echinococcosis disease is much lower, about 0.5% to 4% of the total reported cases. More than 60% of bone hydatid disease occurs in the spine.[5] Spinal echinococcosis disease is difficult to distinguish from x-ray or computed tomography (CT) images of bone tuberculosis, metastases, giant cell tumor, or simple bone cysts. None of these diseases can be readily identified with certainty. We shall attempt to analyze diagnostic pitfalls of spinal hydatid disease.

MATERIALS AND METHODS

Twenty-five cases of spinal hydatid disease were collected in 5721 cases of echinococcosis at the First Affiliated Hospital of Xinjiang Medical University. These comprised 11 males and 14 females, all had undergone debridement operation. The average age was 28.3 years (15 to 56 y). The average duration of infestation with spinal hydatid disease was 3.2 years (0.5 to 12 y). The lesion was located in the cervical vertebrae in 3, the thoracic vertebrae in 11, the lumbar vertebrae in 5, and the sacrum in 6 cases.

Clinical Manifestation

Patients with thoracic spinal hydatid disease often felt pain locally. They may experience lower extremity hyperesthesia, weakness or muscle paralysis, urinary and fecal incontinence, hyperreflexia of knee and ankle-jerks, with a positive Babinski sign. Patients with lumbosacral spinal hydatid disease often feel pain locally, with paresthesia of the lower extremities and perineal region, and/or functional disturbances of urination and defecation. If the lesion becomes infected then abscesses and sinus tracts may form. Sixteen out of 25 cases of spinal hydatid disease had neurologic symptoms of Frankel grade A in 1, grade B in 3, grade C in 3, and grade D in 4 cases.

Laboratory Examinations

The Casoni test was performed in 15 cases and 12 of the 15 were positive. There were 4 cases positive in all of the so-called 8 tests of immunodiagnostic methods.

Imaging

All 25 cases had had x-ray examination. Thirteen cases of the 25 had been scanned by CT and 19 cases were scanned by MR.

Surgical Treatment

Surgical intervention had been used in all of the cases. The basic technique was to expose the relevant lesion, and protect adjacent normal tissue with gauze swabs, if needed access burr holes were made in the area of the lesion and then enlarged carefully with an osteotome. Dexamethasone 10 to 20 mg was injected in the course of operation to prevent allergic shock. The hydatid outer "skin" or peel was removed by aspiration together with any secondary cyst(s) by a combination of spatula dissection and retraction. The compressed normal tissue or "capsule" wall was cleaned by alcoholic phenyl and soaked in 20% hypertonic NaCl solution for 10 minutes. Finally, if necessary, a bone graft was used to rebuild the stability by internal fixation. Ten cases were treated with autogenous bone, 3 cases with allograft bone, 1 case with bone cement, and 5 cases with internal fixation.

Chemotherapy

Chemotherapy with Albendazole was used perioperatively and also for 3 months after operation to prevent disease relapse. The dose of Albendazole tablets or powder was 20 mg/kg per day, or liposomal Albendazole 10 mg/kg per day.

RESULTS

Summary of Clinical Manifestations

All 25 cases were verified by operation and pathology. Eighteen cases were available for follow up and the period ranged from 0.5 to 15 years with an average of 3.6 years. The Casoni test was performed in 15 cases and 12 of the 15 were positive (80%). Four cases were positive in all of the so-called 8 test immunodiagnostic methods. Magnetic resonance imaging (MRI) examination was undertaken in 19 of the 25 cases and 17 cases were diagnosed as having spinal hydatid disease (84.2%). In the 18 cases, which were followed up, 11 cases had relapsed (61.1%). This occurred in the cervical vertebrae in 1 out of 3, the thoracic vertebrae in 4 out of 11, the lumbar vertebrae in 2 out of 5, and the sacrum in 4 out of 6 cases. Five cases relapsed 3 times in the total of 11. Sixteen cases had nerve symptoms, according to the Frankel grading after operation, the symptoms improved differently according to the spinal location. Paresthesia was partially recovered in 1 thoracic vertebral case with A grade. In 3 thoracic vertebrae cases with B grade, 2 cases were recovered totally, and 1 case regressed to D grade because the spinal cord had been irritated during surgery. Three cases with C grade in the thoracic vertebrae recovered and 9 cases with D grade in the lumbosacral vertebrae recovered totally.

Imaging

Spinal hydatid disease was often misdiagnosed by x-ray examination. Thirteen cases were diagnosed as tuberculosis, 6 cases as metastases, 1 case as a chordoblastoma, 1 case as a psoas abscess, and 4 cases were not diagnosed conclusively. The x-ray appearance is nonspecific. In Figure 1A, the sacrum was eroded extensively and virtually destroyed.

The typical appearance for a CE cyst on CT imaging (Fig. 2) is of a round or ovoid space-occupying lesion with "double layer arcuate calcification." This could be considered as specific for hydatid cyst caused by CE infection rather than other cyst diseases. Vertebrae and vertebral arches were destroyed expansively and with multiple cysts. CT images can also recognize rupture of the endocyst by showing a folded detached endocyst. In our series, of the 13 cases scanned by CT, only 5 cases were diagnosed as spinal hydatid disease (23.1%). Under CT scanning, the sacrum was destroyed as shown in Figure 1B. The sacral bone destruction is shown in Figure 1B′ with a 3-dimensional CT scan reconstruction.

Of the 19 cases scanned by MR, 17 were diagnosed as spinal hydatid disease directly. Typically, the vertebral body was destroyed by a cystic, eccentric, expansive, hydatid lesion (Fig. 1C). A hydatid unicysts or single cyst appeared as a round or ovoid space-occupying lesion with a same signal of a long T^1, long T^2 weighted image (WI) and with a smooth border. In this series, there were 2 unicysts and 17 multilocular cases. Secondary cysts occurred in 13 cases out of these 17, all with the same signal in the T^1WI (like water signal). These were located either within the parent cyst or overflowing or lying adjacent to it. The signal of the parent cyst was similar to muscle and higher than the secondary cyst signal (Fig. 3). The capsule had a low signal. Vertebral body destruction with the cysts protruding into the thoracic cavity with both the parent and secondary cysts showing high signals

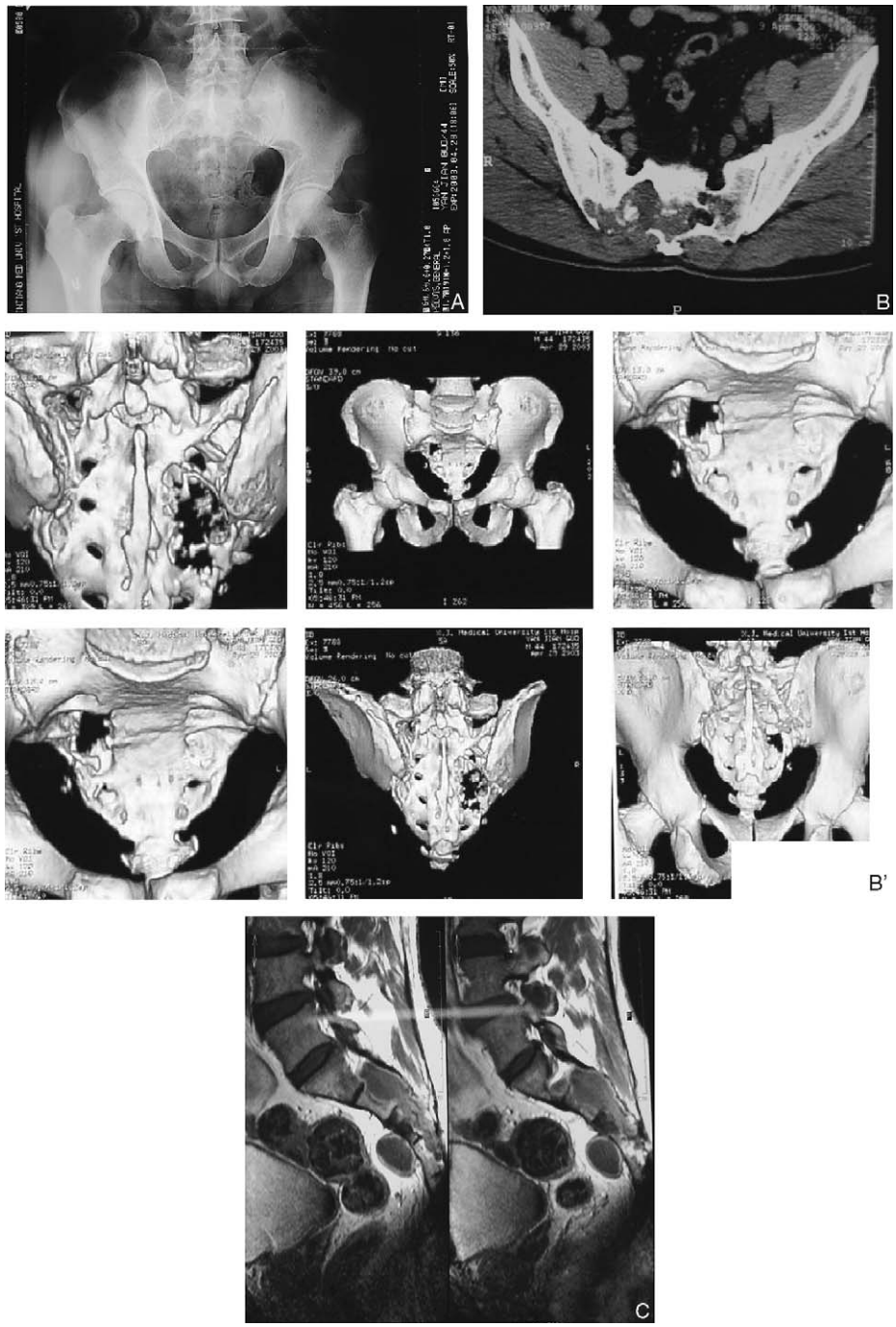

FIGURE 1. A, The radiograph showing the destructive region in the sacrum. B, The sacral bone destruction combined sequestrum on CT scan. B′, The sacral bone destruction on CT scan of 3-dimensional reconstruction. C, MRI showing the occupying lesion in the spinal canal, and in anterior sacrum.

in T^2WI and with secondary cyst false intervals giving the appearance or shapes of roses or wheels (Fig. 4), are sometimes seen. A typical multilocular MR appearance is seen in Figures 5A, B. Enhancement scanning was performed in 12 cases using Magnevist but no enhanced signal was seen. The rupture of concurrently infected thoracic vertebral hydatid disease showed an increased signal with indistinct edges in the T^1WI coronal plane (Fig. 6).

DISCUSSION

Growth Characteristics

Bone hydatid disease often occurs in cancellous bone due to its rich blood supply. The invaded bones are the spine, pelvis, and long bone metaphyses by turn. Spinal hydatid disease is particularly harmful to humans, when it occurs in the vertebrae. The infestation grows along the cancellous bone trabeculae following areas of

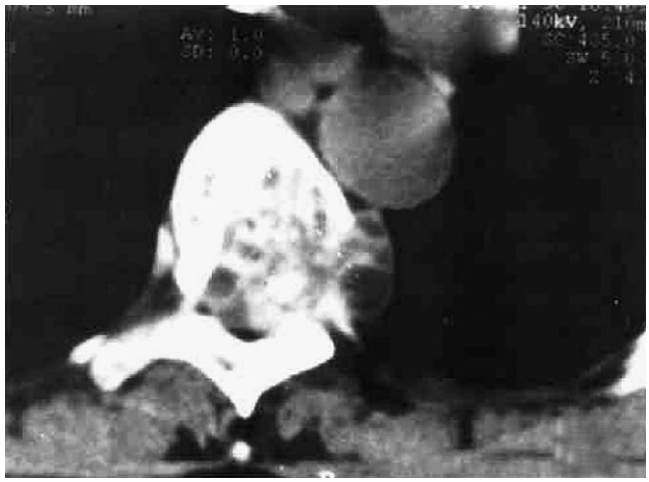

FIGURE 2. The CT appearance of a typical CE cyst as a round or ovoid space-occupying lesion, and double layer arcuate calcification.

low resistance. When the larvae are growing, the spongiform cancellous is enlarged as the bone is eroded and absorbed allowing the cyst/s to dilate and enlarge. The growth pattern determines the imaging characteristics. Bone hydatid disease has no limiting fibrous capsule. It can also grow along the medullary cavity of long bones to the epiphyseal plates and articular cartilage, destroying them and resulting in pathologic fractures or dislocations. New cysts can also be found in soft tissue.[5]

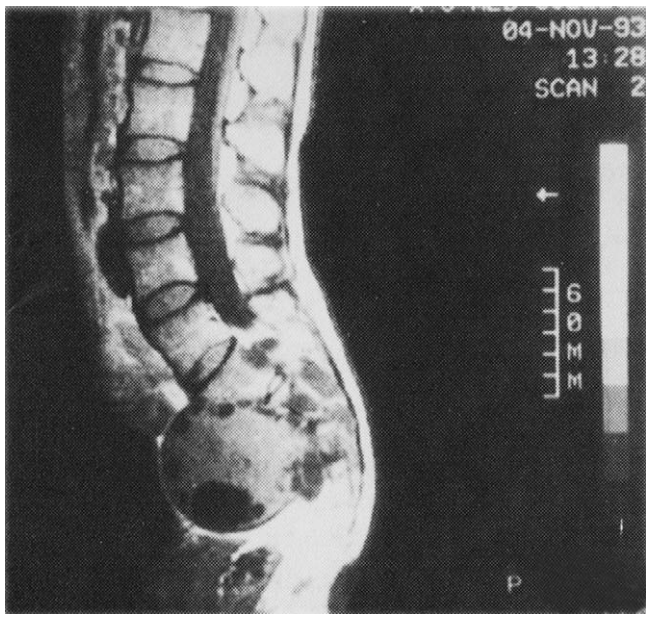

FIGURE 3. MRI showing that the T^1WI, signal of parent cyst is similar to muscle and higher than in the secondary cyst. The signal of the secondary cyst is similar to water, whether located in the parent cyst, overflowing it, or lying adjacent to it.

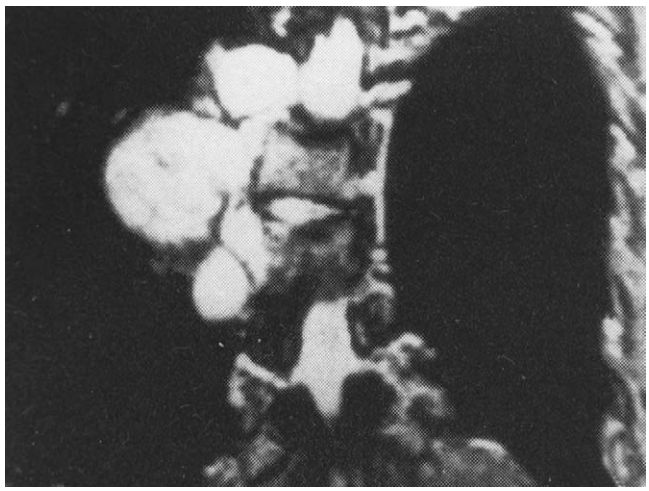

FIGURE 4. The capsule had a low signal. Vertebral body destruction with the cysts protruding into thoracic cavity with both the parent and secondary cysts showing high signals in T^2WI and with secondary cyst false intervals giving the appearance or shapes of roses or wheels.

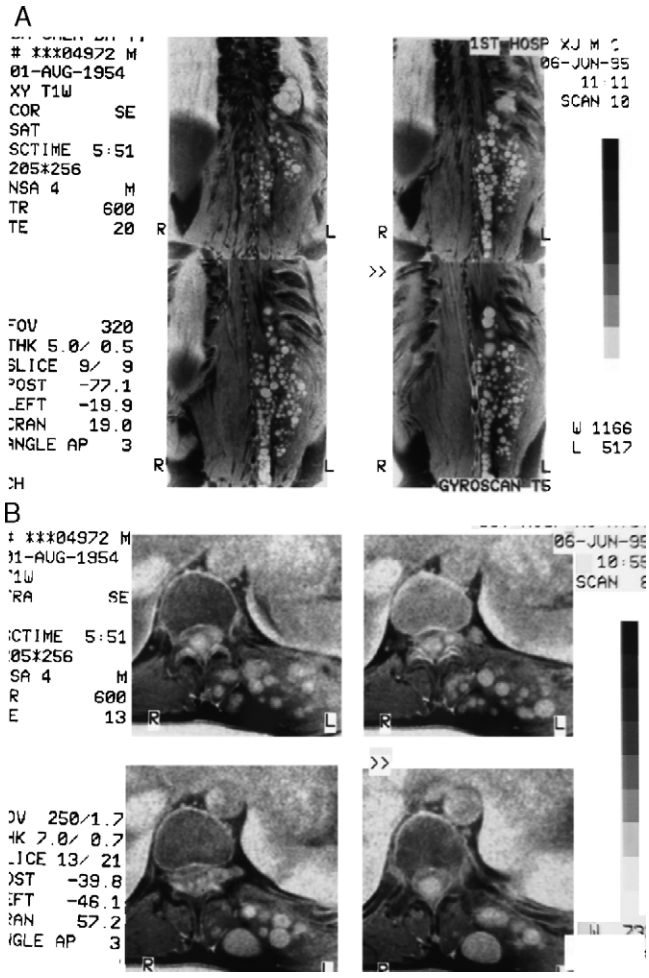

FIGURE 5. A, The saggital views of a multiple cyst of a spinal hydatid disease. B, The transverse multilocular MR views of spinal hydatid disease.

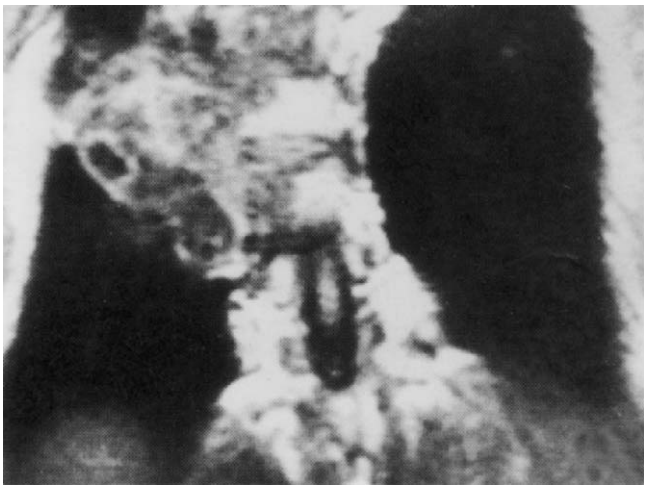

FIGURE 6. The rupture of a concurrent infected thoracic vertebral hydatid lesion showing a signal with indistinct edge in the T^1WI, viewed in the coronal plane.

The Value of Imaging in Diagnosis

The x-ray appearance is that of cystic or irregular destruction of bone. In a few cases, there are arcuate lines of calcification in the "capsule" wall, or there may be multicystic destruction of bone. The above-mentioned characteristics often cause misdiagnosis such as bone cysts and giant cell tumors of bone. In the spine, the appearance is of an irregular destruction of vertebral body and sometimes intervertebral space narrowing. The x-ray appearance of spinal echinococcosis is nonspecific. In our series, 13 cases were diagnosed as tuberculosis, 6 cases as metastases, 1 case as a chordoblastoma, 1 case as a psoas abscess, and 4 cases were not diagnosed conclusively. The nonspecific sacral destruction shown on the x-ray image in Figure 1A is an example.

The typical CT appearance for a CE cyst (Fig. 2) is of a round or ovoid space-occupying lesion with a "double-layered arcuate calcification." This appearance can be considered as specific for hydatid cyst caused by CE infestation rather than any other cyst diseases. Vertebrae and vertebral arches were destroyed multicysticly and expansively. CT imagings can also recognize rupture of the endocyst by showing a folded detached endocyst but the unequivocal images are rarely found. In our series, 13 cases were scanned by CT and only in 5 cases was spinal hydatid disease diagnosed (23.1%). The CT scanning appearance of sacrum destruction seen in Figure 1B is again nonspecific for hydatid disease.

The hydatid cyst has 3 layers: (a) the outer pericyst, composed of modified host cells that form a dense and fibrous protective zone; (b) the middle laminated membrane, which is acellular and allows the passage of nutrients; and (c) the inner germinal layer, where the scolices (the larval stage of the parasite) and the laminated membrane are produced. The middle laminated membrane and the germinal layer form the true wall of the cyst, usually referred to as the endocyst, although the acellular laminated membrane is occasionally referred to as the ectocyst.[6,7] Daughter vesicles (brood capsules) are small spheres that contain the protoscolices and are formed from rest of the germinal layer. The daughter cysts are usually multilocular and because of its slow growth, the bone appears as capsular and distensible, with a smooth and often sclerotic circumscription. The endocyst can develop hyaline degeneration, necrosis, and calcification but these features are not often seen.[8] MRI imaging is the most helpful in diagnosing hydatid cyst disease.[9,10] The multilocular appearance seen in Figures 5A, B is one characteristic of hydatid cyst disease. Another characteristic is that the T^1WI, the signal of the parent cyst is similar to muscle and higher than in the secondary cyst (Fig. 3). The signal of the secondary cyst is similar to water, whether located in the parent cyst, overflowing it, or lying adjacent to it. Both the parent and the secondary cysts show a high signal in the T^2WI sequence and the shape of a rose or a wheel (Fig. 4) due to the interval of the secondary cyst. When the cyst is ruptured or infected, the signal is enhanced because of increased protein in the cyst fluid and there may be an indistinct or vague edge. In addition, MRI is more reliable than CT, because it shows not only the typical signs of a pericystic wall and its multilocular character but also has a special value in showing the relationship of the lesion to the surrounding organs.[8]

Serologic Assay

Serologic tests are important in differential diagnosis. The immunoreaction of the human body is related to the hydatid cyst's integrity, growth vigor, and location. Immunoreaction is heavier in ruptured hydatid cysts and lower when intact. Rupture can result in severe allergic shock and even death. Serologic tests are frequently negative when the hydatid cyst is ageing, calcificied, or dead. Lightowlers and Gottstein[11] found immunoreaction was intense in bone hydatid cyst disease and deduced that this was due to a lack of a fibrous capsule and the cyst contiguity with human tissue. At present, the serologic examinations used in diagnosing hydatid cyst disease are classified into 2 categories. One is detection of antigen from hydatid fluid and protoscoleces, and the main antigenic components are Ag 5 and Ag B,[12] the other is detection of antibodies in the blood serum of patients. Specific antibody examinations are used for diagnosis including the following: the Casoni test, indirect hemagglutination (IHA), counterimmunoelectrophoresis (CIE), enzyme-linked immunosorbent assay (ELISA), and Gold-labeled antibody.[13,14] The Casoni test, IHA, and CIE are called the 3 items of hydatid cyst examination. They show high false positive results and poor sensitivity because the native antigens are prepared directly from hydatid cyst fluid without purification. ELISA is mainly used as a confirmatory test because of its high specificity and sensitivity.[13–15] The so-called 8 tests of immunodiagnosis include ELISA and the Gold-labeled method, which detect 4 types of antigen including the following: the antigen of cyst fluid, the antigen of the cephalomere, the

half-purified antigen of cyst fluid, and the antigen of AE. This 8 test battery provides the most sensitive and specific serologic tests with up to 92.6% sensitivity and 91.9% specificity.[16] In our series, 4 cases were totally positive.

Detection of the specific IgG subclass antibodies of IgG1 and IgG4 isotypes in human CE and AE is also of potential significance[17] and may provide the possibility of detection in early disease and in chronic infections. It may also provide a better correlation with hydatid patient prognosis after medical treatment.[18]

Assessment of posttreatment disease activity among 28 patients with CE was insensitive using detection of CE-specific total IgG antibody. At diagnosis, concentrations of CE-specific total IgG, IgG1, and IgG2 antibodies were significantly elevated compared with IgG3 and IgG4 antibodies by ELISA using crude horse hydatid cyst fluid as antigen. During posttreatment follow up, the IgG2 antibody response provided the best correlate of disease activity.[19]

Analysis of the Reasons for Misdiagnosis

Spinal hydatid disease is often misdiagnosed. The reasons for misdiagnosis were that (a) the spinal hydatid disease is rare and there is therefore a low index of suspicion. (b) x-ray and CT films lack disease-specific characteristics whereas MRI films offer a greater chance of direct diagnosis. (c) Serologic assay methods used for diagnosis only included the following: the Casoni test, IHA, CIE, and complement fixation tests. These tests lack sensitivity and specificity.[20] (d) The absence of a case history. This was important in diagnosis if the patient had had contact with dogs or sheep or had come from a livestock farm.

REFERENCES

1. Szypryt EP, Morris DL, Mulholland RC. Combined chemotherapy and surgery for hydatid bone disease. *J Bone Joint Surg Br*. 1987; 69:141–144.
2. Gemmell MA, Lawson JR, Roberts MG. Towards global control of cystic and alveolar hydatid diseases. *Parasitol Today*. 1987;3: 144–151.
3. Craig PS, Larrieu E. Control of cystic echinococcosis/hydatidosis: 1863 to 2002. *Adv Parasitol*. 2006;61:443–508.
4. Kammerer WS. Echinococcosis affecting the central nervous system. *Semin Neurol*. 1993;13:144–147.
5. Pedrosa I, Saiz A, Arrazola J, et al. Hydatid disease: radiologic and pathologic features and complications. *Radiographics*. 2000;20: 795–817. Review.
6. King CH. Cestodes (tapeworms). In: Mandell GL, Bennett JE, Dolin R. *Principles and Practice of Infectious Diseases*. 4th ed. New York, NY: Churchill Livingstone; 1995:2544–2553.
7. Lewall DB. Hydatid disease: biology, pathology, imaging and classification. *Clin Radiol*. 1998;53:863–874. Review.
8. Wang J, Chen H. Vertebral hydatid disease: MRI diagnosis. *Chin J Med Imaging*. 2002;10:101–102. Chinese.
9. Singh S, Korah IP, Gibikote SV, et al. Sacral hydatidosis: value of MRI in the diagnosis. *Skeletal Radiol*. 1998;27:518–521.
10. Islekel S, Ersahin Y, Zileli M, et al. Spinal hydatid disease. *Spinal Cord*. 1998;36:166–170.
11. Lightowlers MW, Gottstein B. Echinococcosis/hydatidosis; antigens, immunological and molecular diagnosis. In: Thompson RCA, Lymbery AJ, eds. *Echinococcus and Hydatid Disease*. Wallingford: CAB International; 1995:355–410.
12. Barbieri M, Fernandez V, Gonzalez G, et al. Diagnostic evaluation of a synthetic peptide derived from a novel antigen B subunit as related to other available peptides and native antigens used for serology of cystic hydatidosis. *Parasite Immunol*. 1998;20:51–61.
13. Zhong XG, Huang YG, Tang ZR, et al. Immunological diagnosis of echinococcus disease. *Acta Acad Med Shantou*. 2001;14:212–214. Chinese.
14. Han XM. Development of immunological methods in diagnosis of echinococcus disease. *Reports Endemic Dis*. 1997;12:87–90. Chinese.
15. Yao FR, Qiao JY, Yang JH, et al. Comparative study of primarily and postoperation relapse echinococcus disease by four types of immune examinations. *Chin J Parasit Dis Con*. 2002;15:3–4. Chinese.
16. Fu Y, Feng XH, Wen H. Observation in clinical application of the 8- tests immunodiagnosis for human hadatidosis. *Acta Academic Medicine Xinjiang*. 2000;23:242–243. Chinese.
17. Wen H, Craig PS. Immunoglobulin G subclass responses in human cystic and alveolar echinococcosis. *Am J Trop Med Hyg*. 1994;51: 741–748.
18. Huang BC, Jia FJ, Fu TX. Determination of serum specific IgG4 for diagnosing hydatidosis. *Chin J Parasit Dis Con*. 2001;14:283–284. Chinese.
19. Lawn SD, Bligh J, Craig PS, et al. Human cystic echinococcosis: evaluation of post-treatment serologic follow-up by IgG subclass antibody detection. *Am J Trop Med Hyg*. 2004;70:329–335.
20. Wen H, Yang WG, Vuiton D, et al. Status and development of diagnosis and treatment for human echinococcosus. *Acta Acad Med Xinjiang*. 1996;19:183–184. Chinese.

ERRATUM

An error was made in the author listing for "Use of Recombinant Human Bone Morphogenetic Protein-2 as an Adjunct in Posterolateral Lumbar Spine Fusion: A Prospective CT-Scan Analysis at One and Two Years," published in the *Journal of Spinal Disorders and Techniques* (2006:19:416–423). The correct author listing should read Kern Singh, MD, Joseph D Smucker, MD, Sanjitpal Gill, MD, Scott D Boden, MD.

Singh K, Smucker JD, Boden SD. Use of Recombinant Human Bone Morphogenetic Protein-2 as an Adjunct in Posterolateral Lumbar Spine Fusion: A Prospective CT-Scan Analysis at One and Two Years. *J Spinal Disord Tech* 2006;19:416–423.