EDITORIAL

HYDATID DISEASE OF BONE

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Perhaps no other bone infection is more difficult to eradicate, as bone *echinococcosis*. Unfortunately, despite of several years experience in this regard, we still have not found the solution to this zoonotic infection of bone. Every year, several affected people are visited by many orthopedic surgeons and infectious disease specialists all over the country and in referral hospitals and eventually, the skillful neglect seems to be selected as a last resort by most of these visiting physicians. So here remains an important question to be answered: why are we unable to eradicate bone hydatidosis in spite of improvement in our techniques for diagnosis, assessment of the extent of involvement by radiological studies, medical management with new chemotherapeutic agents and surgical resection of the cysts?

Hydatid disease, already known by Hippocrates, is prevalent and widespread in most sheep-raising countries in Asia, Australia, South America, Near East and southern Europe. It is the commonest disease in humans caused by helminthes (1). The disease is most commonly due to *Echinococcus granulosus* and may occur in any organ or tissue. The location is mostly hepatic (75%) and pulmonary (15%), and only 10% occur in the rest of the body. Primary skeletal involvement seldom occurs. Bone involvement is seen in only 1 to 2.5% of cases of hydatidosis (2) and surprisingly musculoskeletal lesions of cystic *echinococcosis* usually occur as isolated findings and without concomitant hepatic or pulmonary involvement (2, 3). Nevertheless, the involvement of other organs should be ruled out in any patient with bone hydatidosis. Spine is the most common location for about 50 percent of osseous hydatidosis, followed by pelvis and hip, the femur, the tibia, the ribs and the scapula. Hydatid disease of bone usually remains asymptomatic over a long period, and it is usually detected after a pathological fracture or secondary infection or the onset of compressive symptoms on adjacent soft tissues. The clinical manifestation may take ten to twenty years to become obvious, since the cyst grows so slowly. So, the diagnosis is difficult and easily overlooked, unless there is a strong element of suspicion (4). In spinal hydatid disease, the most common differential diagnosis problem is tuberculous spondylitis. The absence of damage of the disc surfaces of the vertebral bodies and the spread of the disease, through a subperiosteal and subligamentous path are typical of vertebral hydatid disease.

The most common radiological manifestation of skeletal hydatid disease is of a lucent expansile lesion with cortical thinning. There are no specific radiographic signs of hydatid disease in affected bone; but it should be remembered that, no sclerosis or periosteal reaction is evident in the early stages of the disease. The computed tomography (CT) appearances of bone lesions are similar to those demonstrated on plain films. A well-defined, typically multiloculated osteolytic lesion sometimes with coarse trabeculae within it is usually seen, giving a honeycomb appearance, which is accompanied by expansion of the bone and thinning of its cortex (5). However, CT is more accurate in delineating the area of destruction while making the

interpretation easier. The primary role of CT is in the recognition of the extraosseous spread of the hydatid disease within the soft tissues which may be quite variable. It may have the typical pattern of a cystic lesion shown as a rounded or oval area containing fluid, with sharp and thin margins, exhibiting no contrast enhancement. Alternatively, it may mimic a pattern similar to an abscess or a tumor which is difficult to differentiate from a malignant bone tumor (6). Signs meaningful for a differential diagnosis include lack of osteoporosis and bone thickening in the host bone and the presence of intralesional calcifications (6). The association of bone lesions with soft tissue calcification allows a reliable diagnosis of hydatid disease. The magnetic resonance imaging (MRI) signal intensity pattern of the daughter cysts reflects their contents and may vary in cysts that are dead or alive. The production of hydatid fluid stops when they disintegrate at death (7).

Several patterns of disease have been recognized using various imaging techniques. These include the unilocular cyst, the multilocular lesion and the atypical complex or solid lesion (7). The multilocular lesion with several daughter cysts inside the mother cyst is characteristic, but not pathognomonic of hydatid disease. None of these imaging modalities could determine the extension of the lesion in the bone especially in later stages, helping to delineate a safe margin of resection in preoperative planning.

Immunodiagnosis is useful not only in primary diagnosis but also for follow-up of patients after surgical or pharmacological treatment (8). Detection of circulating *Echinococcus granulosus* antigens in serum is less sensitive than antibody detection, which remains the method of choice. Enzyme linked immunoadsorbent (ELISA), indirect hemagglutination antibody assay, latex agglutination test, and immunoblot test are the most commonly used immunological methods. The immunofluorescence antibody test and arc-5 immunoelectrophoresis are also used. Hydatid cyst fluid antigens are the usual source of antigenic material for immunodiagnosis. Additionally, the lipoproteins antigen B and antigen 5, the major components of hydatid cyst fluid, are widely used in assays for immunodiagnosis of cystic *echinococcosis*. The gene encoding antigen 5 has been cloned and was shown to be closely related to proteases of the trypsin family. The use of both antigens is predominantly restricted to scientific applications, and neither is available for general use. Furthermore, there are difficulties related to their lack of sensitivity and specificity and problems with the standardization of their use. Cross-reactivity with antigens from other parasites, notably other taeniid cestodes, is a major problem. Overall, cystic *echinococcosis* serology may be improved by combining several defined antigens (including synthetic peptides), and the design of new *Echinococcus granulosus* specific peptides that react with otherwise false-negative sera. Currently, however, there is no standard, highly sensitive, and specific test available for antibody detection in cases of the disease. Interleukin-4 detection may be useful in the follow up of patients with cystic *echinococcosis*. Furthermore, this test can be combined with RT-PCR to determine mRNA expression of cytokines in peripheral blood mononuclear cells to complement the biological assays in follow-up. Detection of circulating antigens is also relevant as a method for postsurgical follow-up of patients, and for monitoring the growth dynamics and activity of cysts. In a long-term follow up of hydatid disease of bone, it is important to determine the real status of the cysts since recurrence is usually apparent within 2 or 3 years so the detection of circulating antigen associated with circulating immune complexes (CIC) formation may help to monitor the true state of the parasite, the course of the disease and the outcome (9).

Theoretically, surgery with a broad safety margin is the best treatment for bone hydatidosis (10). But most of times this recommendation is impossible. For example, in most common sites of hydatid disease of bone, spine and pelvis, radical resection of the lesion is practically impossible. In addition, the way *echinococcosis* spreads in bone has not yet been fully determined (11), therefore, it is very hard to establish safety margins in osseous hydatidosis.

Since 1983, comparable data have been collected on the outcome of chemotherapy with benzimidazole carbamate (albendazole) and show encouraging results. Albendazole sulfoxide is better absorbed with higher levels of active metabolite in the cysts compared with other benzimidazoles. The poorest response has, however, been in hydatid disease of bone, although Szypryt *et al.* have reported 5 patients treated successfully by a combination of albendazole and surgery, even though only one or two cycles of chemotherapy were given (12). Other studies have confirmed the effect of albendazole on hydatid disease which correlated with the duration of treatment. It has been shown that 6 courses of albendazole are the minimum needed for circulating hydatid antigen (CAg) levels to become negative which is an indicator of viability and biological activity of the parasite (13). Praziquantel has not been rigorously assessed in the treatment of hydatid disease, but in experimental animals its effect is as good as that of albendazole. Reports suggest that a synergistic effect may occur when albendazole and praziquantel are administered together in humans (14). The evaluation of patients with hydatid disease who are treated with albendazole is difficult because of the long period needed to assess the outcome in this chronic disease. Treatment with albendazole is effective, but at least one cycle should be given before operation and 6 or more courses afterwards.

Hydatid disease of the bone has no pathognomonic clinical or radiographic signs, and thus diagnosis is particularly difficult. Nevertheless, it is important to obtain an early correct diagnosis as the disease cannot be cured easily in its late stages. Inclusion of the disease in the differential diagnosis of destructive bone lesions, especially in endemic areas, will facilitate early diagnosis. On the other hand, it seems that the combination of surgery and long term chemotherapy is the treatment of choice for bone hydatidosis, although it won't be effective in all cases and we need to find the new solutions to this old problem. Adding local chemotherapeutic agents with appropriate carriers can be took into account as an adjunctive measure for late bone hydatidosis.

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