The present issue of the Journal displays eight papers relating to cystic echinococcosis (CE) and alveolar echinococcosis (AE), 2 zoonotic diseases due to the infection by cestodes of the *Echinococcus* genus, Helminths family. *Echinococcus* spp. life cycle develops between carnivores, dogs and other canids, as definitive hosts, which harbour the adult tapeworm in their intestine, and herbivores for *Echinococcus granulosus sensu lato* or small mammals for *Echinococcus multilocularis*, as intermediate hosts where the larva (metacestode) develops in different organs. Humans are dead-end occasional hosts. *Echinococcus* spp. infection are still under-reported and have received so far little attention from international public health institutions [1]. *Echinococcus* spp.-related diseases can be described as chronic, complex and neglected [2]. These characteristics derive from several inter-related factors [3]: i) they are zoonoses with life cycles difficult to interrupt in the absence of sustained, expensive and well-coordinated programs; ii) control of infection in humans does not have impact on global infection spread; however, echinococcosis is not perceived as an important animal health problem, which impairs veterinary control measures; iii) it is difficult to quantify echinococcosis burden because of geographical distribution in vast rural areas, absence of specific symptoms of most infected subjects, and lack of an effective disease record system; and iv) these diseases affect mostly poor pastoral communities. Echinococcosis/CE impact on human health is important, with estimated 1.2 million people affected and 3.6 million DALYs (Disability Adjusted Life Years) lost globally [1,3]. Moreover, *E. granulosus* has major economic impact on agriculture with estimated annual livestock production loss of up to 2190 million US$ [1]. Because of its severity and expensive care management, AE, albeit rare, heavily impacts public health, especially in China where at least 90% of world cases are observed [4]. Definitely, Western China, including Xinjiang, Ningxia and Tibet autonomous regions and Qinghai, Sichuan, and Gansu provinces are among the most endemic areas in the world for both CE and AE [5] and a national Chinese program has been launched to combat the diseases [6]. Chinese reference centers, including their Radiology Departments, have massively contributed to a better knowledge of echinococcosis within the past 25 years, especially the newly designated WHO-Collaborating Centre for Prevention and Care Management of Echinococcosis in Urumqi, Xinjiang Uyghur Autonomous Region, which generated 6 among the 8 studies on echinococcosis published in this issue. The worrisome epidemiological status of China and the crucial role of Imaging Units in the detection of suspicious images to both improve the knowledge on incident cases and accelerate care management of patients are well emphasized by the report of Ding and Li in this issue [7]. With nearly 4000 incident cases per year, China has definitely the highest prevalence rate of CE in the world since a percentage of incident cases slightly lower than in some other endemic countries is widely compensated by the size of the at-risk population in China [8]. We may also doubt that only 3 patients died from their disease in the 2011 to 2015 period [7] since AE as well as complication-associated CE are very severe diseases with high fatality rate and we are personally aware of far more fatalities in Western China endemic areas in the past 5 years. This stresses the importance of accurate reporting, especially for the follow-up of the patients; currently, most of the patients (especially among the nomadic populations) are lost to follow-up, and recording of cases at the international level is clearly inaccurate and should be improved (see discussion on this issue in Vuitton et al., 2015, regarding AE in Europe) [9].

Despite their apparent similarity, CE and AE are quite different diseases, CE being usually considered to present and develop as a benign tumour and AE as a malignant tumour [10]. Although it is usually true, CE may also display extensive and multifocal locations and life-threatening complications. The paper by Fuhrer and Grohowski [11] is a good illustration of the possible severity of CE when the cyst ruptures in the biliary tree, and their description of the ‘string of pearls’ sign in the bile ducts, due to the migration of daughter cysts in the biliary tree, certainly deserves radiologists’ attention. Unusual features of CE at CT and MRI in the liver are also reported by Wang and Liu in this issue [12]: they may be source of radiological misdiagnosis or misclassification, e.g. because of an unusual location that could be confusing, or because of failure of CT to characterize daughter cysts or calcifications. It may be reminded that CT is usually good at
showing calcifications, a characteristic feature of AE and of degenerating CE; MRI is unable to do so but may reproduce characteristic features of CE better than CT [13], and provide pathognomonic evidence for the diagnosis of active AE by showing hyperintense micro-cysts in a ‘honeycomb’ or ‘bunch of grapes’ pattern on T2-weighted sequences [14]. Severity of AE is mostly associated with invasion of hepatic vessels and bile ducts, but also, like cancers, with metastatic dissemination [10]. Brain metastases are rare in Europe (only 3 cases among 329 cases with hepatic AE in France [15]) but more frequent in China (2 cases among 50 surgical cases with hepatic AE in Xinjiang [16]). Differential imaging diagnosis of cerebral AE is not easy: information provided by MR diffusion weighted imaging reported in this issue [17] is an interesting complement that may help differentiate AE brain location from cerebral tuberculosis, usually difficult since conventional MRI features of both diseases are very similar.

AE diagnosis relies on imaging [14], and may be totally confirmed only by pathological or molecular identification of the parasite in the lesion [10]. Specific serology, i.e. presence of specific antibodies against *E. multilocularis*, even when the best antigens and techniques are used, may be positive in subjects without lesions in endemic areas, and may be negative in patients with confirmed AE, especially when they are immunosuppressed [18]. At this point, the main 2 issues are: 1) positive and differential diagnosis, 2) follow-up of the patients, and especially evaluation of the viability of the parasitic larva and of the progression potential of the lesion. The first issue is problematic when the imaging characteristics of the lesions are not recognized by radiologists and physicians, especially in non-endemic areas, which may considerably delay diagnosis and thus proper treatment [19]. The second issue is even more problematic, since all markers of parasite viability are only indirect, including fluoro-deoxyglucose Positron Emission Tomography (FDG-PET), currently the most reliable indicator of lesion metabolic activity [20]. FDG-PET as well as highly specific serology (such as Em18 or Em2PLUS ELISA) actually explore the activity of the associated immune reaction [21]; however, we showed that FDG uptake at the periphery of the lesion was significantly correlated to the presence of the parasitic micro-cysts inside the lesion shown by T2-weighted MR images [22]. As PET is not available in all settings, especially in the most endemic areas, and its cost is an obstacle to its wide use for the follow-up of the patients, in this issue, Wenya Liu and her co-workers from the Xinjiang radiology team explore surrogate imaging markers of disease progression/parasite viability [23,24]. Results are quite encouraging, and the correlation between iodine values obtained at spectral CT and SUV_{max} obtained at FDG-PET was very significant, especially at the portal phase. It may be noted that this correlation only concerned the marginal zone of the lesions, a zone which combines infiltration by immune cells (explored by FDG-PET) and neo-vascularization (explored by enhanced conventional CT, spectral CT and also by CEUS). The zone of the AE lesions where measurements are performed is thus of utmost importance; this is emphasized by the comparison between cholangiocarcinoma and AE also published in this issue [25]. To differentiate AE from cancer, the ‘region of interest’ was defined as the solid portion of the lesion, and only tumour-like type 4 AE lesions were selected for the comparison; the lower mean Apparent Diffusion Coefficient (ADC) of cholangiocarcinoma was due to its relative tissue cellularity higher than that of AE [25]. Use of diffusion weighted MRI to evaluate lesion activity in AE would need measurement in the marginal zone of the lesion, where it would appreciate the cellularity of the immune cell infiltration which surrounds the parasitic lesion, that same area where immune cells do uptake FDG and where neo-vessels were responsible for increased iodine concentration in the studies by Wang et al. and Jiang et al. [23,24].

AE is a severe disease still in search of an optimal treatment, despite active research [26]. Experimental studies are impaired by the rather long pre-patent infection (ranging from 2 to 6 months, depending on the species of experimental rodents) and necessary autopsies of hundreds of animals. Evaluating the feasibility and usefulness of ultrasound examination of *E. multilocularis*-infected rats at the early stages of development of the metacestode is particularly interesting. The study performed by Zeng et al. [27] demonstrates that lesions as small as 1 or 2 mm in diameter can accurately be disclosed and these early lesions are hyperechoic, which confirms findings obtained from early lesions in humans at mass screening [28] or in patients with immune suppression [18]. For ethical as well as scientific reasons, non-invasive imaging evaluation of the parasitic growth in small animal models is a step forward to easier pre-clinical research and wider use of US should be recommended to laboratories actively involved in drug- or vaccine research.

References


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