Short Communication

Cystic echinococcosis in a fox-hound hunt worker, UK

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A male resident in Vanuatu with prior history of employment as a hunt kennel-man in England (1980–2001) was surgically treated for the removal of a hydatid cyst subsequently confirmed as *Echinococcus granulosus* (G1 genotype). This is the first human molecularly identified CE case reported from the UK and a first in a fox-hound handler and indicates a general neglected occupational risk.

Keywords: *Echinococcus granulosus*, Genotype 1, UK, Fox-hound worker, Occupational risk

Introduction

Human cystic echinococcosis (CE) is a neglected zoonotic disease that is endemic in most sheep rearing areas of the world,[1,2] including the British Isles.[3] Slow growing metacestode cysts (hydatids) most commonly occur in the liver and present non-specific symptoms of a space-occupying lesion but may cause significant discomfort and complications.[4] Globally several genotypes of the dog tapeworm *Echinococcus granulosus sensu lato* (s.l.) have been described including the common zoonotic form, or genotype 1 (sheep strain), and also genotype 4 (horse strain or *E. equinus*) which is not considered a zoonosis.[5,6] Genotyping of hydatid surgical isolates is useful from an epidemiological viewpoint,[6] but in the UK to date, despite significant DNA analysis of livestock cyst isolates, no autochthonous human hydatid isolates have been genotyped. Both *E. granulosus sensu stricto* (s.s.) and *E. equinus* are endemic in domestic animals in UK, with sporadic human CE cases occurring primarily in the hill sheep farming areas of mid-Wales and adjacent regions.[7] By contrast, *E. equinus* appears to have a greater UK-wide geographic range and an association with fox-hound packs rather than sheep farming per se.[8] We report a case of hepatic CE in a British male diagnosed in a non-endemic region (South Pacific) and who was treated in Australia. He had a 21-year past history of employment as a kennel man and huntsman in three fox-hound hunting packs on private estates in southwest England. A retrospective analysis of hospital records/case notes from 1997 (Bristol, UK) indicated that he was probably infected in the late 1980s or possibly early 1990s, but despite a suggestive hepatic ultrasound image in 1997, hydatid disease diagnosis was not seriously considered until 2005 in Vila Bay, Vanuatu and, subsequently, in 2008 surgically confirmed in Brisbane, Australia. Histopathological and DNA sequence analysis of archived biopsy material from a liver cystectomy confirmed an *E. granulosus* hydatid cyst of genotype 1 (common sheep-dog strain).

The Case

A 41-year-old male in general good health, with a sport fishing business, was admitted to Vila Bay Health Centre, Vanuatu, in July 2005, with left-side abdominal and chest pains. He also reported that similar symptoms had occurred in 2002. X-ray indicated a raised right hemi-diaphragm with probable pressure on the laryngeal nerve. The physician (Rachel Wells) suspected CE and he was immediately transferred to Mater Private Hospital in Brisbane, where a CT pulmonary angiogram showed the presence of a 7×8 cm cyst with internal septa located in the upper right side of the liver (segment VII). A presumptive diagnosis of hepatic CE was made (JG) and the patient was referred to the Royal Brisbane Women's Hospital for medical anthelmintic treatment with albendazole (physician MW). He was initially treated with three cycles of oral albendazole

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400 mg twice daily for 4 weeks with 2 weeks of rest between cycles beginning 14 July 2005.

A CT scan in November 2006 showed a 7.5 cm cyst in liver segments VI/VII of the right lobe consistent with CE. Serological testing for anti-hydatid antibodies by indirect haemagglutination test in September 2006 was weakly positive (1 : 64 titre). A further three cycles of albendazole was prescribed after consultation on 23 November 2006. A further liver CT scan in January 2008 showed no change in cyst size and little in appearance. Consequently, he was admitted for liver segmental resection the same month. A 7.5 cm diameter cyst (WHO CE type 2)[9] was removed (by BO'L) together with an adherent 4 cm fatty ommental mass (non-hydatid origin). Immediate post-surgery was judged successful with no apparent complications. *E. granulosus* was confirmed as the etiological agent by the microscopic observation of protoscolex hooks in the cyst fluid and by histopathogical staining (with haematoxylin and eosin) of sections from the resected cyst, which showed the presence of a characteristic laminated layer within the cyst wall. Owing to the possibility of viable protoscoleces seen in cyst fluid at the time of hydatid cyst resection, a further three cycles of albendazole 400 mg twice daily for 4 weeks was given commencing on 4 February 2008. The patient made a good overall recovery except for a laparoscopic hernia repair in March 2009 associated with hydatid surgery complications.

Ribbons of formalin-fixed paraffin-embedded pathology blocks of the hydatid cyst recovered from liver cystectomy in 2008 in Brisbane were used for DNA extraction. This was accomplished using the Qiagen DNA FFPE tissue kit as recommended by the manufacturer (Qiagen, Hilden, Germany). Genomic DNA was used in a PCR reaction to amplify a 396-bp fragment within the mitochondrial gene coding for cytochrome *c* oxydase 1.[10,11] Amplified products were separated by electrophoresis on a 1.5% TAE agarose gel, stained with gel red DNA dye (Cambridge Biosciences, UK) and visualized using UV illumination (Syngene G:Box gel documentation and analysis system). Bands of amplified products were cut out under UV light and gel purified using PurLink quick gel purification Kit (Invitrogen, Paisley, UK). Purified PCR products were commercially sequenced (Beckman Coulter, Essex, UK). Nucleotide sequences were analysed using FinchTV software package (Geospiza, Seattle, WA, USA) and compared with those deposited on GenBank database through the use of BLAST (Basic Local Alignment Search Tool, http://www.ncbi.nlm.nih.gov/BLAST/). Nucleotide sequence generated in this study was deposited onto GenBank under accession no. JX870424. Comparison of the generated *cox 1* sequence with those deposited onto Genbank gave a 100% homology with *E. granulosus* G1 genotype (accession no. AB033407).

Human CE can only be acquired by ingestion of microscopic eggs of *E. granulosus* (*s.l.*) voided from the gastrointestinal tract of a dog (or other susceptible carnivore) usually with faeces. Accidental human infection occurs through direct contact with an infected dog, its faeces or faecal- contaminated environment. *E. granulosus s.s.* transmission is principally associated with rural pastoral occupations.[3] Dogs acquire infection from eating livestock liver/lungs or other organs that contain hydatid cysts. Human hepatic CE cysts are usually slow growing (from <0.5 to >2.5 cm per annum) with a long (several years) asymptomatic period,[12,13] and, thus, in adults, it is usually impossible to determine the exact year of infection. We carried out a retrospective assessment of the patient's case notes from November 1997 after his admission to Frenchay Hospital, Bristol (UK) with upper abdominal pain, fever, cough, and dyspepsia. A chest X-ray at that time showed a right hemi-diaphragm and an ultrasound scan revealed a 7 cm liver cyst (with internal lobulations) with associated right side diaphragm displacement. During the clinical examination in 1997, the patient also reported a 4- to 5-year history of upper abdominal pain. A diagnosis of hydatidosis was considered in November 1997, but unfortunately was discounted because of a seronegative blood test for hydatid antibodies. It was considered more likely that cyst origin was due to an amoebic ulcer because of the patient's extensive sport-fishing travel history to tropical coastal regions (which were very low risk for *E. granulosus* transmission). He was treated with metronidazole (no efficacy against CE) and discharged a week after admission in November 1997.

In consideration of exposure period, a 7 cm liver hydatid cyst in an adult would have probably taken 5 or more years to reach that size.[12,13] The case's reported history of upper abdominal pain from the early 1990s would therefore suggest that the hydatid cyst was already large enough (2–3 cm?) to cause symptoms, and thus, he was probably infected in the late 1980s after exposure to an infected dog (s). His employment history showed extensive contact with fox-hounds over a period of 21 years (1980–2001) at three private hunts in the English counties of Wiltshire and Gloucestershire. However, his longest employment was from 1985 to 2001 at a large private estate in Gloucestershire which maintained a fox-hound pack of 150–200 hounds. He reported that in the 1980s and early 1990s, hounds were regularly fed with uncooked raw meat, liver, and lungs from sheep, cattle, and horses (usually fallen stock collected/donated from surrounding farms). He was responsible for cleaning out kennels in the 1980s and later for de-worming

hounds twice per year. He said that he never wore gloves and was unaware of the potential for dogs to carry *Echinococcus* worms. De-wormers used in the 1980s were mainly piperazine- and albendazole-based drugs, which have little or no effect against tapeworms including *Echinococcus* spp. Praziquantel, the drug of choice for canid tapeworm infection, was used to treat fox-hounds by the respective Hunt twice a year from the mid-1990s. He also reported the practice of bringing stallion fox-hounds from outside the Estate for breeding purposes, and also the translocation of sheep to the estate for winter pasture. Both translocated hounds and sheep were not uncommonly brought in from mid-Wales, a region endemic for CE. This activity, together with feeding fox-hounds raw livestock offal, and the use of a sub-optimal de-worming program, probably greatly increased risk of transmission of *E. granulosus* on the Estate where the patient had been employed.

Conclusions

Unlike other reports where travel to endemic areas was associated with CE,[14] the case reported here initially appeared to be at low risk of echinococcosis because of the patient's current occupation (fisherman), absence of high-risk travel, and his residence in Vanuatu (a non-endemic region). However, it is highly probable that the patient contracted CE (genotype 1) as a result of exposure to fox-hound(s) under his care that were infected with the common sheep-dog genotype of *E. granulosus*. This most likely occurred, while he was employed as a fox-hound kennel man/huntsman on private estates in southwest England during the late 1980s and early 1990s. Fox-hounds in the UK may also be exposed to *E. equinus*, but to date there is no conclusive evidence that that species is a zoonosis. Interestingly however, we recently confirmed by DNA sequencing, an *E. equinus* cystic infection in the abdominal cavity of a lemur (a prosimian primate) bred in captivity in the UK.[15] Human CE remains endemic in the UK, but incidence has dropped over the last 40 years, in part due to directed interventions in mid-Wales, but also because of improvements in sheep-dog management and wide availability of praziquantel-based de-wormers.[7,16,17] Nevertheless, sporadic autochthonous human CE cases continue to occur both in the mid-Wales endemic zone as well as occasionally in apparent low-risk regions of England including southwest counties. In 2011, there were 174 hunts listed in England and Wales with fox-hound numbers from 20 to >100. A recent questionnaire survey in 2011 to 16 hunts in England and Wales indicated that 81% fed uncooked livestock offal to fox-hounds and 56% did not use a praziquantel-based de-wormer to treat hounds (W. Lett and P. S. Craig, unpublished).

The human CE case reported here has a high probability of a fox-hound infection source. We therefore strongly recommend: (1) that fox-hounds in the UK (and other CE-endemic regions) are dosed orally with a praziquantel-based de-wormer at least four times per year; and (2) that raw livestock products especially liver/lungs not be fed to dogs at all, or only after appropriate cooking. It is important that fox-hound workers, kennel men, and other hunt staff are made fully aware of the risks of echinococcosis. Advice should come through their employer, any Code of Practice for welfare of hounds in hunt kennels, and the contracted veterinary consultant/practice.

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