INTRODUCTION

The aim of this article is to describe a case of massive eosinophilic granulomatous hepatitis attributed to hepatic cysticercosis in a sheep in the Riverina, NSW, and to briefly report two additional cases with a similar gross presentation from Wodonga, Victoria, and from Shirwal, Maharashtra, India. This condition has been reported once previously in sheep in NSW, but to our knowledge, has not been reported in Victoria, or India. This is a condition that, although rarely encountered, needs to be differentiated from the much more commonly encountered fasciolosis. To our knowledge, the histologic presentation of this condition has only been described in few, if any, reports.

CASE 1
HISTORY

Eight (8) adult sheep including an adult ewe designated as "sheep 3" from the Wagga Wagga saleyards were submitted dead to the Veterinary Diagnostic Laboratory (VDL) of the School of Animal and Veterinary Sciences, Charles Sturt University (CSU), in Wagga Wagga, New South Wales (NSW), Australia, in May 2017, for a necropsy to be performed by veterinary science students, under supervision by four veterinarians (academic staff), for teaching purposes. The history of these sheep was unknown, but common reasons for such submissions include death during transportation to the saleyards or that the animal is deemed unfit for sale and euthanased. This occurs for example when sheep are cachectic, show signs of obvious severe clinical disease, or have been trodden on during transportation.

Gross pathology and parasitology

Sheep 3 was an adult Merino cross in good nutritional condition (body condition score 2.5 to 3 on a scale of 5). On necropsy, multiple discrete, variably sized, spherical pulmonary abscesses were noted throughout the parenchyma. The liver showed remarkable changes (figure 1), being transected by numerous linear or tortuous, whitish or haemorrhagic trajectories, of similar diameter (~1-1.5 cm) but variable length (ranging from 2-12 cm), appearing to be randomly distributed throughout the liver. No parasites were found within the liver parenchyma or the gall bladder.

The other seven (7) sheep necropsied concurrently showed no noteworthy findings in the liver or gall bladder.

Faecal worm egg count for sheep 3 detected 40 strongyle eggs per gram.

HISTOPATHOLOGY

Sections of the liver, gall bladder, myocardium and lungs of "sheep 3" were fixed in buffered formalin, processed routinely, sectioned at 4 µm and stained with haematoxylin and eosin. The gall bladder showed moderate oedema. Hepatic architecture was completely obliterated by the presence of numerous, large, often coalescing, randomly distributed, granulomas, the centre of which was largely necrotic or mildly fibrotic, likely representing the linear or tortuous tracts seen grossly. Granulomas were lined by epithelioid macrophages, lymphocytes and mild fibrosis. The remaining parenchyma was almost diffusely densely infiltrated by large numbers of inflammatory cells, the majority of which were eosinophils (figure 2). No parasites or evidence of Fasciola sp infestations were seen.

In the sections examined, the pulmonary parenchyma was expanded by multiple discrete, large pyogranulomas (figure 3). The myocardium contained one (1) calcified granuloma, most likely a calcified parasitic cyst. Several Sarcocystis sp cysts were also noted, without eliciting any inflammatory response.
DIAGNOSIS

Based on the above findings, the main diagnosis was that of a severe, diffuse, eosinophilic granulomatous hepatitis consistent with subacute massive cysticercosis. Other findings included a focal granulomatous myocarditis of likely parasitic aetiology; myocardial Sarcocystis sp infestation, likely incidental and clinically insignificant; and suppurative / pyogranulomatous pneumonia of undetermined aetiology (likely bacterial).

CASE 2

It should be noted that one of the authors (BM) has seen a single case with almost identical gross presentation in a three-year-old Deccani sheep submitted for necropsy at the KNP College of Veterinary Science, Maharashtra State, India in 1996. The liver showed remarkable linear or tortuous, whitish or haemorrhagic surface trajectories, of similar diameter (~5 mm) but variable length (ranging from 2-12 cm) randomly distributed throughout and over the surface of the liver. However, no further investigations were carried out and no parasites could be detected grossly or histologically.

CASE 3

Another author (DJ), has also seen a single case with almost identical, albeit milder, gross presentation in a batch of condemned ovine livers collected for a student practical from the Wodonga abattoir in Victoria, in 2010-2012. Both authors have only seen a single such case each, in a period covering over 30 years.

DISCUSSION

We report on a case of exceedingly severe, diffuse, massive, eosinophilic granulomatous hepatitis that we presume was the result of subacute hepatic cysticercosis in a sheep from the Riverina region of New South Wales, Australia.

Parasitic infections of the ovine liver are common. Cysticercosis is a common condition of the peritoneal cavity of sheep, usually manifesting as one to several thin fluid-filled parasitic cysts in the peritoneal cavity or liver capsule. It is also commonly seen as calcified remnants of parasitic cysts in the liver. It is caused by Cysticercus tenuicollis, the metacestode form of the adult cestode Taenia hydatigena, which infects the dog. Immature cysticerci travel through the liver, usually not resulting in noteworthy pathology, with the exception of the occasional encapsulated or calcified cyst in the liver, sequelae of cysticercal remnants that did not find their way to the peritoneal cavity, the next site in their life cycle. Apart from sheep, pigs and other mammals may be affected (Yildirim, Ica et al. 2006).

The impressive liver changes seen grossly and the accompanying histopathologic changes described were exceedingly severe and, to our knowledge, have not been described adequately in the literature.
The type of lesion (tortuous or linear trajectories of similar diameter) and the pattern of lesion distribution (random) produced were typical of massive parasitic migration, in the present case, most likely the result of migration of *Cysticercus tenuicollis* through the hepatic parenchyma. Histologically, the nature of the trajectories and the minimal fibrosis pointed to a subacute insult. The diffuse (affecting all lobules) and massive (obliterating normal hepatic architecture) nature of the changes indicate that the mass migration of larvae was almost simultaneous. The accumulation of large numbers of eosinophils may be a result of the large numbers of larvae entering the parenchyma or may represent an idiopathic hypersensitivity reaction in this individual, but is a histologic feature that, to our knowledge, is not seen in fasciolosis. The aggregation of eosinophils to such numbers would presumably require some time to develop and is therefore more consistent with a subacute response. The literature to date is very sparse regarding this presentation, which makes it somewhat difficult to interpret these changes in context.

Both the gross and histologic patterns described here are very rarely encountered in the liver of sheep. Importantly, the gross presentation should be differentiated from the much more common hepatic fasciolosis, namely primarily *Fasciola hepatica* infestations, a condition that is common worldwide, including Australia, with the notable exception of Western Australia. *Fasciola hepatica* infestations are common in the Wagga Wagga area, with the intermediate host, *Lymnea* sp snails considered endemic. The smaller *Dicrocoelium dentriticum* (also known as lancet or small fluke) has not been reported in Australia, although it is common in other countries with substantial sheep industries; it usually produces fibrotic cholangiohepatitis and cholecystitis with intralesional presence of the parasites. The lesions produced with *Fasciola hepatica* infestations are generally similar to the ones produced by the lancet fluke, but the parasites are markedly larger and broader than the lancet fluke. Other liver fluke genuses reported elsewhere are exotic to Australia. No such parasites or other evidence of such parasitism were noted in this case, grossly or histologically. Furthermore, the parasitologic exam was negative for all three of the above; however this finding in itself does not rule out the possibility of past or current presence of *Fasciola* sp or other parasites, firstly, due to the variable time period required for the eggs to be excreted in the faeces and, secondly, because the anthelminthic regime used in this case was not known.

The pulmonary changes were likely incidental; however, the possibility of the pyogranulomas representing secondary bacterial infections following aberrant migration of cysticerci through the lungs cannot be ruled out. Such aberrant migration has been described previously (Yildirim, Ica et al. 2006).

It would be interesting to know the percentage of affected animals on the property of origin of the sheep, however this was not possible due to the absence of any knowledge of the history of the sheep. This type of lesion appears to be a rare occurrence, and has not been observed in carcasses sourced from the Wagga Wagga saleyards or other sheep necropsied at the VDL by the authors over the past several years.

In addition to textbooks (Uzal 2016), (Ferrer, García de Jalón et al. 2002) acute cysticercosis has been reported previously in peer-reviewed
publications in cases from Italy (Scala, Urrai et al. 2016), Greece (Koutsoumpas, Psychas et al. 2013), (a case also examined by one of the authors of the present report (PL)), Turkey (Yildirim, Ica et al. 2006), the UK and Israel (Perl, Edery et al. 2015). In the case from Italy, it was described in association with an acute outbreak of *Taenia hydatigena* cysticercosis, with mortality in 5 of 21 (23.8%) female lambs, with *Cysticercus tenuicollis* being identified as the cause of death. Biochemical parameters in infected lambs confirmed severe hepatitis. Praziquantel, given once at 15 mg/kg body weight, was administered and a dramatic improvement in the clinical condition and biochemical parameters was observed up to 30 days following treatment.

Although rare, at least one other case of (acute) hepatic cysticercosis has been reported in sheep from NSW (Kelly and Staples 2016). Kelly and Staples (2016) reported a case affecting an 8-month-old lamb at Lavington (New South Wales) brought to the district veterinarian by a farmer, who reported that a number of animals in the flock were losing weight. According to the authors, that was the most ill animal; it was found moribund and was euthanased and submitted for necropsy. Unlike the present case, histologic evidence of *T. hydatigena* larvae was produced, and the eosinophilic response was minimal to absent.

To our knowledge, this condition has not been reported in Victoria, or India, and, although rare, should be included in the differential diagnosis of cases with similar liver changes.

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Three gross and two histologic images from this case (sheep 3) were also deposited in “Noah’s Arkive”, a publicly available veterinary pathology image database [noahsarkive.cldavis.org] with the identification numbers F33637, F33657, F33658, and F33659 and F33660 respectively.

FIGURE LEGENDS

Figure 1 (a-e). Gross findings. The liver was transected by numerous linear or tortuous, whitish or haemorrhagic trajectories, of similar diameter (~1-1.5 cm) but variable length, randomly distributed throughout the liver. No parasites were found within the liver parenchyma or the gall bladder.
Figure 2 (a-h). Hepatic architecture was completely obliterated by the presence of numerous, large, often coalescing, randomly distributed, granulomas, the center of which was largely necrotic, likely representing the linear or tortuous tracts seen grossly (a-e). Granulomas were lined by epithelioid macrophages, lymphocytes and fibrosis. The remaining parenchyma was almost diffusely densely infiltrated by large numbers of inflammatory cells, the majority of which were eosinophils (g, h). Haematoxylin and eosin, bar shown in figures.
Figure 2d

Figure 2e
Figure 3 (a, b). The pulmonary parenchyma was expanded by multiple discrete, large pyogranulomas. Haematoxylin and eosin, bar shown in figures.
REFERENCES