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TITLE OF CASE ***Do not include "a case report"***

Mesothelioma in two sheep with pericardial effusion and ascites

SUMMARY ***Up to 150 words summarising the case presentation and outcome (this will be freely available online)***

Mesotheliomas are rare tumours in domestic animals. These tumours have a range of clinical presentations, and a range of gross and microscopic features can be present. We report mesotheliomas in two sheep submitted to APHA's diagnostic pathology service with diverse clinical presentations. The first case was a two-year old ewe with a history of sudden death that had a nodular mass in the wall of the right auricle and marked pericardial effusion and ascites. The second case was a three-year old ewe with a history of recumbency, which had a papillary mass in the peritoneal cavity and marked ascites. A diagnosis of mesothelioma in both cases was confirmed by immunohistochemistry for cytokeratin and vimentin. These cases highlight the diverse presenting signs that can be present with mesothelioma, and this tumour should be considered as a differential diagnosis in sheep with peritoneal, pericardial or pleural effusion at gross post mortem.

BACKGROUND ***Why you think this case is important – why did you write it up?***

Mesotheliomas are rare tumours in domestic animals, and are most commonly described in cattle. We report two cases of mesothelioma in adult sheep with different clinical presentations, but gross post mortem examination revealed marked ascites in both cases, even though the tumours were in different locations. These cases highlight that mesothelioma in sheep should be considered as a differential diagnosis in sheep with peritoneal, pericardial or pleural effusion.

CASE PRESENTATION ***Presenting features, clinical and environmental history***

Case 1 was a two year old Texel cross ewe with 10 day old lambs at foot that was submitted to the Animal and Plant Health Agency (APHA) Veterinary Investigation Centre in Thirsk. The animal had a history of sudden death. Both lambs were healthy with no clinical signs. On post mortem examination, the ewe had marked, generalised subcutaneous oedema. There was approximately 7 litres of pale pink liquid containing a large amount of fibrin strands in

the abdominal cavity and the pericardial sac was massively distended and contained approximately 3 litres of blood stained fluid. The epicardium was uneven with multifocal to coalescing raised roughened plaques. A large, firm, multilobulated, dark red mass, approximately 10cm in diameter, was present in the wall of the right atrium (Figure 1).

Case 2 was a three year old Lleyn ewe that was within one week of its expected lambing date. The ewe had a two day history of recumbency with subcutaneous oedema overlaying the left ventral abdomen, udder and left hindleg. The ewe was treated with an NSAID (Ketoprofen), amoxicillin, enrofloxacin, subcutaneous calcium and magnesium, multivitamins and propylene glycol, but died despite treatment. On post mortem examination, approximately 5L of watery, yellow fluid was present in the abdominal cavity, and the subcutaneous tissue of the left hindleg contained yellow, gelatinous oedema and haemorrhage. A focal, mottled dark red papillary mass (approximately 10cm x 10cm) was present on the peritoneal surface of the ventral abdominal wall. The uterus contained two full term male and female foetuses, weighing 5kg and 4kg, respectively, which were grossly normal.

INVESTIGATIONS ***If relevant***

Histological Findings: On the right atrial wall of Case 1, arising from the epicardium, a papillated, multilobulated, expansile mass was observed. A similar mass was observed arising from the peritoneal wall of Case 2. In both cases, neoplastic cells were arranged in a papillary fashion and were round to polygonal with anisocytosis, anisonucleosis and occasional binucleate cells (Figure 2). Mitoses were rare. There was multifocal haemorrhage, neovascularisation and fibroplasia with small numbers of lymphocytes, siderophages and occasional neutrophils. The central core of many neoplastic nodules in Case 1 were necrotic.

Immunohistochemistry: In both cases, the papillary-like masses showed strong epithelial cytokeratin staining with co-localised vimentin staining (Figure 2).

DIFFERENTIAL DIAGNOSIS ***If relevant***

The main differential diagnosis in these cases was adenocarcinoma. However, due to the co-localisation of cytokeratin and vimentin by immunohistochemical staining, mesothelioma was considered to be the most likely neoplasm present in both cases.

TREATMENT ***If relevant***

OUTCOME AND FOLLOW-UP

Both cases were sporadic with no further incidences in either flock.

DISCUSSION ***Include a very brief review of similar published cases***

Mesothelioma is a rare neoplasm in sheep, and is more commonly seen in cattle, where it is spontaneous and typically found in the peritoneal cavity[1]. In cattle, mesotheliomas have a range of gross presentations, ranging from a single distinct mass to multifocal or coalescing tumours, that can cause diffuse thickening of the peritoneum or a papillary mass[2, 3]. In contrast to farmed species, mesotheliomas in humans and co-habiting pet dogs have been associated with asbestos exposure[4, 5]. Mesotheliomas express both vimentin and cytokeratin, in contrast to epithelial and mesenchymal neoplasms, and they typically metastasise to local lymph nodes and/or are locally infiltrative, so should be considered malignant[1]. Mesotheliomas have rarely been reported in sheep. One previous study described extensive mesothelioma, affecting all serosal surfaces including the pleural cavity, omentum, mesentery, diaphragm and spermatic cord, as well as the peritoneum, in a four month old Suffolk cross lamb[6], with pronounced ascites. A more recent study reported a primary pericardial mesothelioma, with associated pericardial effusion, in a three year old male sheep highlighted during routine meat inspection at an abattoir[7].

LEARNING POINTS/TAKE HOME MESSAGES ***3 to 5 bullet points – this is a required field***

- Mesothelioma is a rare neoplasm in sheep with a range of clinical presentations.
- We describe two cases of mesothelioma in adult sheep, where the neoplasm was located on the epicardium of one animal, and the peritoneal cavity in the other.
- Both animals developed marked ascites, even though the tumours were in different locations, and the animal with epicardial mesothelioma also developed marked pericardial effusion.
- The pathogenesis of the ascites in case 1 was likely due to right sided heart failure resulting in portal hypertension and increased intravascular hydrostatic pressure. In case 2, the cause of the ascites was less clear, however these tumours can metastasise and may block lymphatic drainage. In addition, peritoneal mesotheliomas produce excess peritoneal fluid and have been described as a cause of ascites in humans[8].
- These cases highlight that mesothelioma in sheep should be considered as a differential diagnosis in sheep with peritoneal, pericardial or pleural effusion.

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FIGURE/VIDEO CAPTIONS ***figures should NOT be embedded in this document***

Figure 1. Gross appearance of mesothelioma on the right atrium of Case 1. A large, firm, multilobulated, dark red mass, approximately 10cm in diameter, was present on the wall of the right atrium.

Figure 2. Histologic and immunoreactivity of mesotheliomas in two sheep. Haematoxylin and eosin (HE) staining of formalin fixed, paraffin embedded tissue from both cases revealed neoplastic cells that were round to polygonal with anisocytosis, anisonucleosis and occasional binucleate cells. Cells from both neoplasms were pan-cytokeratin and vimentin positive, differentiating them from a primary carcinoma or sarcoma. Case 1 shows tissue from an epicardial mesothelioma and Case 2 shows tissue from a peritoneal mesothelioma. Bar: 100µm.

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