

# Case Report

## Malignant fibrous histiocytoma of the mammary gland in a mare

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### Summary

**Mammary tumours are uncommon in mares. Sarcomas of the breast account for less than 1% of all human primary malignancies and, among these types of tumours, malignant fibrous histiocytoma (MFH) is very rare. This report describes a 6-year-old uniparous Paint mare that was presented for investigation of right mammary gland enlargement of 3 weeks' duration. The clinical and histopathological findings in this mare with malignant fibrous histiocytoma of the mammary gland as well as complications of bilateral mastectomy are detailed. At one year follow-up there were no clinical signs of recurrence.**

### Introduction

Mammary tumours are uncommon in mares. Previously reported mammary tumours in mares include 16 cases of mammary carcinoma, adenocarcinoma or adenoma (Schmahl 1972; Acland and Gillette 1982; Munson 1987; Foreman *et al.* 1990; Seahorn *et al.* 1992; Reppas *et al.* 1996; Kato *et al.* 1998; Prendergast *et al.* 1999; Hirayama *et al.* 2003; Sparadi *et al.* 2008). To our knowledge, there have been no prior reports of mammary sarcoma in mares. Sarcomas of the breast account for less than 1% of all human primary malignancies and, among these types of tumour, malignant fibrous histiocytoma (MFH) is very rare (De Cesare *et al.* 2005; Pavlovsky *et al.* 2006). MFH has been reported in multiple locations in several domestic animal species, including the soft tissues of the neck, thigh, stifle and forelimb of horses, the skin, bones or viscera (spleen, liver, lung, lymph nodes, kidneys) of dogs and cats, and the soft tissue overlying the cornual process in a cow, but it has never been reported to occur as a primary mammary tumour in domestic animals.

This report describes the clinical and histopathological findings in a mare with malignant fibrous histiocytoma of the mammary gland as well as complications of bilateral mastectomy.

### Case history

A 6-year-old uniparous Paint mare was presented for investigation of right mammary gland enlargement of 3 weeks' duration. The mare's owner detected the enlargement by palpation during routine cleaning of the mammary gland and visual enlargement was not noted. The referring veterinarian had treated the mammary swelling by the administration of an oral diuretic and steroid combination of trichlormethiazide and dexamethasone prior to referral; however, the gland remained enlarged despite therapy. The mare was otherwise systemically healthy based upon physical examination findings.

### Clinical findings

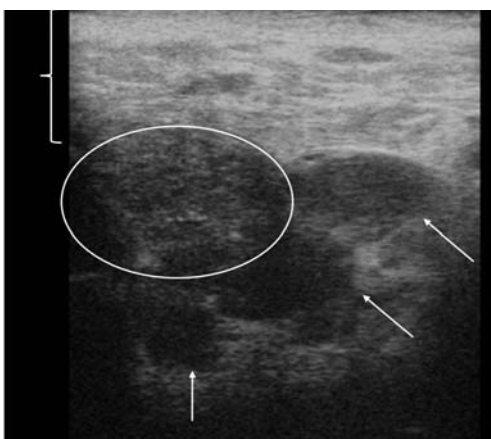
On admission, general physical examination revealed the mare to be in good body condition. Manual palpation of the udder revealed a nodular 2 cm firm mass at the base of the left teat and a 4.5 x 6 cm firm mass within the right mammary gland, dorsal to the right teat. The right teat was normal on palpation. Palpation of the mammary masses did not elicit a pain response from the mare and no secretions were obtained from either teat. Ultrasonographic evaluation using an 8.5 MHz microconvex linear transducer and a 13.5 MHz linear transducer revealed the right mammary mass to be comprised of a 2.5 cm homogenous area surrounded by hyperechoic dense stroma with hypoechoic loculations (**Fig 1**). Several small blood vessels were observed throughout the entire mass, and a thin capsule surrounded the majority of the mass. Ultrasonographic examination of the left mammary gland revealed markedly enlarged (1.69 x 3.48 x 3.72 cm),

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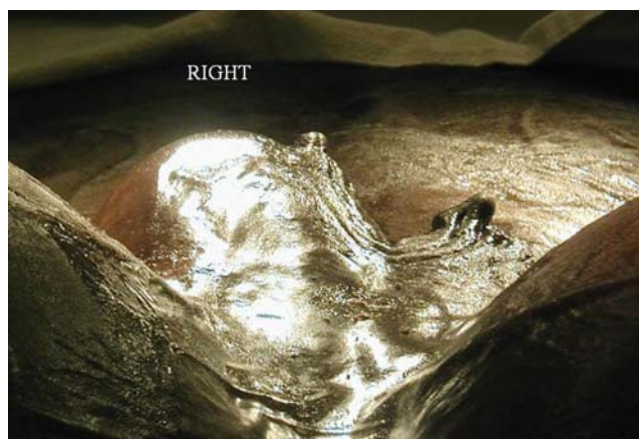
slightly heterogenous intramammary lymph nodes (**Fig 2**). Normal appearing glandular tissue was present dorsal to both mammary masses. Palpation *per rectum* confirmed that the mare was not pregnant, and no enlarged lymph nodes were detected within the pelvic canal. Based on clinical presentation and ultrasonographic findings, mammary neoplasia was suspected and a bilateral mastectomy was recommended. Although a biopsy could have been performed to confirm a diagnosis of mammary neoplasia, the authors were content that excision was warranted on the basis of the ultrasonographic and physical examination abnormalities.

Three weeks later, the mare was readmitted for bilateral mastectomy. The right mammary gland appeared more enlarged, and the mare was mildly sensitive to udder palpation (**Fig 3**). A small amount of serous discharge was obtained by stripping the left teat. Haematological abnormalities included hyperfibrinogenaemia (6 g/l) and mild anaemia ( $6.7 \times 10^{12}$  cells/l). The mare was

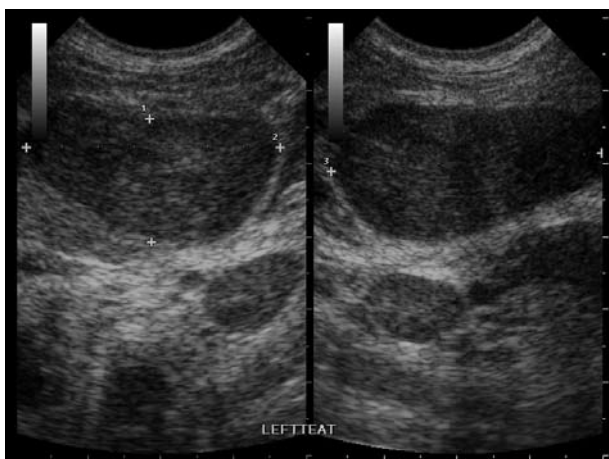
administered preoperative procaine penicillin G (22,000 iu/kg bwt i.m., PenOne Pro)<sup>1</sup> and flunixin meglumine (1.1 mg/kg bwt i.v., Banamine)<sup>2</sup>, followed by xylazine (0.5 mg/kg bwt i.v., Anased)<sup>3</sup> and butorphanol (0.01 mg/kg bwt i.v., Torbugesic)<sup>4</sup> as premedication. The horse was anaesthetised, placed in dorsal recumbency, and a bilateral mastectomy was performed (**Fig 4**). As described in Sysel and Moll (1999), an elliptical incision was performed in a cranial to caudal direction, just lateral to both teats in order to preserve as much skin as possible. The external pudendal artery and vein, obturator vein, internal pudendal veins and caudal superficial epigastric veins were double-ligated with 0 polyglactin 910 (Vicryl)<sup>5</sup>. Both mammary glands, including a single, enlarged lymph node cranial to the right external inguinal ring were removed *en bloc*. The resected tissues were submitted for histopathology. Haemorrhage was not significant, but there was extensive dead space between the fibrous layer of the body wall and the remaining skin. Multiple small, full



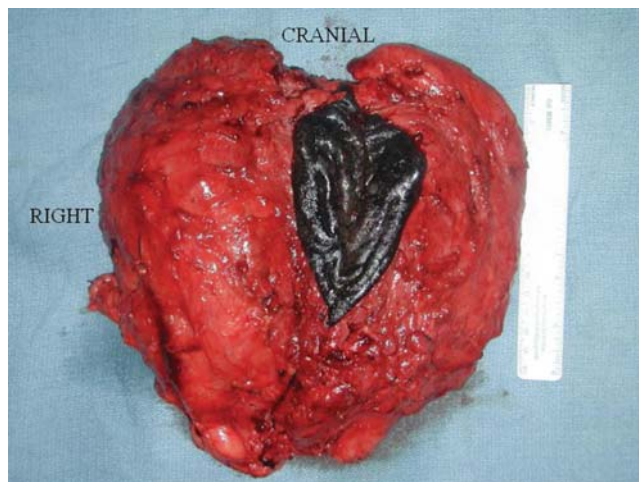
**Fig 1:** Transverse ultrasonographic image of the right mammary gland: 13.5 MHz linear transducer, 7 cm depth. A 2.5 cm homogenous mass (circled) is surrounded by hyperechoic dense stroma (side bar) with hypoechoic loculations (arrows).



**Fig 3:** Enlarged right mammary gland whilst the mare was in dorsal recumbency and anaesthetised, prior to bilateral mastectomy. The right mammary gland had significantly increased in size in the 3 weeks between initial presentation and surgery.



**Fig 2:** Transverse ultrasonographic image of the left mammary gland, revealing markedly enlarged (1.69 x 3.48 x 3.72 cm), slightly heterogenous intramammary lymph nodes.

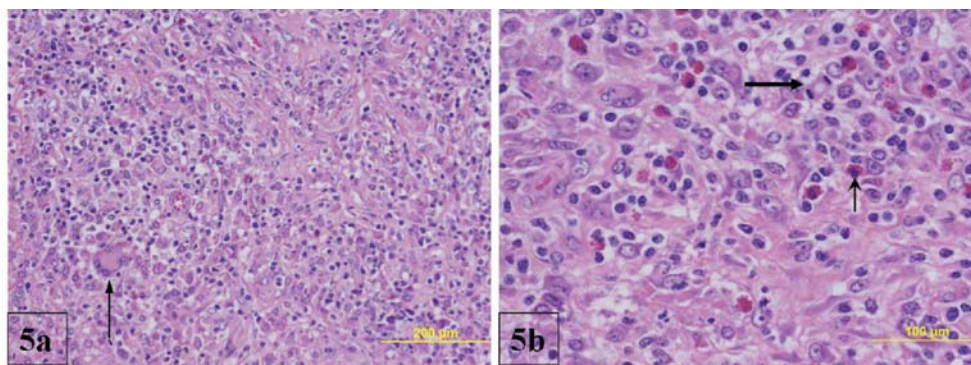


**Fig 4:** Gross appearance of both mammary glands following bilateral mastectomy.

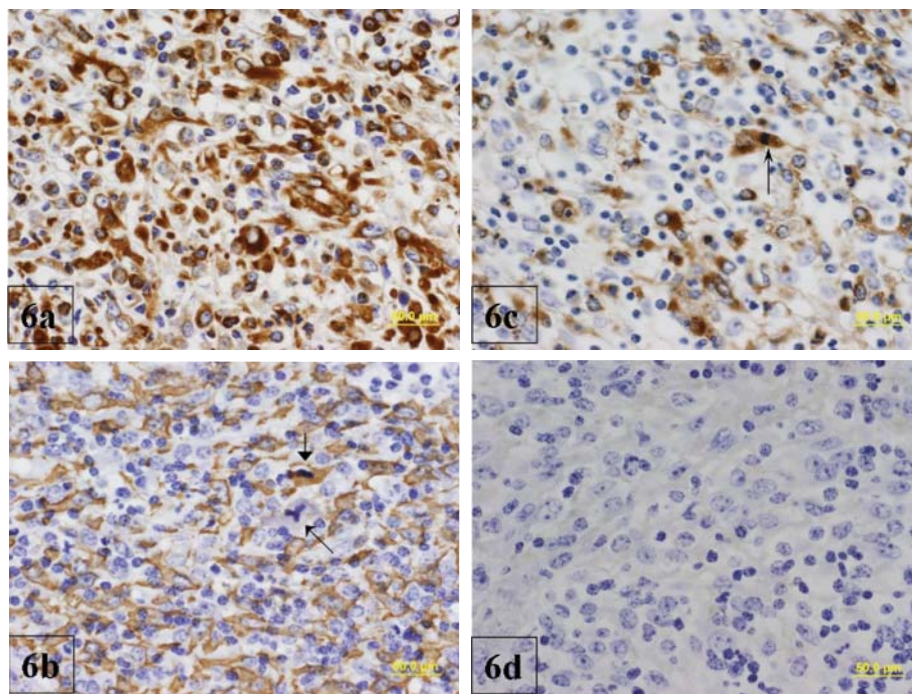
thickness stab incisions were created throughout the skin parallel to the wound edge to relieve tension and encourage drainage post operatively. Sterile gauze packing moistened with saline was placed within the defect exiting the most cranioventral part of the incision to act as a passive drain. The skin was apposed with vertical mattress sutures.

Potassium penicillin (22,000 iu/kg bwt i.v. q. 6 h., Pfizerpen)<sup>6</sup>, gentamicin (8.8 mg/kg bwt i.v. q. 24 h., GentaMax)<sup>7</sup> and phenylbutazone (3.0 mg/kg bwt i.v. q. 12 h., Phenylbute)<sup>8</sup> were administered for 5 days post

operatively, and the packing was removed 2 days post operatively. Attempts were made to apply a compression bandage to the wound by wrapping the material over the lumbar region, but it was difficult to maintain its position, and the compression bandage was discontinued within 2 days. Following the discontinuation of i.v. antimicrobials, oral sulphamethoxazole trimethoprim (30 mg/kg bwt per os q. 12 h)<sup>9</sup> was administered for 7 days. Beginning 8 days post operatively, the amount of serous discharge from the incision began to increase with partial dehiscence of the



**Fig 5:** Photomicrographs of the tumour mass excised from the mammary gland. Haematoxylin and eosin (H&E) stained sections at 10X (a) and 40X (b) magnification. Both demonstrate a pleocellular proliferation composed of fibroblast-like cells arranged in storiform patterns, and histiocytoid cells, which are frequently karyomegalic or multinucleate (a, arrow) with nuclear atypia and frequent mitoses (b, wide arrow). Admixed are inflammatory cells including lymphocytes, plasma cells, eosinophils (b, thin arrow) and neutrophils.



**Fig 6:** Photomicrographs of immunohistochemically stained sections demonstrating variable antigen expression within neoplastic histiocytoid and spindle cell populations. a) Strong expression of vimentin is detected within histiocytoid and spindle cell population, confirming its mesenchymal origin. b) Moderate to strong expression of  $\alpha$ -smooth muscle actin (SMA) is detected within many spindle cells throughout the neoplasm. Note that a cell expressing SMA is undergoing mitosis (upper arrow), as well as an adjacent cell that is not expressing SMA (lower arrow). c) Lysozyme (a histiocytic marker) is also expressed both within atypical spindle cells, one of which is undergoing mitosis (arrow), as well as plump histiocytoid cells. d) Pancytokeratin marker AE1/AE3 is not detected within the neoplastic population, ruling out spindle cell carcinoma as a differential diagnosis.

wound. A swab of the incision was obtained for microbial culture and sensitivity. The microbial culture results yielded multiple Gram-negative and Gram-positive microorganisms, including a methicillin resistant *Staphylococcus aureus*. Adjusting antimicrobial therapy based upon the results of culture and sensitivity patterns, enrofloxacin (7.5 mg/kg bwt *per os* q. 24 h., Baytril)<sup>4</sup> was administered for 10 days; however, the incisional discharge became more purulent, despite daily lavage with dilute povidone-iodine solution and topical application of a solution of dimethylsulphoxide and amikacin. Enrofloxacin was discontinued at this point in time, and therapy with amikacin (15 mg/kg bwt *i.v.*, Amiglyde)<sup>4</sup> was initiated for one week. The wound was beginning to heal well by second intention at this point, and *i.v.* antimicrobial therapy was discontinued. Daily lavage and topical application of dimethylsulphoxide and amikacin was continued. At discharge from the hospital 25 days post operatively, the mare was afebrile and incisional discharge was decreasing.

Follow-up one year later by the referring veterinarian indicated that the incisional infection had resolved and the skin had healed the remaining defect by second intention. No signs of recurrence of swelling in the inguinal region were present; however, the owner had declined follow-up ultrasonography.

### Gross pathology

The right mammary gland was nearly effaced by multifocal, discrete, homogeneous, firm, tan nodules (0.5–2 cm diameter) embedded within poorly demarcated, interwoven bands of firm, white schirrous tissue. Small to medium sized lymph nodes were observed within the tissue, many of which were partially or almost completely effaced by similar firm tan to white nodules, including a large lymph node located close to the caudal surgical margin. Similar firm nodules were observed within the left mammary gland; however, normal glandular tissue could be identified. The excised skin overlying the mammary glands was unaffected.

### Histopathology

Haematoxylin and eosin (H&E) stained, 5 µm thick sections of formalin fixed, paraffin embedded (FFPE) tissues were routinely prepared and examined. On histological evaluation, many sections of both mammary glands were effaced by poorly demarcated, pleocellular neoplastic proliferation comprising atypical spindle cells arranged in interlacing streams and storiform patterns admixed with atypical histiocytoid cells including vacuolated megakaryocytic and multinucleate giant cells (Fig 5a). The spindle cells were often associated with a finely fibrillar to dense collagenous extracellular matrix. Mitoses were frequent within both spindle cell and histiocytoid populations (1–2/40x field) and were sometimes bizarre.

Throughout this proliferation were numerous inflammatory cells including lymphocytes, plasma cells, eosinophils and neutrophils (Fig 5b). In some areas, the lymphocytes formed follicular aggregates. Embedded within this tissue and extending to the surgical margins (including the lymph node resected at the right caudal surgical margin) were many small to medium-sized reactive lymph nodes. Often these nodes contained similar atypical spindle cell/histiocytoid proliferations that extended from the hilar and medullary regions through the capsule. Bacterial, protozoal or fungal microorganisms were not observed with additional histochemical stains (PAS, Gram and Ziehl-Nielsen acid-fast).

Routine immunohistochemical analysis was performed on 5 µm FFPE sections using the following monoclonal antibodies: vimentin<sup>10</sup>, lysozyme<sup>10</sup>, AE1/AE3 pancytokeratins<sup>11</sup> and  $\alpha$ -smooth muscle actin (SMA)<sup>10</sup>. Both spindle cell and histiocytoid cell populations demonstrated strong cytoplasmic expression of vimentin (Fig 6a). Moderate to strong  $\alpha$ -SMA was observed within the cytoplasmic processes of many spindle cells and also some histiocytoid cells. Moderate to strong expression of lysozyme was present within histiocytoid cells and also some spindle cells (Fig 6c). No pancytokeratin expression was observed within any of the sections (Fig 6d). Positive and negative controls were utilised and worked appropriately (data not shown).

### Diagnosis

Based on the storiform pattern of pleomorphic spindle cells, including histiocytes, fibroblasts and multinucleated giant cells, in addition to the results of the special stains, the mammary tumour was diagnosed as a malignant fibrous histiocytoma.

### Discussion

Although mammary neoplasia is uncommon in mares, the case history, ultrasonographic appearance and clinical progression in this mare suggested a locally invasive, neoplastic lesion. In the 3 weeks between initial presentation and surgical excision, the right mammary gland had enlarged dramatically. Histopathological findings were consistent with a diagnosis of malignant fibrous histiocytoma and surgical excision was warranted.

A review of the literature revealed previous reports of mammary carcinomas, adenocarcinomas and one adenoma in mares. Although human mammary neoplasia is common, mammary sarcomas are very rare and, in general, have a poor prognosis (Tse *et al.* 2007). Human mammary sarcomas are characterised by local recurrences and visceral organ metastases, but not lymph node metastases (Tse *et al.* 2007). The treatment of choice is surgical excision, and there is still uncertainty as to the correct role for adjuvant therapy. Radiotherapy is considered in cases where surgical margins are not

adequate, but chemotherapy has been disappointing in the treatment of these neoplasms in women (Pollard *et al.* 1990; Blanchard *et al.* 2003). The percentages of survival reported in the human literature range from 40–60% after 2 years, and from 20–35% after 5 years (Pollard *et al.* 1990). In a report of 6 mares presenting for mammary neoplasia, the time between noticeable enlargement and presentation ranged from one month to 2 years, with a median time of 3.5 months (Sysel *et al.* 1993). Survival time ranged from 3 months to 2 years in the 3 horses not treated surgically and from 3 months to 7 years in the 3 horses treated with hemimastectomy or radical mastectomy. Five of the 6 mares were subjected to euthanasia as a consequence of neoplastic disease.

Malignant fibrous histiocytomas represent a histologically diverse classification of malignant neoplasms that presumably arise from a poorly differentiated population of mesenchymal cells. Based on their histomorphology, MFHs are subclassified into storiform-pleomorphic, inflammatory, giant cell, myxoid and angiomatoid types; however, many tumours often contain more than one or combinations of subtype morphology. Although accepted as a distinct entity in the veterinary literature, there is ongoing debate in the human literature as to whether MFHs should be reclassified as undifferentiated sarcomas (Fletcher 2007). In the veterinary literature, MFH has been reported in several domestic animal species including horses, dogs, cats, mice, rats, rabbits, birds, a pig and a cow (Schneider *et al.* 1999). According to the WHO classification of tumours of domestic animals, only storiform-pleomorphic, inflammatory and giant cell (formerly giant cell tumour of soft parts) types are consistently reported in domestic animals (Goldschmidt and Hendrick 2002). MFH has been most commonly reported in the dog and may arise as a single tumour in the skin or spleen or as a multiorgan disease, involving the lungs, lymph nodes, spleen, liver, bones and kidneys (Meuten 2002). Complete excision can be curative for solitary masses, but there is no recognised successful treatment for multicentric MFH and these animals should be given a very guarded prognosis. In horses, MFHs are rare malignant neoplasms that primarily affect cutaneous regions of the neck, thigh and stifle; however, MFH has never been reported as a primary mammary tumour in horses or any other domestic animal.

Immunohistochemistry and electron microscopy data indicate MFHs comprise cells of myofibroblastic/fibrohistiocytic lineage (Montgomery and Fisher 2001; Morris *et al.* 2002; Yamate *et al.* 2007). The predominant histologic pattern of the tumour in the mammary gland of this horse is consistent with pleomorphic-storiform subclassification of MFH. Positive vimentin expression within neoplastic cells confirms the mesenchymal lineage of this tumour. Variable expression of  $\alpha$ -SMA and lysozyme by spindle cell and histiocytoid tumour cells is also consistent with the immunophenotype of the MFH. A study of a homotransplantable MFH and cloned MFH tumour cells in rats identified the presence of morphologically fibroblast-

like cells which expressed histiocytic markers and also contained lysosomal granules (Yamate *et al.* 2007). These cells were also induced to express inflammatory cytokine TNF- $\alpha$  after incubation with LPS. The authors of this study conclude that these tumour cells demonstrated either multidirectional differentiation or that histiocytic neoplastic cells acquired the appearance and function of fibroblasts. Another study of MFHs from Flat-Coated Retrievers (Morris *et al.* 2002) found that many of the tumours had a significant myofibroblastic component, as evidenced by frequent tumour cell expression of  $\alpha$ -SMA. However, the majority of these sarcomas also expressed MHC class II molecules in greater than 70% of cells, thus further confounding the presumed histogenesis.

In horses, MFHs are uncommon tumours that tend to be raised, solitary, occasionally ulcerated subcutaneous masses. The multicentric form of the disease has not been reported in horses. Previous reports of equine MFH include a case of MFH in the forelimb of a Quarter Horse (Geburek *et al.* 2007), a case of MFH in the forelimb of a Clydesdale cross (Marryatt 2003) and a retrospective case study by Render *et al.* that described a giant cell tumour of soft parts in 6 horses (Render *et al.* 1983). Successful treatment of upper forelimb MFH has been reported in one horse with a combination of surgical excision and Nd:YAG laser irradiation when surgical excision alone resulted in recurrence (Geburek *et al.* 2007). There is also reference to equine MFH by Valentine (2006) in a retrospective survey of equine cutaneous neoplasia in the Pacific Northwest. Although MFH is reported as 1.3% of cutaneous neoplasms in this population of horses, the subtype is listed as 'giant cell tumour' and there is no mention of clinical behaviour. Equine MFHs tend to be locally invasive and post surgical recurrence variable (50% recurrence rate reported in Render *et al.* 1983) but tends to be more frequent when arising within the limbs and with giant cell MFH (Render *et al.* 1983; Marryatt 2003). However, a study that examines and compares the behaviour of MFH giant cell type and storiform-pleomorphic subtypes has not been performed, to our knowledge. Unlike man and other domestic animals, distant metastasis in the horse is not reported. Spindle cell sarcomas tend to invade along fascial planes; depending on the plane of section, surgical margins free of thin tendril-like extensions of neoplastic tissue may be difficult to obtain. Though the resected mammary gland retained a bilobular architecture on gross examination, the dense schirrous neoplastic tissue contained within the right portion of the gland made identification of this septal plane difficult. Therefore, we cannot rule out right to left-sided invasion of the mammary septum by neoplastic tissue, nor a multicentric origin of the neoplasm. However, the extensive regional lymph node involvement identified in this case suggests that local metastasis may have occurred. Although neoplastic cells were not identified within afferent lymphatics, given the concentration of neoplastic tissue within the hilar and medullary regions of the lymph nodes, one could hypothesise that metastasis of

this neoplasm was occurring via blood vessels. However we are unable to definitively confirm this speculation.

Although one year follow-up indicated no gross recurrence of the mammary tumour, the owner declined further diagnostics. Radical surgical excision was warranted in this case; however, bilateral mastectomy resulted in a large wound in a high-motion area with significant dead space. The stab incisions were made to prevent serum accumulation deep to the skin but may have contributed to the development of post operative infection by providing a route for ascending infection. Unfortunately, the extensive defect remaining after bilateral mastectomy is often too deep to the skin to create good contact between the large skin flaps with the underlying soft tissue, and packing with povidone iodine-soaked gauze sponges is recommended (Sysel and Moll 1999). Better preoperative planning for bandaging and using a closed suction drain may have prevented some of the incisional problems seen with this case. Although the mare remained afebrile and systemically healthy while hospitalised, the amount of incisional discharge began to increase post operatively, suggesting incisional infection.

Although bilateral mastectomy was warranted due to the invasive nature and lymph node involvement of the mammary tumour, incisional infection with partial wound dehiscence was a post operative complication. Nonetheless, the wound healed by second intention and the mare was reportedly doing well one year post operatively with no report of post surgical recurrence or metastasis. Further studies better characterising the morphology and behaviour of these neoplasms in horses is warranted.

## Manufacturers' addresses

- <sup>1</sup>MWI Veterinary Supply, Meridian, Idaho, USA.
- <sup>2</sup>Schering-Plough Animal Health Corp, Union, New Jersey, USA.
- <sup>3</sup>LLOYD Inc Shenandoah, Iowa, USA.
- <sup>4</sup>Fort Dodge Animal Health, Fort Dodge, Iowa, USA.
- <sup>5</sup>Johnson & Johnson, Langhorne, Pennsylvania, USA.
- <sup>6</sup>Pfizer Inc, New York, New York, USA.
- <sup>7</sup>Phoenix Pharmaceutical Inc, St Joseph, Missouri, USA.
- <sup>8</sup>Interpharm Inc, Hauppauge, New York, USA.
- <sup>9</sup>Bayer Animal Health LLC, Shawnee Mission, Kansas, USA.
- <sup>10</sup>Dako America, Carpinteria, California, USA.
- <sup>11</sup>Chemicon International, Billerica, Massachusetts, USA.

## References

- Acland, H.M. and Gillette, D.M. (1982) Mammary carcinoma in a mare. *Vet. Pathol.* **19**, 93-95.
- Blanchard, D.K., Reynolds, C.A., Grant, C.S. and Donohue, J.H. (2003) Primary nonphyloides breast sarcomas. *Am. J. Surg.* **186**, 359-361.
- De Cesare, A., Fiori, E., Burza, A., Ciardi, A., Bononi, M., Izzo, L., Volpino, P., Cavallaro, A. and Cangemi, V. (2005) Malignant fibrous histiocytoma of the breast. Report of two cases and review of the literature. *Anticancer Res.* **25**, 505-508.
- Fletcher, D.M. (2007) Soft tissue tumors. In: *Diagnostic Histopathology of Tumors*, Ed: D.M. Fletcher, Elsevier, Philadelphia. pp 1560-1562.
- Foreman, J.H., Weidner, J.P., Parry, B.W. and Hargis, A. (1990) Pleural effusion secondary to thoracic metastatic mammary adenocarcinoma in a mare. *J. Am. vet. med. Ass.* **197**, 1193-1195.
- Geburek, F., von Oppen, T., Hewicker-Trautwein, M. and Ohnesorge, B. (2007) Treatment of a malignant fibrous histiocytoma involving the forelimb of a Quarter Horse mare using conventional and laser surgery. *Equine vet. Educ.* **19**, 19-22.
- Goldschmidt, M.H. and Hendrick, M.J. (2002) Tumors of the skin and soft tissues. In: *Tumors in Domestic Animals*, Ed: D.J. Meuten, Iowa State Press, Ames. pp 89-91.
- Hirayama, K., Honda, Y., Sako, T., Okamoto, M., Tsunoda, N., Tagami, M. and Taniyama, H. (2003) Invasive ductal carcinoma of the mammary gland in a mare. *Vet. Pathol.* **40**, 86-91.
- Kato, M., Higuchi, T., Hata, H., Ishikawa, Y. and Kadota, K. (1998) Lactalbumin-positive mammary carcinoma in a mare. *Equine vet. J.* **30**, 358-360.
- Marryatt, P.A. (2003) Malignant giant cell tumor of soft parts in a mare. *Can. vet. J.* **44**, 743-745.
- Meuten, D.J. (2002) *Tumors in Domestic Animals*, Ed: D.J. Meuten, Iowa State University Press, Ames.
- Montgomery, E. and Fisher, C. (2001) Myofibroblastic differentiation in malignant fibrous histiocytoma (pleomorphic myofibrosarcoma): a clinicopathologic study. *Histopathol.* **38**, 499-509.
- Morris, J.S., McInnes, E.F., Bostock, D.E., Hoather, T.M. and Dobson, J.M. (2002) Immunohistochemical and histopathologic features of 14 malignant fibrous histiocytomas from Flat-Coated Retrievers. *Vet. Pathol.* **39**, 473-479.
- Munson, L. (1987) Carcinoma of the mammary gland in a mare. *J. Am. vet. med. Ass.* **191**, 71-72.
- Pavlovsky, Z., Jandakova, E., Stratil, D. and Hotarkova, S. (2006) Malignant fibrous histiocytoma of the breast: report of two cases. *Cesk. Patol.* **42**, 39-42.
- Pollard, S.G., Marks, P.V., Temple, L.N. and Thompson, H.H. (1990) Breast sarcoma. A clinicopathologic review of 25 cases. *Cancer* **66**, 941-944.
- Prendergast, M., Bassett, H. and Larkin, H.A. (1999) Mammary carcinoma in three mares. *Vet. Rec.* **144**, 731-732.
- Render, J.A., Harrington, D.D., Wells, R.E., Dunstan, R.W., Turek, J.J. and Boosinger, T.R. (1983) Giant cell tumor of soft parts in six horses. *J. Am. vet. med. Ass.* **183**, 790-793.
- Reppas, G.P., McClintock, S.A., Canfield, P.J. and Watson, G.F. (1996) Papillary ductal adenocarcinoma in the mammary glands of two horses. *Vet. Rec.* **138**, 518-519.
- Schmahl, W. (1972) Solid mammary carcinoma in a horse. *Berl. Munch. Tierarztl. Wochenschr.* **85**, 141-142.
- Schneider, P., Busch, U., Meister, H., Qasem, Q. and Wunsch, P.H. (1999) Malignant fibrous histiocytoma (MFH). A comparison of MFH in man and animals. A critical review. *Histol. Histopathol.* **14**, 845-860.
- Seahorn, T.L., Hall, G., Brumbaugh, G.W., Honnas, C.M., Lovering, S.L. and Snyder, J.R. (1992) Mammary adenocarcinoma in four mares. *J. Am. vet. med. Ass.* **200**, 1675-1677.
- Sparadi, A., Valentini, S., Sari, G., Spinella, G. and Millanta, F. (2008) Mammary adenoma in a mare: Clinical, histopathological and immunohistochemical findings. *Equine vet. Educ.* **20**, 4-7.
- Sysel, A.M. and Moll, H.D. (1999) Surgery of the mammary gland. In: *Large Animal Urogenital Surgery*, Eds: D.F. Wolfe and H.D. Moll, Williams & Wilkins, Baltimore. pp 157-164.
- Sysel, A.M., Moll, H.D., Livesey, M.A., Pringle, J. and Slone, D.E. (1993) Mastectomy in three of six cases of equine mammary neoplasia. *Vet. Surg.* **22**, 401-402.
- Tse, G.M., Tan, P.H., Lui, P.C. and Putti, T.C. (2007) Spindle cell lesions of the breast - the pathologic differential diagnosis. *Breast Cancer Res. Treat.* **109**, 199-207.
- Valentine, B.A. (2006) Survey of equine cutaneous neoplasia in the Pacific Northwest. *J. vet. diagn. Invest.* **18**, 123-126.
- Yamate, J., Fumimoto, S., Kuwamura, M., Kotani, T. and Lamarre, J. (2007) Characterization of a rat subcutaneous malignant fibrous histiocytoma and its tumor lines, with reference to histiocytic features. *Vet. Pathol.* **44**, 151-60.