Case Report

Preputial melanoma with systemic metastasis in a pony gelding and disseminated metastatic melanoma in a Thoroughbred gelding

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Introduction

Melanoma is a common (Johnson 1998), generally slow growing, locally invasive tumour, estimated to occur in approximately 80% of ageing grey horses (McFadyean 1933). Valentine (1995) proposed the classification of 4 separate forms of equine melanocytic tumours based on their distinct clinical, histological and behavioural characteristics: melanocytic nevus, dermal melanoma, dermal melanomatosis and anaplastic melanoma. A variety of presenting locations have been reported, but dermal melanomas and melanomatosis typically involve the perineum, ventral tail and external genitalia (MacGillivray et al. 2002), and whilst they may invade only locally, metastasis is considered to be the eventual outcome (Valentine 1995). However, a horse may live for several years with metastatic melanoma, depending on exactly where the metastasis occurs and to what extent. Despite the importance, and relatively common occurrence of this type of tumour, few reports of systemic metastasis of clinical significance can be found in the literature (Kirker-Head et al. 1985; Patterson-Kane et al. 2001; Tarrant et al. 2001; MacGillivray et al. 2002).

This report describes the presenting signs, diagnostic findings and necropsy results of 2 horses subsequently diagnosed with systemic metastatic melanoma.

Case 1

History

A 20-year-old grey pony was admitted to North Carolina State University College of Veterinary Medicine for evaluation of a preputial mass. The referring veterinarian performed biopsies of the mass during the summer of 2004 at which time the mass measured approximately 15 x 14 x 14 cm. A histological diagnosis of melanoma was made by an independent veterinary pathology laboratory. A course of cimetidine (2.5 mg/kg bwt, per os, q. 8 h) was initiated. In the 2 weeks prior to presentation in December 2004, the pony's owner had noticed pain associated with the mass, weight loss, lethargy, an uncharacteristic reluctance to roll and had observed the pony kicking at his abdomen. The owner also suspected the mass to have enlarged significantly and had been unable to ascertain the pony’s ability to urinate.

Clinical examination

On admission, the pony was quiet, but alert and responsive. He weighed 244 kg and had a body condition score of 4 out of 9. A large, firm, nodular black-grey mass measuring approximately 35 x 25 x 25 cm was present at the penile sheath, incorporating the entirety of the penis, which the pony was unable to retract. Palpation revealed the mass to be firmly adhered to the sheath.

Rectal examination revealed no abnormalities. Cardiac auscultation was unremarkable. A rebreathing examination did not precipitate coughing, but the pony exhibited mild signs of stress and increased bronchovesicular sounds were auscultated in the cranioventral lung field. A slight bilateral serous nasal discharge was present.

Clinical pathology

Haematology revealed a mild anaemia (PCV 27%; reference range [rr] 28–42), lymphopenia (0.718 x 10^9/l; rr 1.70–6.10 x 10^9/l), segmented neutrophilia (8.073 x 10^9/l; rr 3.080–7.340 x 10^9/l) and hyperfibrinogenaemia (6 g/l; rr 1–4 g/l). Platelet numbers were within reference range (platelets 140 x 10^9/l; rr 108–272 x 10^9/l). Serum creatinine was measured at 5 mg/l (rr 7–21 mg/l). All other clinical pathological findings were within normal limits.

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**Case progression**

Surgery was planned to remove the mass but was postponed when the pony's rectal temperature rose to 39.1°C. Thoracic radiographs revealed no cardiopulmonary abnormalities. Transtracheal wash cytology revealed mild, chronic suppurative inflammation with haemodilution. More bleeding was elicited by the procedure than was considered normal, and bilateral epistaxis persisted for approximately 6 h. A coagulation profile was performed which was normal. Flunixin meglumine (1.1 mg/kg bwt i.v. q. 12 h), gentamycin (5 mg/kg bwt i.v. q. 24 h) and cephalolin (20 mg/kg bwt i.v. q. 8 h) treatments were begun. PCV and total protein (TP) the following morning were 26% and 70 g/l respectively. Surgery was scheduled for the following day.

**Surgery**

A 100 mg Fentanyl patch was applied topically to the skin of the proximal left forelimb and an epidural of 10 mg morphine was administered prior to surgery. En bloc resection and penile retroversion (Doles 2001) was performed under general anaesthesia without incident or excessive blood loss. Two Penrose drains were placed, exiting the incision laterally. Primary closure of the incision was accomplished using a series of tension sutures (interrupted vertical mattress, 5 m) and appositional sutures (simple interrupted, 3 m). Due to financial constraints, the mass was not submitted for histological evaluation.

**Outcome**

Approximately 6 h post operatively, the pony was found to be tachycardic (80 beats/min), pyrexic (39.4°C) and exhibiting muscle fasciculations. Mucous membranes were pale and capillary refill time prolonged (3 s). A soft heart murmur, not previously detected, was audible on cardiac auscultation (this was presumed to be a haematic murmur, associated with a reduction in blood viscosity). No visible bleeding was present. PCV was 22% and total protein 50 g/l. Fluid therapy consisting of 1 l hypertonic saline, 10 l lactated Ringer's solution and 8 l of 5% lactated Ringer's solution, was administered prior to surgery. En bloc resection and penile retroversion of the penis was performed. Over the course of the next 12 h, the pony's PCV declined steadily and a third crossmatched transfusion was administered 48 h post operatively. The pony was observed urinating without difficulty and appeared bright, with a good appetite. PCV and TP were monitored every 2 h. Seventy-two hours post operatively, a PCV of 6% was measured. The pony became disoriented and weak, and was subsequently subjected to euthanasia.

**Necropsy**

The surgical site was found to contain approximately 11 l of coagulated blood. This extensive haematoma occupied an area of approximately 55 x 30 cm. The spleen was small and irregular with more than 50, relatively uniform, 1.5–2 cm, firm nodules disseminated throughout the parenchyma. On cross section, these nodules appeared mottled tan-black, bulged prominently and were well demarcated from the surrounding splenic parenchyma. Histologically they were composed of neoplastic melanocytes arranged into sheets, cords and loosely formed nests or packets. Individual neoplastic cells were moderately pleomorphic, ranging from a plump, polygonal morphology to a more elongate, spindle-shaped appearance. Occasional multinucleated cells and 1–2 mitotic figures were present, per high power field. The bone marrow of the right humerus contained 3 well-demarcated, 8–10 mm, black, nodular soft tissue masses within the medullary adipose tissue, located within the diaphysis to proximal metaphysis. Histologically, the marrow consisted of a poorly cellular, lipomatous stroma, focally disrupted by a moderately cellular, poorly demarcated aggregate of similar appearing neoplastic melanocytes to those found in the spleen. The left kidney contained a focal, 1.2 cm, well-demarcated, expansive black soft tissue nodule within the cortex. Histologically this consisted of moderately pleomorphic, well-demarcated neoplastic melanocytes with prominent magenta nuclei. Many of the cells contained dark brown cytoplasmic pigment (melanin). The renal cortex of the left kidney was multifocally disrupted by similar appearing neoplastic melanocytes. The left cranial lung lobe was diffusely dark red to brown and slightly emphysematous and exuded a watery, pale red fluid on sectioning. The darkening was poor, demarcated and palpated with a similar consistency to the remaining lung lobes, consistent with pulmonary congestion. The pony was judged to be too unstable for anaesthesia and the likelihood of successfully locating and ligating the bleeding vessels was considered poor. Over the course of the next 12 h, the pony's PCV declined steadily and a third crossmatched transfusion was administered 48 h post operatively. The pony was observed urinating without difficulty and appeared bright, with a good appetite. PCV and TP were monitored every 2 h. Seventy-two hours post operatively, a PCV of 6% was measured. The pony became disoriented and weak, and was subsequently subjected to euthanasia.

**Case 2**

**History**

An 18-year-old grey Thoroughbred gelding presented to North Carolina State University College of Veterinary Medicine for investigation of weight loss and depression of 1 month's duration. The horse's owner also reported a recent episode of colic that responded to medical management.

**Clinical examination**

On presentation, the horse was quiet, but alert and responsive. He weighed 488 kg and was given a subjective...
body condition score of 2/5. A pendulous abdomen, with an appreciable fluid wave on ballottement was noted, and the horse appeared thin over the dorsum. Pronounced preputial oedema was present but the penis appeared grossly normal. The ventral surface of the tail and perineum were covered with approximately 20, roughly circular masses, ranging in diameter from 1–7 cm. The owner was unable to recall when these masses first appeared. Rectal examination revealed a large mass in the caudal abdomen that appeared to be suspended from the dorsal body wall and numerous masses of varying consistency along the pelvic floor. Cardiac and thoracic auscultation was unremarkable. The pelvic lymph nodes were enlarged.

Clinical pathology

Haematology revealed haemoconcentration (PCV 45%; rr 28–42%), an increase in platelet numbers (312 x 10^9/l; rr 94–232 x 10^9/l), leucocytosis (26.7 x 10^9/l; rr 3.40–8.50 x 10^9/l), mature neutrophilia (24.564 x 10^9/l; rr 3.4–8.50 x 10^9/l) and lymphopenia (1.335 x 10^9/l; rr 1.90–6.40 x 10^9/l). Serum biochemistry revealed elevated creatinine (21 mg/l; rr 12–20 mg/l), hypercalcaemia (131 mg/l; rr 113 –125 mg/l), hyperbilirubinaemia (28 mg/l; rr 4–15 mg/l), elevated alkaline phosphatase (199 iu/l; rr 62–197 iu/l) and decreased creatinine kinase (26 iu/l; rr 49–212 iu/l). Bile acids and serum sorbitol dehydrogenase were within reference ranges. Urinalysis revealed trace levels of blood, occasional amorphous crystals and a few calcium oxalate crystals per high power field. All other clinical pathological values were within normal limits.

Additional diagnostics

Abdominocentesis revealed a normal white cell count (1.8 x 10^9 cells/l; rr 1.5–10.1 x10^9 cells/l) and protein (24 g/l; rr 10–24 g/l). The concentrated direct smear contained individual and clumped granulated melanocytes and free granules were observed in the background. Occasional melanophages were noted. Ultrasonographic examination of the spleen revealed numerous hyperechoic nodules throughout. Metastatic nodules ranging from 0.5–2 cm in diameter were identified. This diagnostic test alone may not represent a sufficiently sensitive method for detecting spread of the neoplasia. Abdominocentesis and an ultrasonographic examination of the abdominal viscera may have yielded more prognostic information and when offset against the estimated cost of surgery, would have represented a valuable investment. Biopsy of the mass was originally performed by the referring veterinarian 4 months prior to presentation and the details of the histology that lead to the initial diagnosis was unavailable. Regrettably, following excision, the mass was not submitted for histological examination because of financial constraints.

Necropsy

An excessive volume of low viscosity, red-black abdominal fluid was present in the abdomen. Melanomas were found to extend throughout the perineal vault as 0.5–2 cm diameter nodules located along the rectal and colonic mesentery. A melanoma of approximately 30 cm diameter, weighing 5 kg was firmly attached to the epaxial muscles and encompassed the quadrification of the aorta. The entire mesentery was filled with multifocal to coalescing, black nodules ranging from 0.5–2 cm in diameter. Histologically these were composed of neoplastic melanocytes, arranged in clumps. Cells typically exhibited a single, large, pale nucleus, well demarcated cell borders and small to moderate cytoplasmic volume. Mitotic index was moderately high and numerous neoplastic cells contained large amounts of melanin pigment. The spleen was markedly enlarged and nodular, with numerous surface melanomas of up to 10 cm diameter that bulged through natural and cut surfaces. The surfaces of the lungs, liver and kidneys, the right guttural pouch, the skeletal muscle at the atlantoccipital junction and the tapetum of the right eye also contained melanomas of varying sizes. No histological examination of these latter tumours was performed.

Discussion

Melanoma is a common equine tumour, more frequently affecting older, grey horses (McFadyean 1993; Johnson 1998). Very few reports of systemic metastasis have been published to date, (Kirker-Head et al. 1985; Patterson-Kane et al. 2001; Tarrant et al. 2001; MacGillivray et al. 2002), and the common perception is that metastasis is a rare complication of an almost universally benign neoplasm. Valentine (1995) proposed the subdivision of equine melanocytic tumours into 4 clinically and pathologically distinct categories, of which dermal melanomatosis and anaplastic melanoma represent the most invasive and/or metastatic. The 2 cases reported here, however, highlight the importance of keeping in mind the possibility of clinically and prognostically significant metastasis, regardless of the location of the mass with which the horse presents.

To the authors’ knowledge, no reports exist of penile or preputial melanomas resulting in systemic metastasis and there are few published reports of metastasis of other equine penile neoplasias (Patterson et al. 1990; Mair et al. 2000). In the first case, we feel that evidence of metastatic neoplasia could have been gathered preoperatively and that this would have significantly influenced the decision to perform a complicated, irreversible, costly procedure (Markel et al. 1988; Doles et al. 2001) on an elderly pony. Although thoracic radiographs and a rectal examination were performed, no further investigation of the internal organs was carried out. Rectal examination was performed to palpate the regional lymph nodes draining the penis and prepuce, as metastasis commonly commences with spread to the lymph nodes. However, in this instance, no abnormalities were identified. This diagnostic test alone may not represent a sufficiently sensitive method for detecting spread of the neoplasia. Abdominocentesis and an ultrasonographic examination of the abdominal viscera may have yielded more prognostic information and when offset against the estimated cost of surgery, would have represented a valuable investment. Biopsy of the mass was originally performed by the referring veterinarian 4 months prior to presentation and details of the histology that lead to the initial diagnosis was unavailable. Regrettably, following excision, the mass was not submitted for histological examination because of financial constraints.

However, the clinical outcome of this case highlights the potential importance of this information since histological
features predictive of widespread metastasis may have been present. Case 2 illustrates the clinical benefit of performing these diagnostic tests, as an ante mortem knowledge of the severity of multiple organ involvement resulted in a poor prognosis and the horse’s subsequent euthanasia.

The cause of pyrexia and apparent inability to create appropriate haemostasis in the pony were never definitively diagnosed. Pyrexia was hypothesised to have resulted either from pre-existing lung disease, or as a result of increased levels of TNFα in systemic circulation. In the face of a normal clotting profile, the prolonged bleeding is postulated to be the result of disruptive invasion of the bone marrow, by neoplastic cells and became clinically more significant due to infiltration of the spleen by neoplastic melanocytes. This may also have contributed to a poor regenerative response in the immediate aftermath of haemorrhage and transfusion.

MacGillivray et al. (2002) concluded that metastatic melanoma should be considered a differential diagnosis of almost any grey horse that presents for veterinary evaluation. We believe that a basic database, including abdominocentesis and ultrasonographic examination of the abdominal viscera, should be gathered for all cases of melanoma that present for surgical evaluation prior to resection, to investigate the possibility of metastatic spread before extensive surgical procedures are embarked upon. In essence, a form of staging should be performed to plan appropriate treatment and avoid pointless and costly resection where metastases are already present.

Manufacturer’s address

1B. Braun Medicinal, Irvine, California, USA.

References


